UDC 547.873〔547.792.9〕

150. **Kiyoshi Futaki and Senji Tosa**: Studies on the Synthesis of 3-Alkyl-5,6,7,8-tetrahydro-*s*-triazolo[4,3-*b*][1,2,4]triazine-6,7-diones.

(*Photographic Division, Mitsubishi Paper Mill Co., Ltd.*[*1])

A new series of compounds, 3-alkyl-5,6,7,8-tetrahydro-*s*-triazolo[4,3-*b*][1,2,4]triazine-6,7-diones (III), were synthesized as possible addition agents to photographic emulsion and developer. The steps of syntheses are shown in Chart 1.

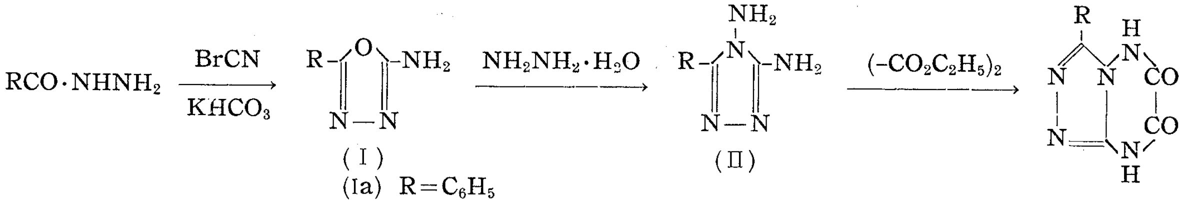


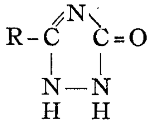
Chart 1.

Acylhydrazides were reacted with cyanogen bromide to produce 2-alkyl-5-amino-1,3,4-oxadiazoles (I). The condition employed was essentially the same as that of Gehlen,1) but he assigned an incorrect chemical structure to the product.

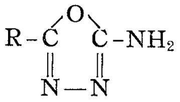
In 1949, Gehlen1) studied the reactions of acylhydrazides with cyanogen bromide and reported the chemical structure of its products as 1-cyano-2-acylhydrazines (structure (A)). Later, from the basis of the infrared spectroscopic findings, Mautner and Kumler2) assigned, instead of structure (A), 3-alkyl-Δ^3-1,2,4-triazolin-5-ones (structure (B)) to the products, because the infrared spectra of the compounds showed no absorption of C≡N (near 4.5 μ).

RCO-NHNH·C≡N

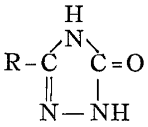
(A)
1-Cyano-2-acylhydrazine



(B)
3-Alkyl-Δ^3-1,2,4-triazolin-5-one



(C)
2-Alkyl-5-amino-1,3,4-oxadiazole



(D)
3-Alkyl-Δ^3-1,2,4-triazolin-5-one

With reference to the synthesis of intermediates for triazolotriazines, there was the problem of these chemical structures. The so-called N′-cyanobenzohydrazide or 3-phenyl-Δ^2-1,2,4-triazolin-5-one (compound X) prepared by Gehlen's method was found to be insoluble in *N* sodium hydroxide solution. This fact is astonishing, since it is known that benzohydrazide, dibenzohydrazide, 1-benzoylsemicarbazide, and "3-phenyl-Δ^2-1,2,4-triazolin-5-one[*2]" (D) are all soluble in *N* sodium hydroxide solution. The infrared spectrum of compound (X) showed strong absorption at 6.1 μ (Fig. 1) to which Mautner and Kumler assigned the absorption of C=O. However, their assignment of 6.1 μ seems incorrect, since absorption of a carbonyl group in a five-membered ring ordinarily appears in a region of further shorter wave length, as shown by the absorption of carbonyl (5.8 μ) of "3-phenyl-Δ^2-1,2,4-triazolin-5-one" (D).

[*1] Nagaoka-cho, Otokuni-gun, Kyoto (二木 清, 土佐宣治).

[*2] According to H. Gehlen, "N′-cyano-2-benzohydrazine (compound X)" was converted by treatment with boiling alkali into its isomer, 5-phenyl-1,2,4-triazol-3-one. Later, H. Mautner and W. Kumler assigned the structure 3-phenyl-Δ^2-1,2,4-triazolin-5-one (D) to this compound. See references (1) and (2).

1) H. Gehlen: Ann., **563**, 185(1949).

2) H. Mautner, W. Kumler: J. Am. Chem. Soc., **77**, 4076(1955).

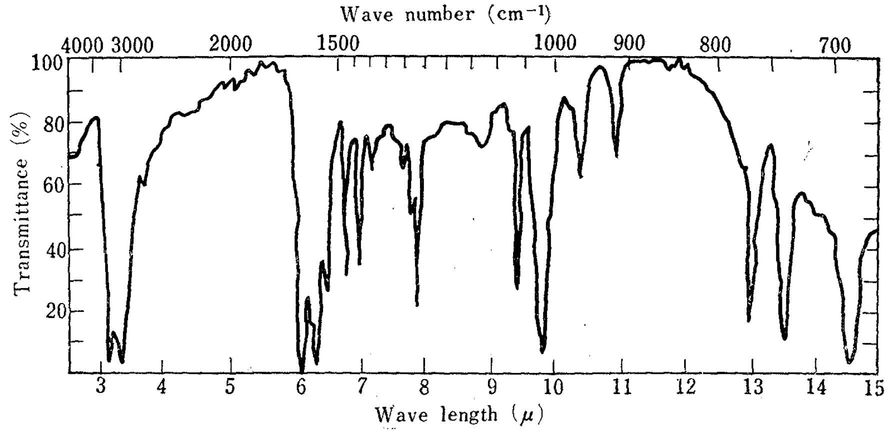
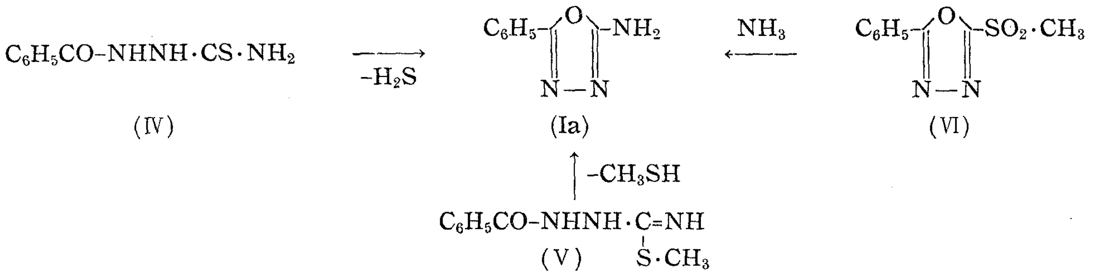


Fig. 1. Infrared Absorption Spectrum of 2-Amino-5-phenyl-1,3,4-oxadiazole (KBr disk)

It was further found that a green color resulted on mixing compound (X) with sodium pentacyanoaquoferriate solution (test for primary aromatic amines[3]), and that a deep reddish violet color resulted on mixing the compound with sodium 1,2-naphthoquinone-4-sulfonate in alkaline solution (test for reactive $-CH_2-$ and $-NH_2$ groups[4]). These observations led to the assumption that the compound would have an amino group. Therefore, amino-phenyl-oxadiazole (structure C) is assumed as the most possible structure for compound (X).

2-Amino-5-phenyl-1,3,4-oxadiazole (Ia) was already described by Fhrenbach and Stollé[5] who synthesized (Ia) by thermal elimination of hydrogen sulfide from 1-benzoylthiosemicarbazide (IV). Later, Hoggarth[6] reported the synthesis of (Ia) by thermal elimination of methanethiol from 1-benzoyl-S-methylisothiosemicarbazide (V). Although the products by these two procedures were reported as 2-amino-5-phenyl-1,2,4-oxadiazole (Ia), their experimental basis for assigning the structure (Ia) to the product was insufficient.

(Ia) was synthesized in the present work by the reaction of 2-methylsulfonyl-5-phenyl-1,3,4-oxadiazole (VI) with ethanolic ammonia at room temperature and the three products from (IV), (V), and (VI) were found to be identical.



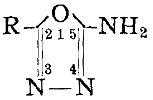
It was found from mixed melting point (no depression) and from infrared spectrum that compound (X) was identical with the authentic sample of 2-amino-5-phenyl-1,3,4-oxadiazole (Ia). On the basis of these findings, the proposed structure (C) should be assigned to the product obtained by the reaction of acylhydrazide with cyanogen bromide. The absorption of (Ia) at 6.1 μ is assumed to be due to the amino group.

In order to synthesize triazolotriazines (III), 2-alkyl-5-amino-1,3,4-oxadiazoles (I) were further converted to 3-alkyl-4,5-diamino-1,2,4-triazoles (II) by heating with hydrazine hydrate according to the method of Gehlen and Elchlepp.[7]

---

[3] V. Anger : Mikrochim. Acta, **2**, 3(1937); cf. F. Feigl : "Spot Tests in Organic Analysis" (1956).
[4] P. Ehrlich, C. Herter : Z. Physiol. Chem., **41**, 329(1904); cf. also F. Feigl (*loc. cit.*).
[5] K. Fhrenbach, R. Stollé : J. prakt. Chem., **122**, 289(1929).
[6] E. Hoggarth : J. Chem. Soc., **1949**, 1918.
[7] H. Gehlen, H. Elchlepp : Ann., **594**, 14(1955).

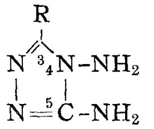
TABLE I. 2-Alkyl-5-amino-1,3,4-oxadiazoles



No.	R	m.p. (°C)[a]	Crystal form[b]	Mol. formula	Analyses (%) Calcd. C	Calcd. H	Calcd. N	Found C	Found H	Found N
(Ib)	C_4H_9	136.5～137.5	needles	$C_6H_{11}ON_3$	51.04	7.85	29.77	50.98	7.62	29.98
(Ic)	C_5H_{11}	146.5～147	leaflets	$C_7H_{13}ON_3$	54.17	8.44	27.08	54.18	8.15	27.50
(Id)	C_7H_{15}	151.5～152.5	〃	$C_9H_{17}ON_3$	58.98	9.35	22.93	59.02	9.14	22.32
(Ie)	C_8H_{17}	148～148.5	needles	$C_{10}H_{19}ON_3$	60.88	9.71	21.30	61.07	9.80	21.43
(If)	C_9H_{19}	148～149	〃	$C_{11}H_{21}ON_3$	62.52	10.02	19.89	62.27	9.74	19.78
(Ig)	$C_{11}H_{23}$	148～149	leaflets	$C_{13}H_{25}ON_3$	65.23	10.53	17.56	65.24	10.36	17.11

a) All m.p.s are uncorrected.
b) All compounds are colorless.

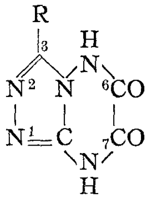
TABLE II. 3-Alkyl-4,5-diamino-1,2,4-triazoles



No.	R	m.p. (°C)	Crystal form[a]	Mol. formula	Analyses (%) Calcd. C	Calcd. H	Calcd. N	Found C	Found H	Found N
(IIa)	C_4H_9	183.5～185	leaflets	$C_6H_{13}N_5$	46.43	8.44	45.13	46.26	8.33	44.56
(IIb)	C_5H_{11}	184～185	〃	$C_7H_{15}N_5$	49.68	8.93	41.39	49.58	8.89	41.54
(IIc)	C_7H_{15}	188～189	〃	$C_9H_{19}N_5$	54.79	9.71	35.50	55.23	9.69	35.48
(IId)	C_9H_{19}	189～190	〃	$C_{11}H_{23}N_5$	58.63	10.29	31.08	58.85	10.05	30.45

a) All compounds are colorless.

TABLE III. 3-Alkyl-5,6,7,8-tetrahydro-*s*-triazolo[4,3-*b*][1,2,4]triazine-6,7-diones



No.	R	m.p. (°C) (decomp.)	Crystal form[a]	Mol. formula	Analyses (%) Calcd. C	Calcd. H	Calcd. N	Found C	Found H	Found N
(IIIa)	CH_3	ca. 315	prisms	$C_5H_5N_5O_2$	35.93	3.02	41.91	36.03	3.15	42.28
(IIIb)	C_2H_5	〃 292	leaflets	$C_6H_7N_5O_2$	39.78	3.89	38.66	39.55	3.94	38.52
(IIIc)	C_4H_9	285.5	〃	$C_8H_{11}N_5O_2$	45.93	5.30	33.48	46.04	4.96	—
(IIId)	C_5H_{11}	276	needles	$C_9H_{13}N_5O_2$	48.42	5.87	31.38	48.31	5.53	—
(IIIe)	C_7H_{15}	272	plates	$C_{11}H_{17}N_5O_2$	52.57	6.82	27.87	52.50	6.58	27.95
(IIIf)	C_9H_{19}	267	〃	$C_{13}H_{21}N_5O_2$	55.89	7.58	25.07	55.60	7.43	25.10
(IIIg)	$PhCH_2$	289.5	leaflets	$C_{11}H_9N_5O_2$	54.32	3.73	28.80	54.66	3.72	28.97
(IIIh)	$PhCH_2CH_2$	308	〃	$C_{12}H_{11}N_5O_2$	56.02	4.31	27.23	55.71	4.26	27.54

a) All compounds are colorless.

In Tables I and II are listed 2-alkyl-5-amino-1,3,4-oxadiazoles (I) and 3-alkyl-4,5-diamino-1,2,4-triazoles (II) which have not been reported in any literature. These *o*-diaminotriazoles (II) reacted easily with diethyl oxalate by heating together and produced 3-alkyl-5,6,7,8-tetrahydro-*s*-triazolo[4,3-*b*][1,2,4]triazine-6,7-diones (III). Physical and analytical data of these compounds (III) are listed in Table III.

The effect of these compounds on development of photographic emulsion was found to be very interesting,[8,9] but this is not included in this paper.

Experimental

2-Butyl-5-amino-1,3,4-oxadiazole (Ib)—A solution of 5.08 g. of CNBr in 80 cc. of H_2O was added to the solution of 5.58 g. of valeryl hydrazide and 5.5 g. of $KHCO_3$ in 50 cc. of H_2O. After standing overnight, the precipitate was collected and washed with H_2O. Two recrystallizations from H_2O yielded 2.8 g. of (Ib) (Table I).

2-Pentyl-5-amino-1,3,4-oxadiazole (Ic)—A solution of 1.06 g. of CNBr in 16 cc. of H_2O was added to the solution of 1.3 g. of caproyl hydrazide and 1.05 g. of $KHCO_3$ in 10 cc. of H_2O. The mixture was allowed to stand overnight and the precipitate was collected. Two recrystallizations from H_2O yielded 0.6 g. of (Ic).

2-Heptyl-5-amino-1,3,4-oxadiazole (Id)—A solution of 1.06 g. of CNBr in 16 cc. of H_2O was added to the hot solution (35°) of 1.58 g. of caprylyl hydrazide and 1.05 g. of $KHCO_3$ in a mixture of 50 cc. of H_2O and 35 cc. of MeOH. After standing overnight, the precipitate was collected and recrystallized from 50% MeOH. Yield, 1.2 g.

2-Octyl-5-amino-1,3,4-oxadiazole (Ie)—A solution of 2.12 g. of CNBr in 60 cc. of 50 (v/v)% MeOH was added dropwise over a period of 10 min. into the stirred solution prepared from 3.44 g. of pelargonyl hydrazide, 2.1 g. of $KHCO_3$, 50 cc. of H_2O, and 50 cc. of MeOH, keeping the reaction temperature at 38~42°. Stirring was further continued for 1 hr. at the same temperature and then the reaction mixture was allowed to stand overnight. The precipitate was collected, washed with H_2O, and recrystallized from MeOH. Yield, 2.0 g.

2-Nonyl-5-amino-1,3,4-oxadiazole (If)—A solution of 1.06 g. of CNBr in 16 cc. of H_2O was added dropwise over a period of 5 min. into the stirred solution prepared from 1.82 g. of capryl hydrazide, 1.05 g. of $KHCO_3$, 30 cc. of H_2O, and 50 cc. of MeOH, keeping the reaction temperature at 45~50°. Stirring was further continued for 30 min. at the same temperature and then the reaction mixture was allowed to stand overnight. The precipitate was collected, washed with H_2O, and recrystallized from 50% MeOH. Yield, 1.48 g.

2-Undecyl-5-amino-1,3,4-oxadiazole (Ig)—A solution of 5 g. of $KHCO_3$ in 50 cc. of H_2O was added to the hot solution of 10 g. of lauryl hydrazide in 300 cc. of MeOH. To this mixture, a solution of 5 g. of CNBr dissolved in a mixture of 100 cc. of H_2O and 50 cc. of MeOH was added at 50° and the whole was stirred for 1 hr. After standing overnight, the precipitate was collected, washed with H_2O, and recrystallized from MeOH. Yield, 9.8 g.

2-Amino-5-phenyl-1,3,4-oxadiazole (Ia) from 2-Methylsulfonyl-5-phenyl-1,3,4-oxadiazole (VI)—One g. of 2-methylsulfonyl-5-phenyl-1,3,4-oxadiazole[6] (VI) was suspended in a mixture of 20 cc. of benzene and 20 cc. of EtOH saturated with dry NH_3, and the mixture was allowed to stand at room temperature for 2 days. About 3/4 of the solvent was then evaporated under a reduced pressure and insoluble crystals were collected. After washing with hot benzene, the crystals were purified by recrystallization from EtOH. Yield, 0.2 g. m.p. 236°(decomp.). Mixed m.p. with the sample prepared by Gehlen's[1] or Hoggarth's[6] method showed no depression and infrared spectroscopic data of these three samples were in good agreement.

3,4-Diamino-5-butyl-1,2,4-triazole (IIa)—A mixture of 0.5 g. of (Ib) and 0.5 cc. of 82% hydrazine hydrate was refluxed for 7 hr. and allowed to stand overnight at room temperature. The precipitate was collected and recrystallized from dioxane. Yield, 0.3 g. (Table II).

3,4-Diamino-5-pentyl-1,2,4-triazole (IIb)—By a procedure similar to synthesis of (II), 0.1 g. of pure (IIb) was obtained from 0.6 g. of (Ic) and 0.6 cc. of 82% hydrazine hydrate.

3,4-Diamino-5-heptyl-1,2,4-triazole (IIc)—By a procedure similar to synthesis of (IIa), 0.25 g. of pure (IIc) was obtained from 0.6 g. of (Id) and 0.6 cc. of 85% hydrazine hydrate.

3,4-Diamino-5-nonyl-1,2,4,-triazole (IId)—A mixture of 1.2 g. of (Ie) and 1.2 cc. of 85% hydrazine hydrate was refluxed for 9 hr. and allowed to stand overnight at room temperature. The precipitate was collected and recrystallized from dioxane. Yield, 0.4 g.

---

[8] K. Futaki, Y. Ohyama, T. Iwasaki: Phot. Sci. Eng., **4**, 97(1960).

[9] K. Futaki: Nippon Shashin Gakkai Kaishi, in press.

3-Methyl-5,6,7,8-tetrahydro-*s*-triazolo[4,3-*b*][1,2,4]triazine-6,7-dione (IIIa)—A mixture of 0.9 g. of 3,4-diamino-5-methyl-1,2,4-triazole[8] and 4.6 g. of diethyl oxalate was heated in an oil bath (160~165°) for 4 hr. and allowed to stand overnight at room temperature. The precipitate was collected and washed with Et_2O. The crystals were dissolved in 5 cc. of 3*N* NaOH, the solution was then acidified to pH 3 with conc. HCl, and the precipitate was collected and washed with MeOH. Recrystallization from a large volume of H_2O gave 0.2 g. of (Ⅲa) (Table Ⅲ).

3-Ethyl-5,6,7,8-tetrahydro-*s*-triazolo[4,3-*b*][1,2,4]triazine-6,7-dione (IIIb)—A mixture of 1.25 g. of 3,4-diamino-5-ethyl-1,2,4-triazole[7] and 5.75 g. of diethyl oxalate was heated in an oil bath (160~165°) for 3.5 hr., cooled, the precipitate was collected, washed with Et_2O, and dissolved in 2*N* NaOH. The solution was then acidified with 6*N* HCl and the precipitate was collected. Recrystallization from MeOH gave 0.8 g. of (Ⅲb).

3-Butyl-5,6,7,8-tetrahydro-*s*-triazolo[4,3-*b*][1,2,4]triazine-6,7-dione(IIIc)-A mixture of 0.6 g. of (Ⅱa) and 2.08 g. of diethyl oxalate was heated in an oil bath (160~165°) for 3 hr. and allowed to stand overnight at room temperature. The precipitate was collected, washed with Et_2O, and dissolved in 2*N* NaOH. The solution was then acidified to pH 2 with 6*N* HCl and separated crystals were collected. Recrystallization from 50% EtOH gave 0.3 g. of (Ⅲc).

3-Pentyl-5,6,7,8-tetrahydro-*s*-triazolo[4,3-*b*][1,2,4]triazine-6,7-dione (IIId)—A mixture of 1.2 g. of (Ⅱb) and 3.2 g. of diethyl oxalate was heated in an oil bath (160~165°) for 4 hr., cooled, the preciptiate was collected, washed with Et_2O, and dissolved in 20 cc. of 2*N* NaOH. The solution was then acidified with 6*N* HCl and separated crystals were collected. Recrystallization from MeOH gave 0.4 g. of (Ⅲd).

3-Heptyl-5,6,7,8-tetrahydro-*s*-triazolo[4,3-*b*][1,2,4]triazine-6,7-dione (IIIe)—By a procedure similar to synthesis of (Ⅲd), 0.5 g. of (Ⅲe) was obtained from 0.96 g. of (Ⅱc) and 2.9 g. of diethyl oxalate.

3-Nonyl-5,6,7,8-tetrahydro-*s*-triazolo[4,3-*b*][1,2,4]triazine-6,7-dione (IIIf)—A mixture of 1.13 g. of (Ⅱd) and 2.9 g. of diethyl oxalate was heated in an oil bath (160~165°) for 6 hr. and allowed to stand overnight at room temperature. The precipitate was collected, washed with Et_2O, and dissolved in 10 cc. of *N* NaOH at 40~45°. The solution was then acidified with 6*N* HCl and separated crystals were collected. Recrystallization from 90% EtOH gave 0.5 g. of (Ⅲf).

3-Benzyl-5,6,7,8-tetrahydro-*s*-triazolo[4,3-*b*][1,2,4]triazine-6,7-dione (IIIg)—A mixture of 0.63 g. of 3,4-diamino-5-benzyl-1,2,4-triazole[7] and 1.95 g. of diethyl oxalate was heated in an oil bath (160~165°) for 4.5 hr. and allowed to stand overnight at room temperature. The precipitate was collected, washed with Et_2O, and dissolved in *N* NaOH at 40~45°. The solution was then acidified with 6*N* HCl and separated crystals were collected. Recrystallization from 50% EtOH gave 0.2 g. of (Ⅲg).

3-Phenethyl-5,6,7,8-tetrahydro-*s*-triazolo[4,3-*b*][1,2,4]triazine-6,7-dione (IIIh)-A mixture of 2.4 g. of 3,4-diamino-5-phenethyl-1,2,4-triazole[7] and 7.3 g. of diethyl oxalate was heated in an oil bath (160~165°) for 4 hr., cooled, the precipitated crystals were collected, washed with Et_2O, and dissolved in 40 cc. of 2*N* NaOH. The solution was then acidified with 6*N* HCl and separated crystals were collected. Recrystallization from 50% ethoxyethanol gave 0.8 g. of (Ⅲh).

The authors' thanks are due to Prof. S. Uyeo of the University of Osaka and Dr. Y. Ohyama, the Chief of the Research Section of their Division, for giving them many facilities, and also due to Mr. M. Fukuda of the University of Osaka for microanalytical data.

Summary

The chemical structure of the compounds found by the reaction of cyanogen bromide and acylhydrazines was determined as 2-alkyl-5-amino-1,3,4-oxadiazoles (I).

3-Alkyl-5,6,7,8-tetrahydro-*s*-triazolo[4,3-*b*][1,2,4]triazine-6,7-diones (Ⅲ), which are listed in Table Ⅲ, were prepared from 4,5-diamino-1,2,4-triazoles (Ⅱ) and diethyl oxalate. Several unreported intermediates of these compounds —— 2-alkyl-5-amino-1,3,4-oxadiazoles (I) and 4,5-diamino-1,2,4-triazoles (Ⅱ) —— were also prepared and are listed in Tables I and Ⅱ.

(Received February 11, 1960)