[Chem. Pharm. Bull. 16(7)1244—1250(1968)] UDC 547.852.07

Studies on the Synthesis of Pyridazine Derivatives. XI.[1] Reaction of 3,6-Dialkoxypyridazine 1-Oxide with Alkylhalides, Haloketones and Haloacid Esters, and Decomposition of Reaction Products[2]

Mitsuji Yanai and Masa-aki Yamaguchi

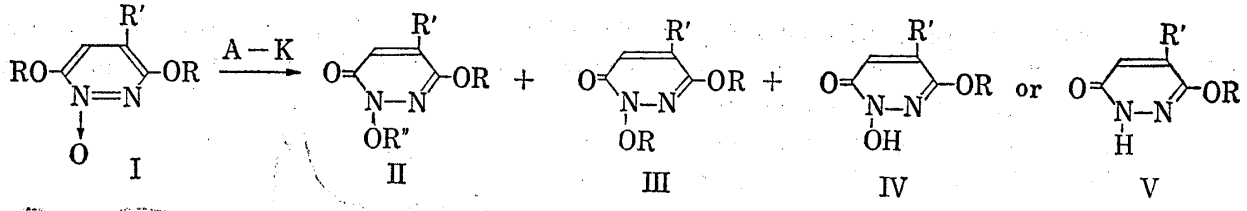
Faculty of Pharmaceutical Sciences, Nagasaki University[3]

(Received September 11, 1967)

Reaction of 3,6-dialkoxypyridazine 1-oxides (I) with halogeno compounds afforded corresponding esters of cyclic hydroxamic acid (II). Decomposition of II with acids, alkalines and pyrolysis gave aldehydes and 3-alkoxy-6(1*H*)pyridazinones (V), or conjugated carbonyl olefines and 1-hydroxy-3-alkoxy-6(1*H*)pyridazinones (IV), respectively.

Meisenheimer[4] reported that N-alkoxyammonium hydroxides were decomposed into tertiary amines and aldehyde with alkalines. Herz,[5] Ochiai, *et al.*[6] showed that N-alkoxy aromatic quarternary ammonium salts were decomposed into aldehydes and aromatic tertiary amines, and they were similar to the Meisenheimer's salts. Moreover, recently Kato, *et al.*[7] developed this reaction into synthesis of ketoaldehydes.

In a preceding paper,[8] the authors reported the decomposition of 1-phenacyloxy-3-alkoxy-6(1*H*)pyridazinone into phenylglyoxal and 3-alkoxy-6(1*H*)pyridazinone. That

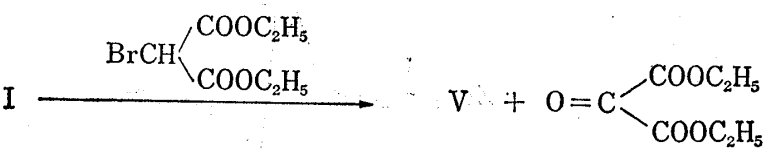


I II III IV V

a : R=CH_3, R'=H
b : R=C_2H_5, R'=H
c : R=CH_3, R'=CH_3
d : R=C_2H_5, R'=CH_3

A : $Cl\cdot COOC_2H_5$
B : $Br\cdot CH_2COOC_2H_5$
C : $Br\cdot CH_2CH_2COOC_2H_5$
D : $Br\cdot CH_2CH_2CH_2COOC_2H_5$

E : $BrCH_2CH_2CH_2CH_2COOC_2H_5$
F : $BrCH_2CH_2CO\cdot C_6H_5$
H : $BrCH_2CH_2C_6H_5$
K : $ClCH_2C_6H_5$[8]



X

Chart 1

1) Part X: *Chem. Pharm. Bull.* (Tokyo), **16**, 1221 (1968).
2) This work was presented at Kyushu Branch Meeting of Pharmaceutical Society of Japan, September 17, 1966.
3) Location: *4-23 Burkyo-machi, Nagasaki.*
4) J. Meisenheimer, *Ann.*, **397**, 273 (1913); **399**, 371 (1913).
5) M. Herz, *Chem. Ber.*, **70**, 1270 (1937).
6) E. Ochiai, M. Katada, and T. Naito, *Yakugaku Zasshi*, **64**, 210 (1944); E. Ochiai and T. Kato, *Yakugaku Zasshi*, **71**, 156 (1951).
7) T. Kato, Y. Goto, and Y. Yamamoto, *Yakugaku Zasshi*, **84**, 287 (1964).
8) M. Yanai, T. Kinoshita, and M. Yamaguchi, *Yakugaku Zasshi*, **86**, 81 (1966).

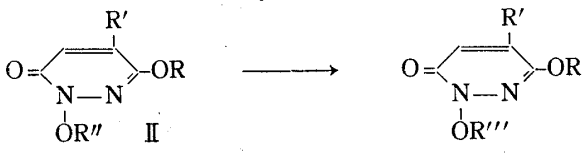
paper showed that decomposition of esters of cyclic hydroxamic acid type were similar to the Meisenheimer's salts and N–alkoxy aromatic quaternary ammonium salts.

This paper describes the syntheses of ester of cyclic hydroxamic acid and decomposition of the esters. General reaction formula was showed at Chart 1, the reaction of I with halogeno compounds afforded coresponding esters of cyclic hydroxamic acid (II). In case of higher reaction temperature, 1,3–dialkoxy–6(1*H*)pyridazinone (III) and 1–hydroxy–3–alkoxy–6(1*H*) pyridazinone (IV) (or 3–alkoxy–6(1*H*)pyridazinone (V)) were obtained, on some occasion.

Preparation of Esters of Hydroxamic Acid

1–Ethoxycarbonyloxy–3–alkoxy–6(1*H*)pyridazinones (II–A) or 1–ethoxycarbonylmethoxy–3–alkoxy–6(1*H*)pyridazinones (II–B) were afforded by reaction of I with ethyl chlorocarbo-

Table I. Reaction of II with pri. Amines, Methanol–hydrochloric Acid and dil. Hydrochloric Acid



Starting Materials	R	R′	R‴	Products m.p. (°C)	Yield (%)	Formula
IIa–B	CH_3	H	CH_2CONH_2	155—157	55	$C_7H_9O_4N_3$
IIb–B	C_2H_5	H	CH_2CONH_2	114—115	57	$C_8H_{11}O_4N_3$
IIc–B	CH_3	CH_3	CH_2CONH_2	162—163	50	$C_8H_{11}O_4N_3$
IId–B	C_2H_5	CH_3	CH_2CONH_2	133—134.5	61	$C_9H_{13}O_4N_3$
IIa–B	CH_3	H	$CH_2CONHNH_2$	144—145.5	70	$C_7H_{10}O_4N_4$
IIb–B	C_2H_5	H	$CH_2CONHNH_2$	126.5—127.5	65	$C_8H_{12}O_4N_4\cdot\frac{1}{2}H_2O$
IIc–B	CH_3	CH_3	$CH_2CONHNH_2$	174.5—175.5	89	$C_8H_{12}O_4N_4$
IIc–B	CH_3	CH_3	$CH_2\cdot COOH$	143.5—145	70	$C_8H_{10}O_5N_2$
IIc–B	CH_3	CH_3	$CH_2\cdot COOCH_3$	136.5—138	61	$C_9H_{12}O_5N_2$
IIa–C	CH_3	H	$(CH_2)_2\cdot COOH$	140—141	77	$C_8H_{10}O_5N_2$
IIa–D	CH_3	H	$(CH_2)_3\cdot COOH$	128—130	54	$C_9H_{12}O_5N_2$
IIb–D	C_2H_5	H	$(CH_2)_3\cdot COOH$	104.5—105.5	81	$C_{10}H_{14}O_5N_2$
IIa–E	CH_3	H	$(CH_2)_4\cdot COOH$	94.5—95.5	80	$C_{10}H_{14}O_5N_2$
IIb–E	C_2H_5	H	$(CH_2)_4\cdot COOH$	119—120	82	$C_{11}H_{16}O_5N_2$

Starting Materials	Analysis (%) Calcd. C	H	N	Found C	H	N
IIa–B	42.21	4.55	21.10	42.51	4.64	20.99
IIb–B	45.08	5.20	19.71	45.18	5.09	19.46
IIc–B	45.08	5.20	19.71	45.13	5.27	19.49
IId–B	47.57	5.77	18.45	47.27	5.78	18.20
IIa–B	39.25	4.71	26.16	39.54	4.61	25.81
IIb–B	41.10	5.52	23.61	41.38	5.39	23.89
IIc–B	42.10	5.30	24.55	42.38	5.33	24.81
IIc–B	44.86	4.71	13.08	45.01	4.68	12.75
IIc–B	47.37	5.30	12.28	47.65	5.18	12.32
IIa–C	44.86	4.71	13.08	44.85	4.51	13.21
IIa–D	47.37	5.30	12.28	47.24	5.03	12.44
IIb–D	49.58	5.83	11.57	49.33	5.64	11.79
IIa–E	49.58	5.83	11.57	49.72	5.84	11.90
IIb–E	51.56	6.29	10.93	51.89	6.23	11.07

nate (A) or ethyl bromoacetate (B), respectively, by heating at 95—100° on a water bath, in good yield.

Reaction with ethyl 3-bromopropionate (C) gave 1-ethoxycarbonylethoxy-3-alkoxy-6(1*H*)pyridazinones (II-C), by heating at 130° for 6—10 hr, in 50—60% yield. Similarly reaction with ethyl 4-bromobutyrate (D) or ethyl 5-bromovalerate (E) afforded 1-ethoxycarbonylpropyloxy-3-alkoxy-6(1*H*)pyridazinones (II-D) or 1-ethoxycarbonylbutyloxy-3-3-alkoxy-6(1*H*)pyridazinones (II-E), accompanied with III respectively, by heating at 130—140° for 10 hr in 50% yield.

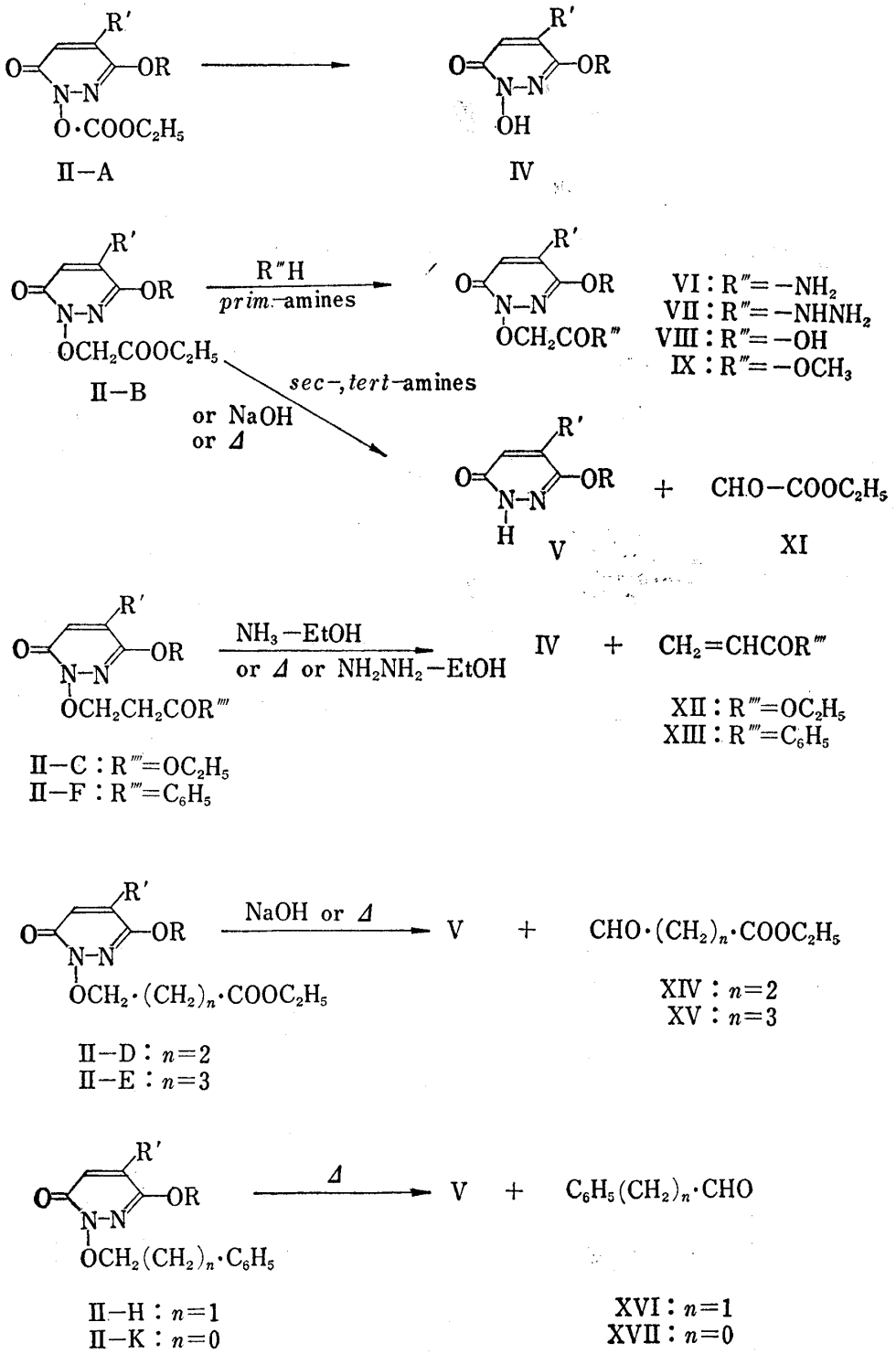
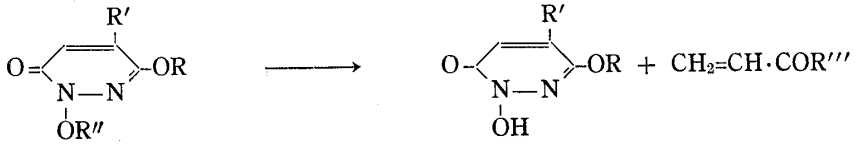


Chart 2

In the reaction of I and β-bromopropiophenone (F), following different results were obtained by reactionary condition, 1-hydroxy-3-alkoxy-6(1*H*)pyridazinones (IV) and vinyl phenyl ketone were obtained at above 100°, 1-benzoylethoxy-3-alkoxy-6(1*H*)pyridazinones (II-F) were afforded at 60—65°, reflux of chloroform solution of I and F afforded II-F (a,b,c,d) accompanied with starting material and a small amount of IV.

Reaction of I with diethyl bromomalonate (G) gave not esters of hydroxamic acid, but 3-alkoxy-6(1*H*)pyridazinones (V) and diethyl mesooxalate even at boiling point of chloroform solution. It was suggested that reaction product of I with G was decomposed in V and diethyl mesooxalate very easily at boiling point of chloroform.

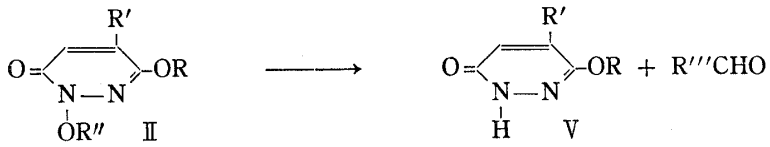
Table II-1. Decomposition of II to IV and Conjugated Carbonyl Olefines



II-A, II-C, II-F IV

Starting Materials	Methods	Reaction Temp (°C)	Reaction Time (hr)	Reaction Products (%) IV	olefines	
IIc-A	H_2O	100	3	93	—	
IIc-A	NH_3-MeOH	0—5	2	93	—	
IIa-C	heat	180—220	2	51	40	CH_2=CH·COOEt
IIb-C	$NH_2NH_2\cdot H_2O$-EtOH	40	3	34	—	
IIb-C	NH_3-EtOH	0—5	2	98	—	
IIb-F	NH_3-EtOH	0—5	2	95	33	CH_2=CH·CO·C_6H_5
IIb-F	heat	100—120	3	32	—	

Table II-2. Decomposition of II to V and Aldehydes



Starting Materials	Methods	Reaction Temp. (°C)	Reaction Time (hr)	Products (%) V	Aldehyde	
IIa-B	NaOH-EtOH	20	over night	24		
IIa-B	Me_2NH-EtOH	25	24	32		
IIa-B	heat	160—170	13	37		
IIb-B	NaOH-EtOH	25	72	39		
IIb-B	Me_2NH-EtOH	25	7	57	62	CHO·COOEt
IIb-B	M*-EtOH	reflux	3	78		
IIb-B	M*-EtOH	22	3	29		
IIc-B	Me_2NH-EtOH	25	3	48		
IIc-B	P*-EtOH	reflux	3	51		
IIc-B	heat	170—180	8	54	42	CHO·COOEt
IIa-D	10% NaOH	100	3	40		
IIa-D	heat	230—245	2.5		40	CHO·$(CH_2)_2$·COOEt
IIa-E	heat	250—260	2	30	42	CHO·$(CH_2)_3$·COOEt
IIa-H	heat	230—260	2	50	37	$C_6H_5\cdot CH_2CHO$
IIb-K	heat	220—240	2	63	51	C_6H_5·CHO

M*: Morpholine P*: Piperidine

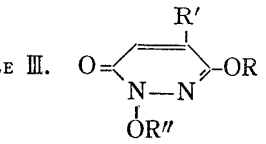
Reaction with β-bromoethylbenzene (H) afforded 1-phenethyloxy-3-alkoxy-6(1*H*)pyridazinones (II-H) (50%) and III (24%), by heating at 140—150° for 10 hr.

The structure of reaction products were identified by measurement of elementary analyses, infrared and ultraviolet spectra. Infrared spectra showed ring carbonyl at 1650—1690 cm^{-1}, ultraviolet spectra showed characteristic absorption curve and absorption maximum at 303—316 mμ. Moreover, liquid compounds of ester of carboxylic acid derivatives were measured nuclear magnetic resonance (NMR) spectra, and hydrolyzed to free carboxylic acids with dil. hydrochloric acid, which were identified with elementary analysis, infrared and ultraviolet spectra. 1-Phenethyloxy-3-methoxy-6(1*H*)pyridazinone (IIa-H) was identified with infrared (C=O, 1675 cm^{-1}), ultraviolet (315 mμ) and NMR (CCl_4, δ 3.03, 2H, triplet: $CH_2\underline{CH}_2C_6H_5$: δ 4.30 2H, triplet: $OC\underline{H}_2CH_2C_6H_5$; δ 3.76, 3H, singlet: OCH_3; δ 6.80, 2H, singlet: pyridazinone ring proton; δ 7.16, 5H, singlet: phenyl proton) spectra.

Decomposition of Esters of Hydroxamic Acid

II-A were hydrolyzed with water and ethanolic ammonia to IV easily, it was similar to 1-acetoxy-3-alkoxy-6(1*H*)pyridazinones.[8] In case of II-B, transesterification, amination and hydrazination were occurred by treatment with alcholic hydrochloric acid, ethanolic ammonia or hydrazine hydrate, respectively. While secondary and tertiary amines, sodium hydroxide and heating gave V and ethyl glyoxylate.

Table III.



Starting Materials	R	R′	R″	mp (°C) or bp (°C/mmHg)	Yield (%)	Formula	Analysis (%) Calcd. C	H	N	Found C	H	N
IIa-A	CH_3	H	$COOC_2H_5$	60—61	94	$C_8H_{10}O_5N_2$	44.86	4.71		45.20	4.71	
IIb-A	C_2H_5	H	$COOC_2H_5$	92—94	80	$C_9H_{12}O_5N_2$	47.37	5.30	12.28	47.34	5.10	12.34
IIc-A	CH_3	CH_3	$COOC_2H_5$	80—82	73	$C_9H_{12}O_5N_2$	47.37	5.30	12.28	47.34	5.03	12.45
IId-A	C_2H_5	CH_3	$COOC_2H_5$	64—65	25	$C_{10}H_{14}O_5N_2$	49.58	5.83	11.57	49.86	5.80	11.70
IIa-B	CH_3	H	$CH_2\cdot COOC_2H_5$	74—75.5	71	$C_9H_{12}O_5N_2$	47.37	5.30	12.28	47.53	5.71	12.56
IIb-B	C_2H_5	H	$CH_2\cdot COOC_2H_5$	79—80.5	55	$C_{10}H_{14}O_5N_2$	49.58	5.83	11.57	49.78	5.74	11.70
IIc-B	CH_3	CH_3	$CH_2\cdot COOC_2H_5$	80—81.5	71	$C_{10}H_{14}O_5N_2$	49.58	5.83	11.57	49.72	5.77	11.64
IId-B	C_2H_5	CH_3	$CH_2\cdot COOC_2H_5$	75—76.5	72	$C_{11}H_{16}O_5N_2$	51.56	6.29	10.93	51.70	6.41	10.85
IIa-C	CH_3	H	$(CH_2)_2\cdot COOC_2H_5$	69—71.5	50	$C_{10}H_{14}O_5N_2$	49.58	5.83	11.57	49.80	5.78	11.40
IIb-C	C_2H_5	H	$(CH_2)_2\cdot COOC_2H_5$	57.5—58.5	34	$C_{11}H_{16}O_5N_2$	51.56	6.29	10.93	51.66	6.28	11.00
IIc-C	CH_3	CH_3	$(CH_2)_2\cdot COOC_2H_5$	66—67	57	$C_{11}H_{16}O_5N_2$	51.56	6.29	10.93	51.68	6.37	10.79
IId-C	C_2H_5	CH_3	$(CH_2)_2\cdot COOC_2H_5$	61—62	51	$C_{12}H_{18}O_5N_2$	53.32	6.71	10.37	53.32	6.71	10.50
IIa-D	CH_3	H	$(CH_2)_3\cdot COOC_2H_5$	166—170/2—3	55							
IIb-D	C_2H_5	H	$(CH_2)_3\cdot COOC_2H_5$	170—171/3	51							
IIa-E	CH_3	H	$(CH_2)_4\cdot COOC_2H_5$	175—180/3	59							
IIb-E	C_2H_5	H	$(CH_2)_4\cdot COOC_2H_5$	175—178/2	52							
IIb-F	C_2H_5	H	$CH_2CH_2COC_6H_5$	89—90	28	$C_{15}H_{16}O_4N_2$	62.49	5.59	9.72	62.80	5.44	9.63
IId-F	C_2H_5	CH_3	$CH_2CH_2COC_6H_5$	97—98.5	24	$C_{16}H_{18}O_4N_2$	63.56	6.00	9.27	63.72	5.81	8.93

II-C were decomposed with ethanolic ammonia to IV, but in this case ethyl acrylate was not isolated, instead IV and ethyl acrylate were obtained by heating. By sodium hydroxide or heating, II-D and II-E afforded to V and corresponding aldehyde, which was ethyl 3-formyl propionate and ethyl 4-formylglutarate, while the esters of hydroxamic acids resisted to secondary amines for example morpholine and piperidine. II-F were decomposed to IV and vinyl phenyl ketone with primary amines (for example ammonia, hydrazine hydrate) and heat-

ing. II–H, II–K afforded V and corresponding aldehyde by heating (phenylacetaldehyde or benzaldehyde).

Structure of aldehydes were identified as 2,4–dinitrophenylhydrazones, they were verified by elemental analyses. Benzaldehyde was identified with authentic sample of 2,4–dinitrophenylhydrazone of benzaldehyde. Ethyl acrylate was identified with infrared and NMR spectra comparison. Vinyl phenyl ketone afforded 1,3–diphenyl–Δ_2–pyrazoline mp 152—153° by reaction with phenylhydrazine, it was identified with elementary analysis and NMR spectrum.

These results suggested that esters of hydroxamic acid were decomposed to V and corresponding aldehydes, in general. While in case of II–C and II–F afforded IV and coresponding conjugated carbonyl olefines by β–elimination and II–A gave IV by hydrolysis.

Experimental

1-Ethoxycarbonyloxy-3-methoxy-6(1*H*)pyridazinone (IIa-A)——A mixture of 2.0 g of Ia and 7.0 ml of A was heated at 95—100° on a water bath for 3 hr. Reaction mixture was evaporated to dryness under reduced pressure. The residue was recrystallized from ether–pet.ether to give 2.6 g of colorless prisms (IIa–A), mp 60—61°.

1-Ethoxycarbonylmethoxy-3-methoxy-6(1*H*)pyridazinone (IIa-B)——A mixture of 2.367 g of Ia and 5 ml of B was heated at 95—100° on a water bath for 8 hr. After cool, reaction mixture was washed with ether–pet.ether. The crystals were recrystallized from ether to give 2.45 g of colorless needles (IIa–B), mp 74—75.5°.

Reaction of 3,6-Diethoxypyridazine 1-Oxide (Ib) with Ethyl 3-Bromopropionate (C)——A mixture of 5.0 g of Ib and 4.9 g of C was heated at 120—125° for 4.5 hr. Reaction mixture was added ether–pet.ether and chilled with ice–water. The deposited crystals were recrystallized from ether–pet.ether to give 1.63 g of colorless needles (IIb–C), mp 57.5—58.5°. Mother liquor was separated with fractional distillation in three fraction, the initial fraction gave C at bp 80—100° (8 mmHg) (oil bath), the second fraction gave 1.02 g of Ib at bp 80—140°(4 mmHg) (oil bath), the final fraction gave 0.7 g of IIb–C at bp 160—170° (4 mmHg) (oil bath).

Reaction of 3,6-Dimethoxypyridazine 1-Oxide (Ia) with Ethyl 4-Bromobutyrate (D)——A mixture of 5.0 g of Ia and 6.25 g of D was heated at 130° for 13 hr. Reaction mixture was separated with fractional distillation in three parts. The initial fraction was obtained at bp 51—54° (2—3 mmHg). The crystals were obtained from the second fraction at bp 90—122° (2—3 mmHg), they were recrystallized from ether to give 0.4 g of colorless needles, mp 68—70°, it was identified with IIIa by mixed melting point and infrared (IR) comparison. The final fraction gave 4.8 g of pale yellow oil (IIa–D), at bp 170—171° (3 mmHg).

Reaction of 3,6-Diethoxypyridazine 1-Oxide (Ib) with β-Bromopropiophenone (F)——A solution of 5.0 g of Ib, 5.8 g of F and dry $CHCl_3$ was refluxed for 1 hr. Reaction mixture was evaporated to dryness under reduced pressure, the residue was added a little of ether and chilled. The deposited crystals were recrystallized from acetone to give 1.38 g of colorless needles, mp 120—122°, it was identified with IVb by mixed melting point and IR comparison. Mother liquor was evaporated to dryness, the residue was recrystallized from ether to give colorless cubes (IIb–F). Moreover mother liquor was distilled under reduced pressure, pale yellow oily product was obtained (0.82 g, bp 90—100° (2—3 mmHg)(oil bath)), it was identified with vinyl phenyl ketone. Reaction of the oil and phenylhydrazine afforded 1,3–diphenyl–Δ_2–pyrazoline mp 152—153° yellowish green needles. *Anal.* Calcd. for $C_{15}H_{14}N_2$: C, 81.05; H, 6.35; N, 12.60. Found: C, 80.72; H, 6.33; N, 12.30.

Reaction of 3,6-Dimethoxypyridazine 1-Oxide (Ia) with Diethyl Bromomalonate (G)——A mixture of 2.0 g of Ia and 3.22 g of G was heated at 95—100° on a water bath for 7 hr. After chilled, reaction mixture was added a little ether. The deposited crystals (0.3 g) were recrystallized from acetone to give colorless needles, mp 163°, it was identical with Va by mixed melting point and IR comparison. Mother liquor and ether solution were combined, and evaporated to dryness. After the residue was dissolved in ether, and poured on alumina for chromatography. The initial fraction eluted with ether, pale yellow oily material was obtained, 2,4–dinitrophenylhydrazone of oily material was recrystallized from MeOH to give yellow leaves, mp 118—118.5°. *Anal.* Calcd. for $C_{13}H_{14}O_8N_4$: C, 44.07; H, 3.98; N, 15.82. Found: C, 44.39; H, 4.12; N, 16.12. And then, the column was eluted with acetone, the residue from the fraction eluted with acetone was recrystallized from ether to give 70 mg of mp 68—70°, it was identified with IIIa by mixed melting point and IR comparison.

Reaction of 3,6-Dimethoxypyridazine 1-Oxide (Ia) with Phenylethyl Bromide (H)——A mixture of 1.85 g of Ia and 2.3 g of H was heated at 140—155° for 10 hr. Reaction mixture was separated with fractional distillation in two parts. The crystals were obtained from the initial fraction at bp 150—160° (4—7 mmHg), they were recrystallized from ether to give 0.435 g of colorless needles, mp 68—70°, it was identified

with IIIa by mixed melting point and IR comparison. The final fraction gave 1.45 g of pale yellow viscous oil (IIa–H) at bp 195° (4—7 mmHg). UV λ_{max}^{EtOH} 315 mμ, IR $\nu_{C=O}^{KBr}$ 1675 cm^{-1}.

Reaction of IIa-A and Water——A mixture of 0.252 g of IIa–A and 1 ml of H_2O was heated on a boiling water bath for 2 hr. After cool, the deposited crystals were recrystallized from MeOH to give 0.145 g of colorless needles, mp 170—172°. It was identified with IVa by mixed melting point and IR comparison.

1-Carbamoylmethoxy-3-methoxy-6(1*H*)pyridazinone (VIa)——A solution of 0.3 g of IIa–B and 4 ml of EtOH was chilled with crashed ice, absorbed ammonia gas for 2 hr. The deposited crystals were recrystallized from acetone to give 0.14 g of colorless needles, mp 154—156°.

1-Hydrazinocarbonylmethoxy-3-methoxy-6(1*H*)pyridazinone (VIIa)——A solution of 0.5 g of IIa–B, 0.18 g of hydrazine hydrate (80%) and 4 ml of MeOH was heated at 40° for 2 hr. The deposited crystals were recrystallized from MeOH to give 0.33 g of colorless needles, mp 143—145°.

1-Carboxymethoxy-3-methoxy-4-methyl-6(1*H*)pyridazinone (VIIIc)——A solution of 0.3 g of IIc–B and 2 ml of 1% HCl was heated at 70—80° for 1 hr. Reaction mixture was evaporated to dryness under reduced pressure, the residue was recrystallized from AcOEt to give 0.18 g of colorless cubes, mp 143.5—145.5°.

1-Methoxycarbonylmethoxy-3-methoxy-4-methyl-6(1*H*)pyridazinone (IXc)——A solution of 0.5 g of IIc–B, 0.2 ml of conc. HCl and 5 ml of MeOH was allowed to stand for over night at room temperature. The deposited crystals were recrystallized from AcOEt to give 0.29 g of colorless cubes, mp 136.5—138°.

Pyrolysis of IIc-B——In a small sausage flask 0.8 g of IIc–B was heated at 170—180° for 8 hr. Oily product (0.25 g.) was distilled in accepter, 2,4-dinitrophenylhydrazone was recrystallized from EtOH to give yellow leaves, mp 123—124°. *Anal.* Calcd. for $C_{10}H_{10}O_6N_4$: C, 42.56; H, 3.57; N, 19.85. Found: C, 42.65; H, 3.51; N, 19.91.

Reaction of IIc-B with Piperidine——A solution of 0.3 g of IIc-B, 0.316 g (3 eq.) of piperidine and 5 ml of EtOH was refluxed for 3 hr. Reaction mixture was evaporated to dryness under reduced pressure. After the residue was washed with ether, recrystallized from MeOH to give 90 mg of colorless needles, mp 206—208°, it was identified with Vc by mixed melting point and IR comparison.

Reaction of IIb-C with Ammonia——A solution of 0.3 g of IIb–C and 5 ml of EtOH was chilled with crashed ice, and absorbed ammonia gas. The deposited crystals were recrystallized from EtOH to give colorless needles, mp 123°, it was identified with IVb by mixed melting point and IR comparison.

Pyrolysis of IIa-C——In a small sausage flask 1.2 g of IIa–C was heated at 180—220° for 1 hr, 220 mg of colorless liquid was obtained in accepter. It was identified with ethyl acrylate by IR and NMR comparison. The distilled residue was recrystallized from MeOH to give 360 mg of IVa, mp 172°.

Pyrolysis of IIb-D——In a small sausage flask 860 mg of IIb–D was heated at 230—245° under reduced pressure (25—45 mmHg) for 2.5 hr, 210 mg of colorless liquid was obtained. The distilled residue was recrystallized from EtOH to give 175 mg of Vb, mp 173—174°. Redistillation of the liquid gave 100 mg of pure product, bp 87°(19 mmHg). 2,4-Dinitrophenylhydrazone of the product was recrystallized from EtOH to give yellow leaves, mp 112—113°. *Anal.* Calcd. for $C_{12}H_{14}O_6N_4$: C, 46.45; H, 4.55; N, 18.06. Found: C, 46.83; H, 4.50; N, 18.05.

Reaction of IIb-F with Ammonia——To a cold solution of EtOH (4 ml) and IIb–F (300 mg) ammonia gas was injected for 1.5 hr. The deposited crystals were collected, and filtrate was added ether, moreover deposited crystals were collected, which were combined to former crystals. Recrystallization from MeOH gave colorless needles, mp 122—123°. It was identified with IVb by mixed melting point and IR comparison. The filtrate was condensed, and added a little of EtOH and 100 mg of phenylhydrazine. The mixture was refluxed for 2 hr, the reaction mixture was evaporated to dryness. The residue was dissolved in ether and passed through Al_2O_3 column, eluted with ether. Recrystallization from EtOH gave 65 mg of pale yellow needles, mp 152—153°. It was identified with 1,3-diphenyl-Δ_2-pyrazoline by mixed melting point and IR comparison.

Pyrolysis of IIa-H——In a small sausage flask 700 mg of IIa–H was heated at 230—260° for 3 hr, 100 mg of colorless liquid was obtained in accepter. The liquid was purified by vacuum distillation, bp 85—90° (20 mmHg), 2,4-dinitrophenylhydrazone was recrystallized from EtOH to give yellow leaves, mp 118—120°. *Anal.* Calcd. for $C_{14}H_{12}O_4N_4$: C, 56.00; H, 4.03. Found: C, 55.99; H, 3.93. Moreover 190 mg of colorless crystals were obtained under reduced pressure (20—30 mmHg), recrystallization from acetone gave colorless needles, mp 162—163°, it was identified Va by mixed melting point and IR comparison.

Acknowledgement The authors are indebted to Mrs. H. Mazume for elementary analysis and to Miss K. Ohta for the measurement of nuclear magnetic resonance spectra and to Mr. H. Ishikawa for the measurement of infrared and ultraviolet spectra.