Summary

Biogenesis of oospolactone (I) and oosponol (II) from a fungus, *Oospora astringenes* were studied by using glucose-[1-^{14}C], glucose-[6-^{14}C], malonate-[2-^{14}C], formate-[^{14}C], and uniformly labelled glucose-[^{14}C]. Degradation methods of the two metabolites were established and the progress of cultivation was also studied.

The isotope experiments suggest that the skeletons of the two metabolites are synthesized from five C_2-units according to the "acetate-malonate condensation" and one C_1-unit. C_1-unit is incorporated as methyl-C (carbon 11) in I, on the other hand, as =CH- (carbon 9) which participates to form the lactone ring in II. It is interesting that these two isocoumarins from the same culture have the different origin of lactone ring.

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51. **Tetsuji Kametani and Osamu Umezawa**: A Novel Dehydrazination Reaction. V.[*1] The Formation of Various Amides from Aliphatic and Aromatic Carboxylic Acid Hydrazides in the Presence of Chloral.

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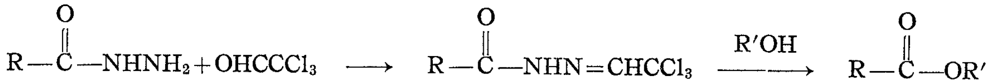
It has been previously observed that ethyl 2-bromo-4,5-dimethoxyphenylacetate was produced by the reaction between 2-bromo-4,5-dimethoxyphenylacetic acid hydrazide and either chloral or bromal in ethanol.[1a] Accordingly, the reactions between aromatic,[1b,2] aliphatic[3] and heterocyclic[*1] carboxylic acid hydrazides and either chloral or bromal in various alcohols were attempted and respective esters were obtained.



$$\underset{\text{I}}{R-\overset{O}{\overset{\|}{C}}-NHNH_2}+\underset{\text{II}}{OHCCCl_3}\longrightarrow\underset{\text{III}}{R-\overset{O}{\overset{\|}{C}}-NHN=CHCCl_3}\xrightarrow{R'OH}\underset{\text{IV}}{R-\overset{O}{\overset{\|}{C}}-OR'}$$

The purpose of the present investigation was to study the reaction of various acid hydrazides with chloral in the presence of various amines instead of alcohols previously reported by the authors,[*1,1a,1b,2,3] leading eventually to reveal that the formation of corresponding acid amides was recognized by the reactions between aliphatic and aromatic acid hydrazide and chloral in various amines.

After a reddish-brown mixture of 1-(benzoyl)-2-(2,2,2-trichloroethylidene)hydrazine[2] (III : $R=C_6H_5$-) and an excess of butylamine had been refluxed for 5 hr., removal of an excess of amine and alumina-chromatography of the residue gave the anticipated amide

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[*1] Part IV. T. Kametani, O. Umezawa, H. Yagi, S. Asagi : Yakugaku Zasshi, **85**, 518 (1965).

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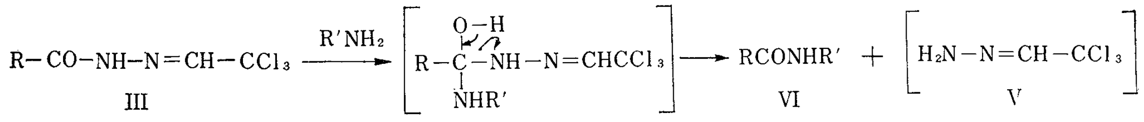
3) *Idem* : *Ibid.*, **85**, 514 (1965).

(Ⅵ : $R=C_6H_5-$, $R'=C_4H_9-$), whose infrared spectrum was identical with that of an authentic sample.[4~7] It was therefore considered that the intermediate (Ⅲ : $R=C_6H_5-$) was formed by the condensation between acid hydrazide and chloral and the -CO-NH- bond will be cut off by the electron attractivity of trichloro-ethylidene radical in the amidolysis.

Accordingly, a mixture of hydrazine (Ⅲ : $R=C_6H_5-$) and aniline was heated without solvent in an oil-bath at 180~190°, giving the expected amide (Ⅵ : R, $R'=C_6H_5-$) (75.39%) which was identical with an authentic sample[8] (Ⅵ : R, $R'=C_6H_5-$) by mixed melting point test and infrared spectrum. In this case the reaction of the above hydrazine with aniline in the presence of ether or ether-dioxane recovered a starting material. Furthermore, aniline was added in small portions to a cooled yellow mixture of benzoic acid hydrazide[9] (I : $R=C_6H_5-$) and chloral (1.2 moles), giving the same amide as above in 72.48% yield. Following derivation of the above carboxylic acid hydrazide to amide, the latter reaction was carried out in the aromatic and aliphatic carboxylic acid hydrazides as is shown in Table I and Ⅱ. That is, the reaction of the hydrazide (I) with amine in the presence of chloral was held without taking out the hydrazine (Ⅲ).

Perhaps the simplest mechanism to explain the formation of Ⅵ would initially involve condensation of hydrazide (I) and chloral (Ⅱ) to yield Ⅲ. In the presence of a large amount of amines, amidolysis would lead to Ⅵ and V, the latter of which would decompose immediately as in case of esterification.[2,3] A detailed mechanism is under examination.



$$\underset{\text{III}}{R-CO-NH-N{=}CH-CCl_3} \xrightarrow{R'NH_2} \left[R-\overset{\overset{O-H}{|}}{\underset{\underset{NHR'}{|}}{C}}-NH-N{=}CHCCl_3 \right] \longrightarrow \underset{\text{VI}}{RCONHR'} + \underset{\text{V}}{\left[H_2N-N{=}CH-CCl_3 \right]}$$

$R=C_6H_5-$, $C_6H_5CH_2-$, $C_6H_5CH_2CH_2-$, $CH_3(CH_2)_n$ ($n=1\sim4$)
$R =C_6H_5-$, $C_6H_5CH_2-$, $C_6H_5CH_2CH_2-$, $C_6H_{11}-$, C_4H_9-, $C_6H_{13}-$

In case of aliphatic acid hydrazide, for example, propionic and butyric acid hydrazide, the heat formation was so hard that an admixture of hydrazide with chloral must be held carefully. If not, a large amount of resinous substance formed and the yield of amides decreased. Furthermore, the addition of amines, for instance, butylamine and benzylamine, to a mixture of the hydrazide and chloral must be done very slowly in order to prevent from the formation of a black resinous substance by instantaneous reaction. On the other hand the heat formation during the dropwise addition in case of aniline was not recognized, but the reaction proceeded explosively when the cooled mixture was suddenly heated at 40~60°. Accordingly, careful treatment must be taken also in the above case.

The reaction time on heating in case of aromatic amines, for instance, aniline, benzylamine and phenethylamine, needed about three hours, but it took much time for the completion of the reaction in case of aliphatic amines, namely, butylamine, *n*-hexylamine and cyclohexylamine. Furthermore, the reaction of hydrazine (Ⅲ : $R=C_6H_5-$) with aniline in the presence of ether recovered a starting material as described

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Table I. The Reaction of the Aromatic Acid Hydrazides with Chloral in Various Amines[a]

Acid hydrazide	Hydrazide used (g.)	Chloral used (g.)	Amine used (ml.)		Time of reaction (hr.)	Yield of amide (%)	m.p. (℃)	b.p. (℃)
Benzoic acid hydrazide[9]	2	3	$C_6H_5NH_2$	30	3	72.48	159~161[b,8]	
	2	3	$C_6H_5CH_2NH_2$	30	5	20.93	104~106[12]	
	2	3	$C_6H_5CH_2CH_2NH_2$	30	5	40.79	114~115[13]	
	2	2.8	$C_6H_{11}NH_2$	40	4	11.72	147~149[14]	
	6	9	$C_4H_9NH_2$	60	12	21.77	37~38[b,4,5]	b.p$_{18\sim19}$ 185~188[5,6]
	6	9	$C_6H_{13}NH_2$	60	10	26.53	41~42[15]	
Phenylacetic acid hydrazide[10]	1.5	1.55	$C_6H_5NH_2$	30	4	45.02	114~115[16,17]	
	2	2.1	$C_6H_5CH_2NH_2$	40	4	68.33	120~121[18]	
	3	3.1	$C_6H_5CH_2CH_2NH_2$	30	4	61.71	91~93[19]	
	3	3.1	$C_6H_{11}NH_2$	30	9	19.58	134~135[20]	
	3	3.1	$C_4H_9NH_2$	30	9	22.25	52~53[21]	
	3	3.1	$C_6H_{13}NH_2$	40	4	76.46	53~54[c]	
Hydrocinnamic acid hydrazide[11]	3	3	$C_6H_5NH_2$	40	4.5	33.75	95~96[22]	
	3	3	$C_6H_5CH_2NH_2$	40	4.5	30.88	83~84[23,24]	
	3	3	$C_6H_5CH_2CH_2NH_2$	40	4.5	38.89	96~97[c]	
	5	5	$C_6H_{11}NH_2$	50	10	37.07	110~111[c]	
	5	5	$C_4H_9NH_2$	60	12	49.59	29~31	b.p$_{8\sim9}$ 184~185[6]
	5	5	$C_6H_{13}NH_2$	50	10	63.33	37~38.5[c]	b.p$_9$ 202~203

a) The reaction was done under reflux. *b*) The details were described in the experimental section as a typical example.
c) Since these compounds were unknown in the literature, the details were described in the experimental section.

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TABLE II. The Reaction of the Aliphatic Acid Hydrazides with Chloral in Various Amines[a]

Acid hydrazide	Hydrazide used (g.)	Chloral used (g.)	Amine used	(ml.)	Time of reaction (hr.)	Yield of amide (%)	m.p. (°C)	b.p. (°C)
Propionic acid hydrazide[25]	5	10	$C_6H_5NH_2$	40	4.5	12.27	103~104[c,28]	
	5	10	$C_6H_5CH_2NH_2$	40	4.5	56.18	46~47[23,24]	b.p$_{7\sim8}$ 151~153
	5	10	$C_6H_5CH_2CH_2NH_2$	40	4.5	46.30	49~51[29,30]	b.p$_{7\sim8}$ 154.5~156
	4.65	9.3	$C_6H_{11}NH_2$	40	3	29.30	89~90[28]	
	5	10	$C_4H_9NH_2$	28	4.5	53.14		b.p$_{12}$ 124~126[31,32]
	5	10	$C_6H_{13}NH_2$	40	6	65.00		b.p$_{7\sim8}$ 122~123.5[d]
Butyric acid hydrazide[26]	4	6.9	$C_6H_5NH_2$	40	3	39.88	94~95[33]	
	4	6.9	$C_6H_5CH_2NH_2$	40	3	51.86	46~48[6,23,24]	b.p$_9$ 168~170
	4	6.9	$C_6H_5CH_2CH_2NH_2$	40	3	49.39[b]	46~48[29,34]	b.p$_6$ 152~156
	1.9	3.5	$C_6H_{11}NH_2$	25	4	41.28	63~64[28,34,35]	
	8	13.8	$C_4H_9NH_2$	80	4	22.29		b.p$_{10}$ 137[32,34]
	5	8.65	$C_6H_{13}NH_2$	40	4	34.59		b.p$_5$ 135~138[34]
Valeric acid hydrazide[27]	2	2.8	$C_6H_5NH_2$	30	4	64.23[c]	60~61[36]	
	2	2.8	$C_6H_5CH_2NH_2$	30	4	54.32[a]	46~48[c,24,27]	
	4	5.6	$C_6H_5CH_2CH_2NH_2$	30	4.5	45.27	43~44[29]	
	2	2.8	$C_6H_{11}NH_2$	30	4.5	24.08[b]	65~67[29]	
	1.5	2.1	$C_4H_9NH_2$	30	5	34.48		b.p$_{13}$ 138~140[d]
	4.6	6.5	$C_6H_{13}NH_2$	70	4.5	38.10		b.p$_{13}$ 164~166[d]
Hexanoic acid hydrazide[27]	3	3.7	$C_6H_5NH_2$	30	4	71.47	94~95[38,39]	
	3	3.7	$C_6H_5CH_2NH_2$	30	4	64.47	50~51[24,37]	
	3	3.7	$C_6H_5CH_2CH_2NH_2$	30	4	33.64	38~41[d]	b.p$_6$ 170~172[d]
	5	7	$C_6H_{11}NH_2$	40	0.5	29.04	72~73	b.p$_{11}$ 148~150[d]
	5	7	$C_4H_9NH_2$	40	2	12.49		b.p$_{15}$ 164~165[d]
	5	7	$C_6H_{13}NH_2$	40	2	28.31		b.p$_{13}$ 168~170[d]

a) The reaction was done under reflux. *b*) Purified by alumina column chromatography.
c) The details were described in the experimental section as a typical example.
d) Since these compounds were unknown in the literature, the details were also described in the experimental section.

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above. These facts reveal that since the reaction temperature is low in case of the amine having a lower boiling point the yield would decrease.

Attempted amidation in case of dodecyl-, hexadecyl- and octadecylamine resulted in failure for the sake of difficulties in separation and removal of amines.

The authentic samples, which were used for the identification of amides, were prepared by Schotten-Baumann reaction of acid chloride with various amines in the presence of 10% sodium hydroxide solution.

Experimental*3

N-Phenylbenzamide——Aniline (30 ml.) was added dropwise to a cooled yellowish mixture of 2 g. of benzoic acid hydrazide[9] and 3 g. of chloral (1.2 moles). After being allowed to stand for a while, the mixture was heated under reflux in an oil-bath at 180° for 3 hr. The reaction mixture was acidified with conc. HCl solution and extracted with EtOAc. The extract was washed with 10% aq. HCl, 10% aq. NaOH solution and H_2O, and dried on Na_2SO_4. Removal of the solvent gave a pale brown residue, which was recrystallized from H_2O-EtOH to afford 2.1 g. (72.48%) of the amide as pale brown scales, m.p. 159~161°. This amide was identical with an authentic sample,[8] m.p. 161~162°, by mixed melting point test and infrared spectrum.

N-Butylbenzamide——A reddish-brown mixture of 6 g. of benzoic acid hydrazide, 9 g. of chloral (1.4 moles) and 60 ml. of butylamine was mildly warmed on a water-bath in order to dissolve all the crystals and then heated in an oil-bath at 100~120° for 12 hr. The above reaction mixture was treated with 240 ml. of H_2O, acidified with conc. HCl solution and extracted with EtOAc. The extract was washed with H_2O, dried on Na_2SO_4, and distilled *in vacuo* to give 2.8 g. of a pale yellow oil, b.p$_{8\sim9}$ 168~169°, which was dissolved in benzene, filtered in order to remove an insoluble substance*4 and chromatographed on alumina. Evaporation of 50 ml. of the first yellow eluate gave a syrup, which was distilled *in vacuo* to afford 1.7 g. (21.77%) of a pale yellow oil, b.p$_{18\sim19}$ 185~188° (b.p$_{0.5}$ 128°,[5] b.p$_{0.1}$ 125~137°[6]). The infrared spectrum was identical with that of an authentic sample, b.p$_{8\sim9}$ 167~167.5°, m.p. 37~38.5° (colorless needles) (m.p. 28°,[4] m.p. 39.5~40.5°[7]). *Anal.* Calcd. for $C_{11}H_{15}ON$: C, 74.54; H, 8.53; N, 7.90. Found : C, 74.56; H, 8.53; N, 7.87.

N-Hexylphenylacetamide——A mixture of 3 g. of phenylacetic acid hydrazide[10] 3.1 g. of chloral and 40 ml. of hexylamine was heated under reflux at 140~150°. The reaction mixture was extracted with benzene. The extract was washed with 10% aq. HCl and 10% NaOH solution, dried on Na_2SO_4 and distilled off, to give a solid, whose recrystallization from dil. EtOH and then hexane gave colorless scales, m.p. 53~54°. *Anal.* Calcd. for $C_{14}H_{21}ON$: C, 76.66; H, 9.65; N, 6.39. Found : C, 76.60; H, 9.64; N, 6.62.

N-(β-Phenethyl)hydrocinnamide——A mixture of 3 g. of hydrocinnamic acid hydrazide,[11] 3 g. (1.2 moles) of chloral and 40 ml. of β-phenethylamine was heated in an oil-bath at 190° for 4.5 hr. After the reaction mixture had been treated as usual, recrystallization of the resultant product from benzene-hexane gave 1.8 g. (38.89%) of the amide as pale yellow needles, m.p. 96~97°, which was identical with an authentic sample, m.p. 97~98° (colorless scales from EtOH) by mixed melting point test and infrared spectrum. *Anal.* Calcd. for $C_{17}H_{19}ON$: C, 80.57; H, 7.56; N, 5.53. Found : C, 80.73; H, 7.39; N, 5.51.

N-Cyclohexylhydrocinnamide——A mixture of 5 g. of the preceding hydrazide, 5 g. of chloral and 50 ml. of cyclohexylamine was heated at 170~180° for 10 hr. The reaction mixture was treated as usual and extracted with EtOAc. Removal of the solvent and recrystallization from EtOAc-petr. ether gave 2.6 g. (37.07%) of the amide as colorless needles, m.p. 110~111°, which was identical with an authentic sample. *Anal.* Calcd. for $C_{15}H_{21}ON$: C, 77.88; H, 9.15; N, 6.05. Found : C, 77.69; H, 9.32; N, 5.95.

N-Hexylhydrocinnamide——A mixture of the preceding hydrazide, 5 g. of chloral and 50 ml. of hexylamine was heated at 170~180° for 10 hr. The reaction mixture was treated as above and extracted with EtOAc. Distillation of the solvent gave a pale yellow oil, b.p$_9$ 202~203°, which solidified on cooling to give pale yellow needles, m.p. 37~38.5°. This was identical with an authentic sample, b.p$_9$ 106~107°, m.p. 37~38° (colorless needles). *Anal.* Calcd. for $C_{15}H_{23}ON$: C, 77.20 ; H, 9.94 ; N, 6.00. Found : C, 76.69; H, 9.75; N, 5.72.

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*3 Melting points were not corrected.

*4 This formed colorless scales, m.p. 148~150°, which was different from benzoic acid hydrazide (m.p. 116~117°) and 1,2-bisbenzoylhydrazine (m.p. 237~239°), but the structure of this compound was not recognized.

N-Phenylpropionamide——Aniline (40 ml.) was added dropwise to a cooled yellow mixture, which was obtained by mixing 5 g. of propionic acid hydrazide[25] with 10 g. (1.2 moles) of chloral on cooling. In this case addition of aniline must be held very carefully in order to avoid a severe heat formation. After the mixture had been allowed to stand at room temperature for a while, it was heated in an oil-bath at 150~160° for 4.5 hr. The reaction mixture was decomposed with 400 ml. of H_2O, acidified with conc. HCl solution and extracted with benzene. Filtration and removal of the solvent gave a pale brown solid, which was recrystallized from benzene to afford 1.9 g. (12.27%) of the amide as pale yellow needles, m.p. 103~104°. This was identical with an authentic sample,[28] m.p. 103°.

N-Hexylpropionamide——After a mixture of 5 g. of the preceding hydrazide, 10 g. of chloral and 40 ml. of hexylamine had been warmed for a while on a water-bath and no heat formation recognized, the mixture was heated under reflux at 150~160° for 6 hr. The reaction mixture was decomposed with 400 ml. of H_2O, acidified with conc. HCl solution and extracted with benzene. Removal of the extract and distillation *in vacuo* gave 5.8 g. (65.0%) of amide as a colorless oil, b.p$_{7\sim8}$ 122~123.5°, whose infrared spectrum was identical with that of an authentic sample, b.p$_{9\sim10}$ 134~134.5°. *Anal.* Calcd. for $C_9H_{19}ON$: C, 68.74; H, 12.18; N, 8.91. Found : C, 68.23; H, 12.20; N, 8.79.

N-Benzylvaleramide——A mixture of 2 g. of valeric acid hydrazide,[27] 2.8 g. of chloral and 30 ml. of benzylamine was heated in an oil-bath at 180° for 4 hr. After treatment as usual, the benzene extract was condensed, chromatographed on alumina and removal of the benzene eluate gave the amide as a brown residue, which was recrystallized from hexane to give 1.77 g. (54.32%) of pale yellow needles, m.p. 46~48° (m.p. 42~43°,[24] m.p. 41.1~41.8°[15])). This compound was identical with an authentic sample on mixed melting point test and infrared spectrum. *Anal.* Calcd. for $C_{12}H_{17}ON$: C, 75.35; H, 8.96; N, 7.32. Found : C, 75.61; H, 9.05; N, 7.39.

N-Butylvaleramide——After a mixture of 1.5 g. of the preceding hydrazide, 2.1 g. of chloral and 30 ml. of butylamine was allowed to stand at room temperature overnight and then refluxed in an oil-bath at 95~100° for 5 hr. After treatment as usual, removal of the benzene extract and distillation *in vacuo* gave 0.7 g. (34.4%) of a colorless oil, b.p$_{13}$ 138~140°, whose infrared spectrum was identical with that of an authentic sample, b.p$_{11}$ 136~138°. *Anal.* Calcd. for $C_9H_{19}ON$: C, 68.74; H, 12.18; N, 8.91. Found : C, 69.02; H, 12.26; N, 8.68.

N-Hexylvaleramide——A mixture of 4.6 g of the preceding hydrazide, 6.5 g. of chloral and 70 ml. of hexylamine was refluxed in an oil-bath at 120~130° for 4.5 hr. The reaction mixture was treated as usual and extracted with benzene. Removal of the solvent and distillation *in vacuo* gave a colorless oil, b.p$_{13}$ 164~166°, whose infrared spectrum was identical with that of an authentic sample, b.p$_9$ 150~151°. *Anal.* Calcd. for $C_{11}H_{23}ON$: C, 71.30; H, 12.51; N, 7.56. Found : C, 69.89; H, 12.37; N, 7.35.

N-(β-Phenethyl)hexanamide——β-Phenethylamine (30 ml.) was added dropwise to a cooled mixture of 3 g. of hexanoic acid hydrazide[27] and 3.7 g. (1.2 moles) of chloral. After being allowed to stand at room temperature for a while, the mixture was heated in an oil-bath at 160~180° for 4 hr. After treatment as usual, distillation *in vacuo* of the benzene extract gave 1.7 g. (33.64%) of a colorless oil, b.p$_6$ 170~172°, which solidified on cooling to afford colorless needles, m.p. 38~41°. The infrared spectrum of this amide was superimposable on that of an authentic sample. *Anal.* Calcd. for $C_{14}H_{21}ON$: C, 76.66; H, 9.65; N, 6.39. Found : C, 76.38; H, 9.50; N, 6.51.

N-Cyclohexylhexanamide——A mixture of 5 g. of the preceding hydrazide, 7 g. of chloral and 40 ml. of cyclohexylamine was refluxed at 150°. The same treatment as above of the reaction mixture and distillation of the resultant residue gave 14.15 g. of a yellowish brown oil, b.p$_{12}$ 148~150°, which was dissolved in benzene. The solvent layer was washed with 10% aq. NaOH and $NaHCO_3$ solution. Removal of the solvent and distillation of the residue afforded 2.2 g. (29.04%) of a colorless oil, b.p$_{11}$ 148.5~150°, which solidified on cooling to yield colorless needles, m.p. 72~73°. This compound was identical with an authentic sample, m.p. 73~74°, by mixed melting point test and infrared spectrum. *Anal.* Calcd. for $C_{12}H_{23}ON$: C, 73.04; H, 11.75; N, 7.10. Found : C, 73.12; H, 11.65; N, 6.95.

N-Butylhexanamide——After a mixture of 5 g. of the preceding hydrazide, 7 g. of chloral and 40 ml. of butylamine had been heated at 170° for 2 hr. and treated as above, distillation *in vacuo* of the resultant product gave 2.1 g. of a colorless oil, b.p$_{12}$ 100~138°, which was dissolved in a small amount of benzene. The benzene extract was washed with 10% aq. HCl and $NaHCO_3$ solution and evaporated. Distillation *in vacuo* of the above residue gave 0.85 g. (12.49%) of a colorless oil, b.p$_{15}$ 164~165°, whose infrared spectrum was identical with an authentic sample, b.p$_{24}$ 172.5~173°. *Anal.* Calcd. for $C_{10}H_{21}ON$: C, 70.12; H, 12.36; N, 8.18. Found : C, 69.93; H, 12.30; N, 7.93.

N-Hexylhexanamide——After a mixture of 5 g. of the preceding hydrazide, 7 g. of chloral and 40 ml. of hexylamine had been refluxed at 170° for 2 hr., the reaction was treated as usual and extracted with benzene. Removal of the solvent and distillation *in vacuo* of the residue gave 5.9 g. of colorless oil, b.p$_{12}$ 110~145°, which was dissolved in a small amount of benzene, washed with 10% aq. HCl and $NaHCO_3$ solution, and evaporated. Redistillation of the above residue gave 2.17 g. (28.31%) of the amide as a colorless oil, b.p$_{13}$ 168~170°, whose infrared spectrum was identical with that of an authentic sample, b.p$_{20}$ 191°. *Anal.* Calcd. for $C_{12}H_{25}ON$: C, 72.30; H, 12.64; N, 7.03. Found : C, 72.10; H, 12.71 ; N, 7.25.

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Summary

In the previous papers the reactions between aromatic, aliphatic and heterocyclic carboxylic acid hydrazides and either chloral or bromal in various alcohols were attempted and respective esters were obtained. In this paper the reactions of aromatic and aliphatic acid hydrazide with chloral in the presence of various amines were examined, leading eventually to reveal the formation of our expected acid amides as are shown in Table I and Ⅱ. The intermediates in this reaction, 1-benzoyl-2-(2,2,2-trichloroethylidene) hydrazine (Ⅲ : $R=C_6H_5-$, $X=Cl$) was found to form the amides (Ⅵ) when heated in amines. This fact indicated that the acid hydrazides converted to their amides through Ⅲ.

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52. **Shirō Takahashi and Hideo Kanō** : Benzimidazole N-Oxides. VI.[*1] Reaction of 3-Methoxy-1-methyl- and 1,2-dimethylbenzimidazolium Iodide with Various Nucleophiles.

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The chemistry of N-alkoxy quaternary salts of pyridine and its related systems has been studied by several workers in recent years.1) In almost all the reactions reported, the formation of diverse products is best understood as resulting from various nucleophilic attacks on the quaternary salts *via* the following four courses (Chart 1).

The reaction of the quaternary salts with each of cyanide ion,2) Grignard reagents3) and some of ketones4) has been shown to yield the corresponding α- or α- and γ-substituted compound (course A). In some of these reactions, the decomposition *via* course C occurs concurrently. The reaction of 1-alkoxy-3- and 4-picolinium salts with thiophenoxide ions proceeds *via* course B, giving the corresponding arylmercaptomethylpyridines.5) When the quaternary salts are treated with alkali, the parent bases and an aldehyde are produced6) (course C). N-Alkoxypyridinium halides decompose gradual-

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