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Indoles. II.[1] Oxidation of N-Phthaloyl-l-acetyltryptophan with Chromium Trioxide

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Oxidation of N-phthaloyl-l-acetyltryptophan (**1**) with chromium trioxide afforded the kynurenine derivative (**4**) in 35% yield and the dioxindole lactone (**6**) in 20% yield. The latter substance was separated into the two epimers (**6a** and **6b**) and their configuration was examined.

N-Bromosuccinimide (NBS) in *tert*-butanol converted N-phthaloyltryptophan (**7**) to the corresponding oxindole (**9**) in 51% yield when a 1:1 mole ratio of NBS to indole was used. When a 2:1 ratio of reactants was used and its products were treated with sodium hydrogen carbonate, the dioxindole lactone (**8**) was obtained, and acetylation of **8** afforded **6** that agreed with the oxidation product.

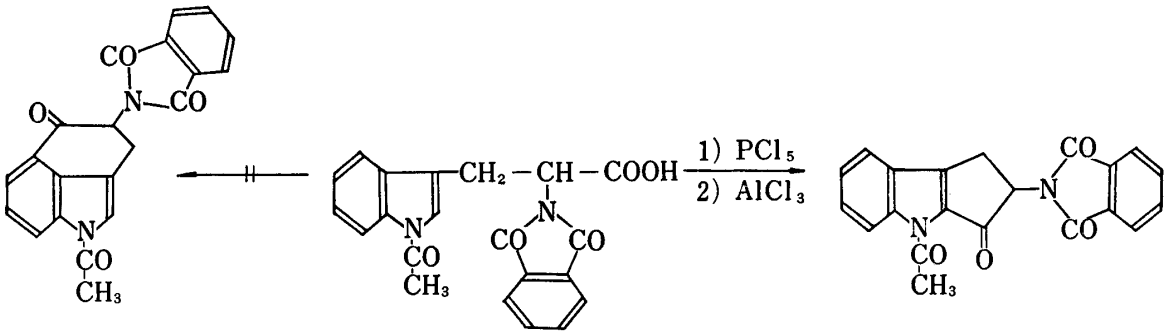
The mass spectra of **8** and **9** are discussed.

In a preceding work of this series,[1] 1-acetyltryptophan and its derivatives were synthesized in order to obtain compounds related to lysergic acid and their Friedel–Crafts reaction was examined. According to Szmuszkovicz's report,[3] Friedel–Crafts reaction of N-phthaloyl-1-acetyltryptophan (**1**) should give a product (**2**) cyclized to the 4-position of the indole ring but, unexpectedly, a compound (**3**) cyclized selectively to the 2-position was obtained (Chart 1). However, the decreased nucleophilic activity of 2-position in these compounds was confirmed from their reaction with *o*-nitrophenylsulfenyl chloride.[1]

In the present series of work, examinations were made on the oxidation of **1** which constitutes subject of this paper.

Tryptophan is known to be easily oxidized by oxidation agents like periodic acid,[4] persulfate,[5] permanganate,[6] chromic acid,[7] peroxide,[8] iodine,[9] peracid,[10] selenium dioxide,[11] and ozone,[12] but the reaction is complicated and examples are rare for efficient isolation of the products.[10,12] Atkinson and others[13] found that the oxidation of indole compounds with chromium trioxide resulted in a markedly increased yield when their 1-position is acetyl-

1) Part I: S. Ohki and T. Nagasaka, *Chem. Pharm. Bull.* (Tokyo), **19**, 545 (1971).
2) Location: *Ueno Sakuragi*-1-chome, *Taito-ku*, *Tokyo*.
3) J. Szmuszkovicz, *J. Org. Chem.*, **29**, 843 (1964).
4) K. Arakawa, *J. Biochem.* (Tokyo), **44**, 217 (1957); J. R. Clamp and L. Hough, *Biochem. J.*, **94**, 17 (1965).
5) E. Boyland, P. Sims, and D. C. Williams, *Biochem. J.*, **62**, 546 (1956).
6) W. J. Haas, I. W. Sizer, and J. R. Loofbourow, *Biochim. Biophys. Acta*, **6**, 601 (1951); O. G. Pokrovskaya, *Tr. Novosib. Med. Inst.*, 33, 162 (1959).
7) J. García-Blanco and A. M. Pascual-Leone, *Rev. Espan. Fisiol.*, **11**, 143 (1955) [*C. A.*, **50**, 4702a (1956)].
8) B. C. Kar, *J. Indian Chem. Soc.*, **14**, 291 (1937); G. Toennies and R. P. Homiller, *J. Am. Chem. Soc.*, **64**, 3054 (1942); Y. Hachimori, H. Horinishi, K. Kurihara and K. Shibata, *Biochim. Biophys. Acta*, **93**, 346 (1964).
9) F. J. Hartdegen and J. A. Rupley, *Biochim. Biophys. Acta*, **92**, 625 (1964).
10) C. A. Benassi, E. Scoffone, and F. M. veronese, *Tetrahedron Letters*, **1965**, 4389.
11) E. Neuzil, M. Labadie, and J. C. Breton, *Bull. Soc. Pharm. Bordeaux.*, **104**, 200 (1965) [*C. A.*, **65**, 13816h (1966)].
12) *a*) B. Witkop and G. Graser, *Ann.*, **556**, 103 (1944); *b*) J. L. Warnell and C. P. Berg, *J. Am. Chem. Soc.*, **76**, 1708 (1954); *c*) A. Previero, E. Scoffone, P. Pajetta, and C. A. Benassi, *Gazz. Chim. Ital.*, **93**, 849 (1963).
13) C. M. Atkinson, J. C. E. Simpson, and A. Taylor, *J. Chem. Soc.*, **1954**, 165.

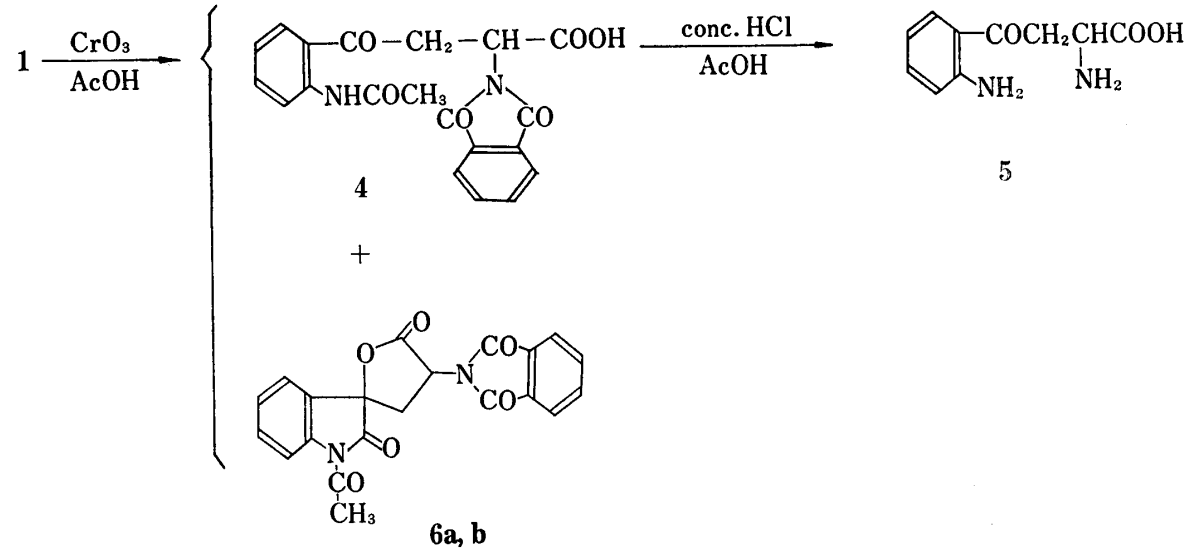


2 1 3

Chart 1

ated. Therefore, oxidation of **1** and N-phthaloyltryptophan (**7**) with chromium trioxide was compared.

Oxidation of **7** with chromium trioxide in acetic acid failed to give any crystalline substance but oxidation of its acetylated compound (**1**) under the same condition afforded colorless prisms, mp 237—238° (decomp.) in 35% yield and a neutral substance of mp 228—233° (decomp.) in 20% yield. The analytical values of the former product corresponded to $C_{20}H_{16}O_6N_2$, its infrared (IR) spectrum exhibited absorption for OH group in its carboxyl at 3000—2200 cm^{-1}, and its nuclear magnetic resonance (NMR) spectrum (in trifluoroacetic acid) had signals at 7.51 τ (singlet, 3H, $COCH_3$), 5.91 τ (singlet, 1H, NH), 5.90 τ (octet, 2H, CH_2), 6.03 τ (quartet, 1H), 1.80—2.60 τ (multiplet, aromatic protons), and 1.70 τ (doublet, 1H), indicating that the product is the expected kynurenine derivative (**4**) (Chart 2). Hydrolysis of **4** with conc. hydrochloric acid in acetic acid gave a product whose sulfate was identified with the sulfate of kynurenine (**5**), obtained by ozonolysis of N-acetyltryptophan by the method of Warnell and Berg.[12b] This proved that the said product is Nα-phthaloyl-N-acetylkynurenine (**4**).



4 5 6a, b

Chart 2

The latter neutral substance was found to be approximately equal mixture of two substances from the measurement of NMR spectrum (in $CHCl_3$). This mixture was therefore submitted to silica gel chromatography and elution with chloroform successfully separated the product into two kinds of crystals; one of fine needles (**6a**), mp 250° (decomp.), and the

other of prisms (**6b**), mp 235°. Both corresponded to analytical values of $C_{21}H_{14}O_6N_2$, and they showed only a slight difference in the finger-print region in their IR spectra. These were therefore considered to be epimers. The NMR spectra of these substances are shown in Fig. 1 and 2.

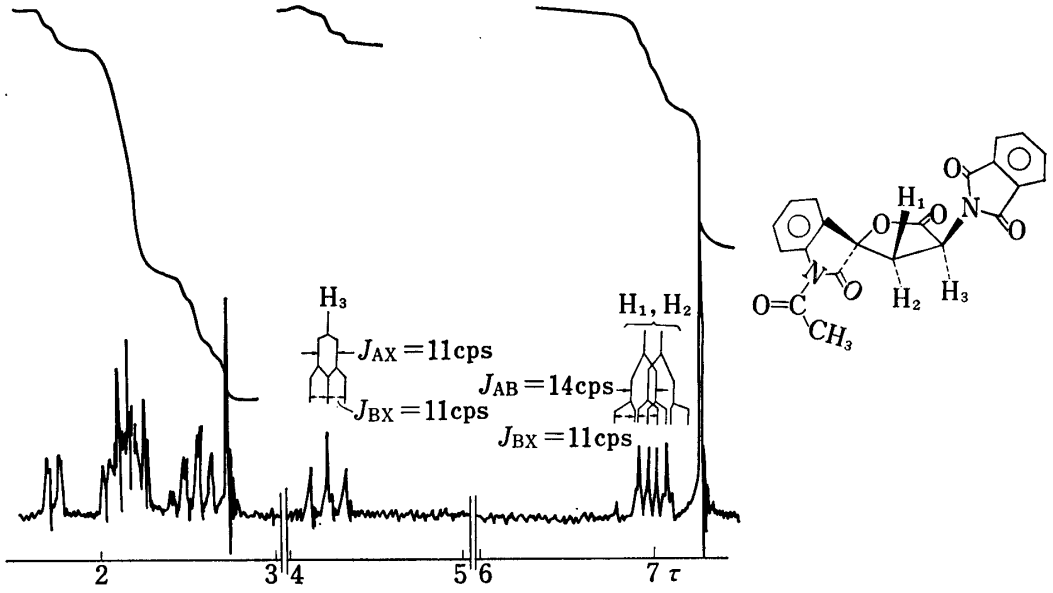


Fig. 1. NMR Spectrum of **6a** in $CDCl_3$

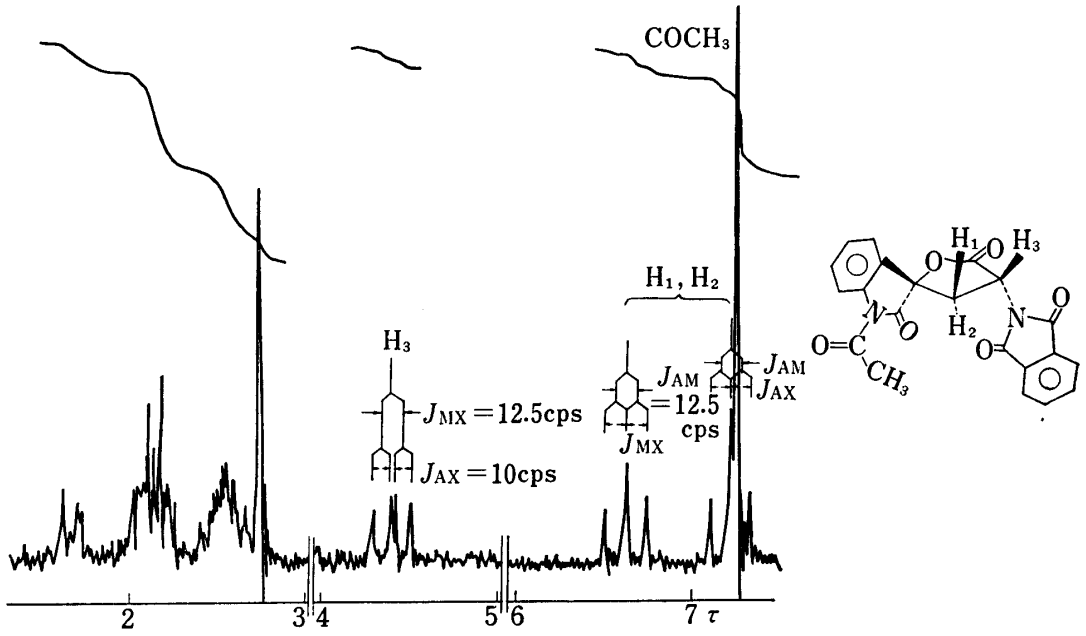


Fig. 2. NMR Spectrum of **6b** in $CDCl_3$

It has been reported that the reaction of indole-3-propionic acid with 2 moles of N-bromosuccinimide and treatment of its product with sodium hydrogen carbonate affords dioxindole lactone.[14] Therefore, **7** was reacted with 2 moles of N-bromosuccinimide in *tert*-butanol and treated with sodium hydrogen carbonate. The product thereby obtained was acetylated with acetic anhydride and chromatographic purification of its product afforded two kind of

14) *a*) W. B. Lawson, A. Patchornik, and B. Witkop, *J. Am. Chem. Soc.*, **82**, 5918 (1960); *b*) R. L. Hinman and C. P. Bauman, *J. Org. Chem.*, **29**, 1206 (1964).

crystals in a good yield. These products agreed completely with **6a** and **6b** (Chart 3). In this case, **6a** and **6b** were obtained respectively *via* **8a** and **8b**, and this fact proves that the neutral substance obtained from the oxidation of **1** with chromium trioxide is 1-acetyldioxindole-3-(α-phthalimido)propionic acid lactone (**6**) in Chart 2.

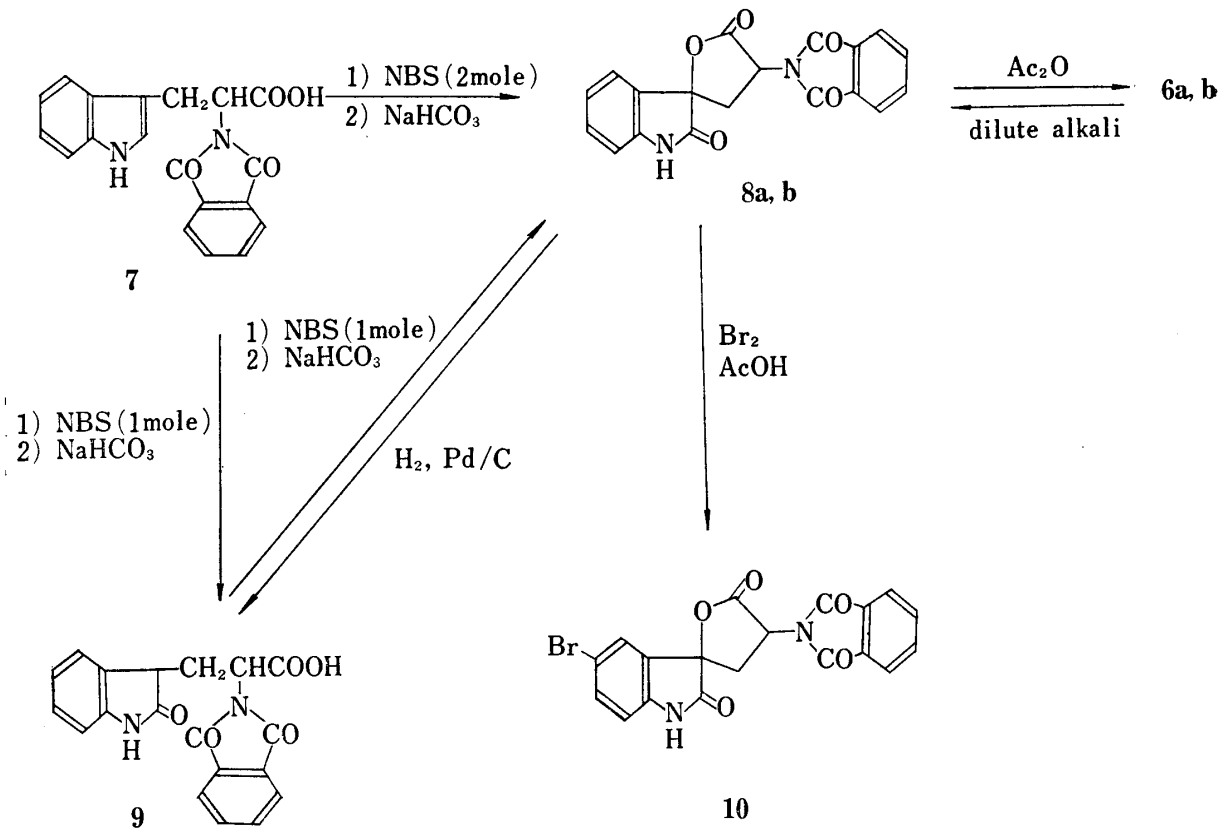


Chart 3

The reaction whereby spirolactone (**8**) is formed from **7** would probably give a different product according to the amount of N-bromosuccinimide used[14,15] and this point was examined. One mole of N-bromosuccinimide was reacted with **7** in *tert*-butanol, the product was treated with alkali, and **9** was obtained in *ca.* 51% yield, together with **8** in 16% yield. Similar reaction of **9** with 1 mole of N-bromosuccinimide afforded **8** in 62% yield, with **10** in 12% yield. Bromination of **8** with bromine in acetic acid afforded **10** in 90% yield but **10** resisted further bromination, the starting material being recovered. Catalytic reduction of **8** over palladium-carbon gave **9** in 7.5% yield. This low yield of the product is rather unexpected since Witkop and others[14a,15] obtained oxindole-3-propionic acid in a good yield by the application of 3 moles of N-bromosuccinimide to indole-3-propionic acid and subsequent catalytic reduction of its product.

Oxidation of tryptophan to 2-oxotryptophan is generally in a low yield[16] and the best yield obtained to date was 14% (based on unrecovered starting material) of N-acetyl-2-oxotryptophan by the application of N-bromosuccinimide to N-acetyltryptophan.[14b] The good yield of **9** from N-phthaloyltryptophan (**7**) is probably due to the difficult occurrence of farther reaction to the eserine type compound.[17]

15) W. B. Lawson and B. Witkop, *J. Org. Chem.*, **26**, 263 (1961).
16) B. Witkop, *Ann.*, **558**, 98 (1947); T. Wieland, O. Weiberg, and W. Dilger, *Ann.*, **592**, 69 (1955); K. Freter, H. Weissbach, B. Redfield, S. Udenfriend, and B. Witkop, *J. Am. Chem. Soc.*, **80**, 983 (1958).
17) M. Ohno, J. F. Spande, and W. Witkop, *J. Am. Chem. Soc.*, **92**, 343 (1970).

Acetylation of **9** with acetic anhydride and sodium acetate affords, besides an acid substance, a neutral substance in 20% yield. This latter substance melts at 139°, its analytical values correspond to $C_{14}H_{13}O_4N$, its IR spectrum exhibits absorptions at 1776, 1748, and 1706 cm^{-1}, and its NMR spectrum (in $CDCl_3$) shows signals at 7.60 τ (singlet, 3H), 7.32 τ (singlet, 3H), and 7.30 τ (singlet, 3H). Since these data agreed entirely with those for **11** reported in literature,[18] this product was identified with a authentic sample through IR spectra and admixture (Chart 4). Substitution of the alkyl group in 3-position of oxindole ring with an acyl group is rather rare but, considering the fragmentation reaction of the side chain, its mechanism may be assumed as follows:

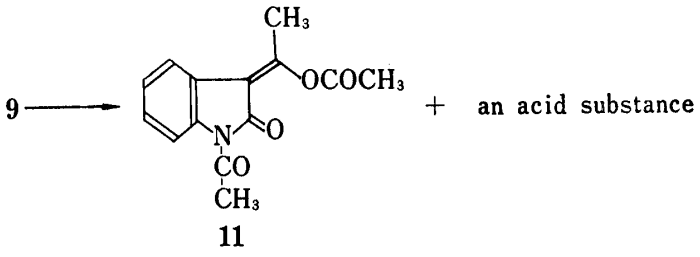


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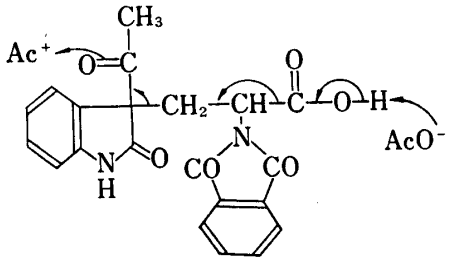
Chart 4



Chemical structure of the acid substance is now being examined.

The configuration of the two epimers, **6a** and **6b**, was considered as follows. When **6a** and **6b** are each warmed for 1 hr with 5% hydrochloric acid in acetic acid, both are quantitatively deacetylated to **8a**, mp 265—268° (decomp.), and a mixture of **8a** and **8b**, mp 220—262° (decomp.), respectively. Because thin-layer chromatography over alumina and elution with chloroform showed the latter to form two spots containing **8a** and **8b**, and comparison of NMR spectra also indicated that the latter contains **8a** and **8b** (Fig. 3 and 4). Further warming of a mixture of **8a** and **8b** with 5% hydrochloric acid in acetic acid for 5 hr in a water bath and thin-layer chromatography of the product showed the same spot for **8a**, and NMR

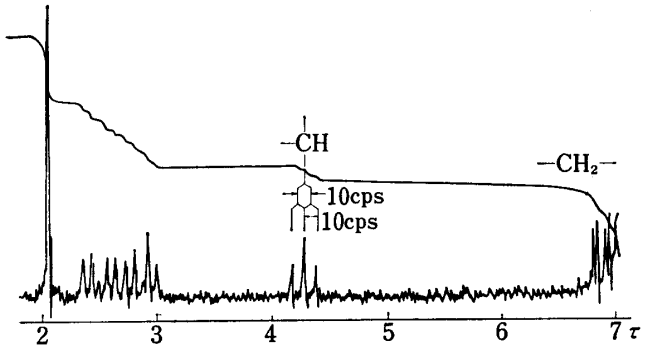


Fig. 3. NMR Spectrum of **8a** in d_6-Acetone

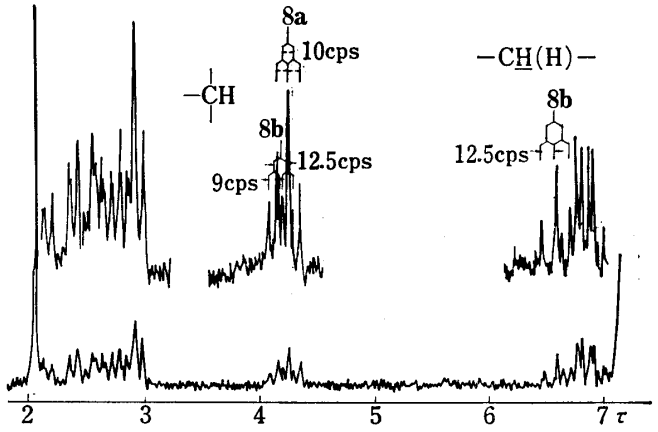


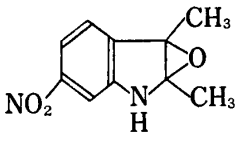
Fig. 4. NMR Spectrum of a Mixture of **8a** and **8b** in d_6-Acetone

18) T. Kato, H. Ichikawa, and M. Okita, *Yakugaku Zasshi*, **87**, 986 (1967).

spectrum of the isolated substance was entirely identical with that of **8a**. It is considered that the less stable **8b** underwent isomerization to **8a** under hydrolytic condition.

Comparison of the NMR spectra of **6a** and **6b** (Fig. 1 and 2) showed that the signal for methin proton in **6a** appeared in a lower magnetic field than that of **6b** by 0.15 ppm. Since the methin proton in the same plane as the carbonyl group in oxindole is considered to be under the strong anisotropic effect, it is assumed that the carbonyl group in oxindole and phthalimide are in *trans* with respect to the lactone ring in **6a**, while these groups will be in *cis* configuration in **6b**. There is still a problem in the conformation of the spirolactone but, considering its molecular model, the more stable type is the *trans* which fact supports the assumption made from the NMR data.

There has been no example, as far as is known, of the direct formation of oxindole compound from indole by oxidation with chromium trioxide. Further oxidation of **6** with chromium trioxide in acetic acid does not give **4** and the starting material is recovered so that **6** could not be an intermediate for kynurenine. Atkinson and others[13] carried out oxidation of 2,3-dimethyl-6-nitro-oxindole with chromium trioxide and obtained 2,3-epoxy-2,3-dimethyl-6-nitroindole (**12**). If this kind of an epoxide compound were to exist as an intermediate in 1-acetylindole compounds, formation mechanism shown in Chart 5 might be considered.



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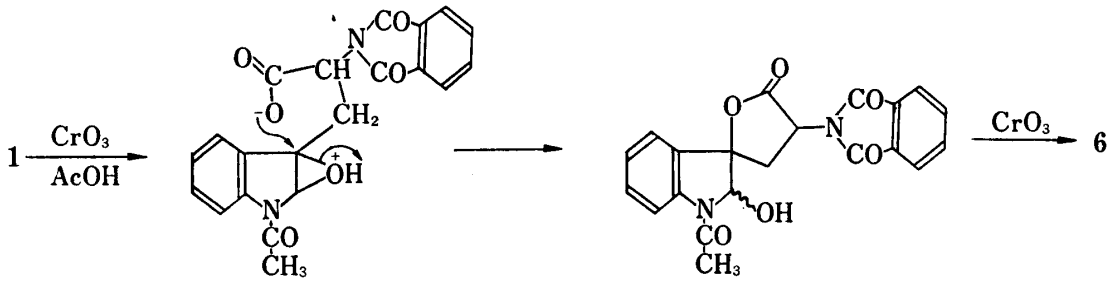


Chart 5

Mass Spectra of 8 and 9

The mass spectrum of **9** exhibits M^+ and simply fragmented ion peaks at *m/e* 132, 146, and 305, and strong signals of fragments at *m/e* 133 and 205 due to McLafferty transition,

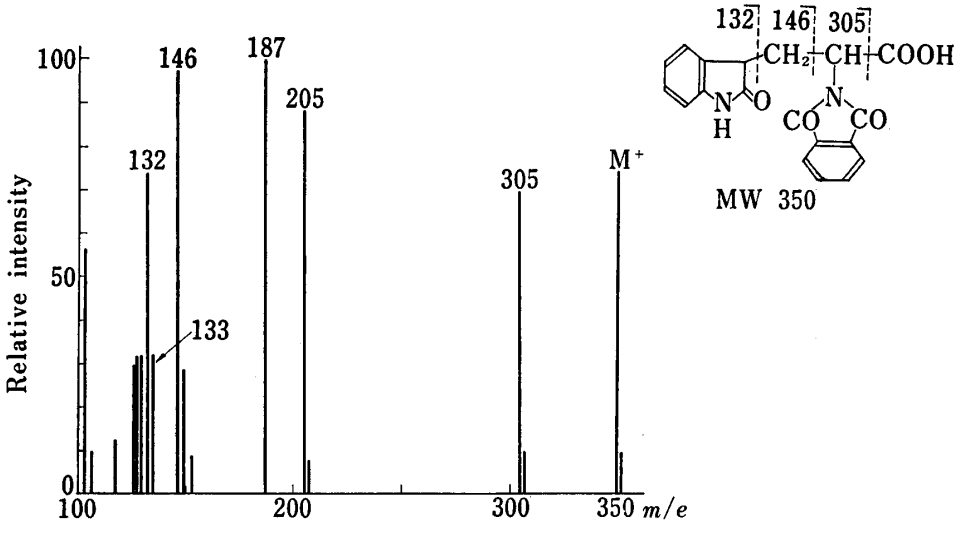
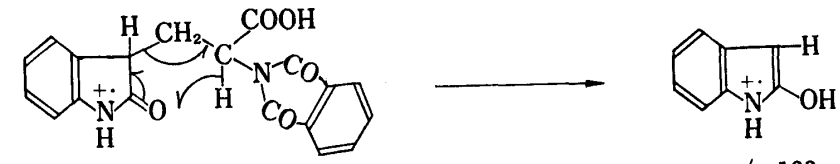


Fig. 5. Mass Spectrum of **9**



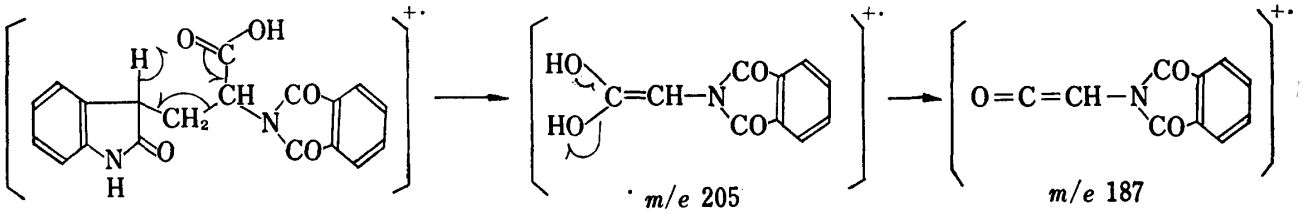


Chart 6

with a base peak at *m/e* 187 (Chart 6 and Fig. 5). The composition of main ion peak of **8** by high-resolving mass spectrum is shown in Table I. **8** shows a strong M^+ ion with a base peak at *m/e* 304 (M^+-CO_2) (Fig. 6). Liberation of carbon dioxide can be produced from the phthalimido group[19a] and the lactone[19b] but, since the decarboxylation peak is weak in **9**, it is considered to be due to the lactone cyclized in a spiro type. Main fragments may be considered to be those shown in Chart 7. The signal at *m/e* 330 (M^+-H_2O) is rather unexpected but there is a report of the loss of water from the peak of **13**.[20]

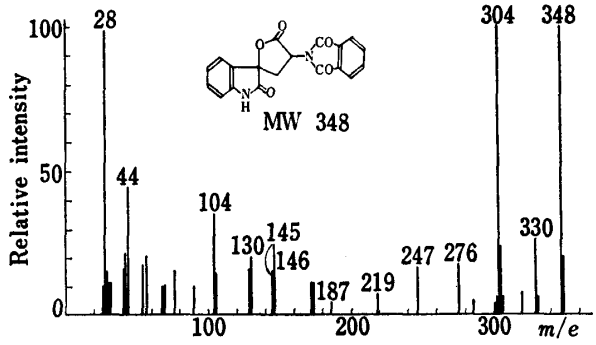
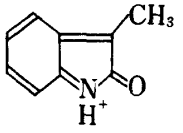


Fig. 6. Mass Spectrum of **8**



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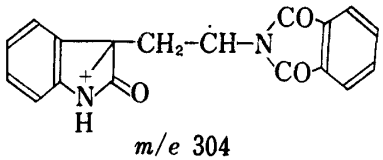
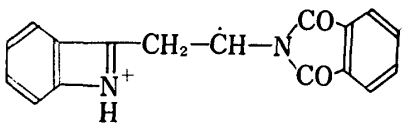
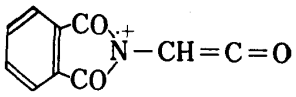


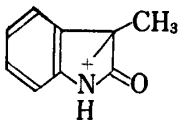
m/e 304



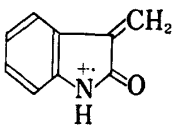
m/e 276



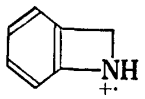
m/e 187



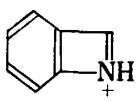
m/e 146



m/e 145



m/e 105



m/e 104

Chart 7

19) *a*) H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Mass Spectrometry of Organic Compounds," Holden-Day, Inc., 1967, p. 364; *b*) *Ibid.*, p. 206.
20) J. C. Powers, *J. Org. Chem.*, 33, 2044 (1968).

Table I. The Composition of Main Ion Peak of **8** by High-Resolving Mass Spectrum

Observed (*m/e*)	Calculated	Observed (*m/e*)	Calculated
348.0708	348.0746 ($C_{19}H_{12}O_5N_2$)	219.0898	219.0923 ($C_{15}H_{11}N_2$)
330.0618	330.0641 ($C_{19}H_{10}O_4N_2$)	187.0286	187.0270 ($C_{10}H_5O_3N$)
304.0873	304.0849 ($C_{18}H_{12}O_3N_2$)	146.0599	146.0606 (C_9H_8ON)
276.0887	276.0899 ($C_{17}H_{12}O_2N_2$)	145.0999	145.0529 (C_9H_7ON)
247.0843	247.0873 ($C_{16}H_{11}ON_2$)	130.0627	130.0659 (C_9H_8N)

Experimental [21]

Oxidation of N-Phthaloyl-l-acetyltryptophan (1) with Chromium Trioxide——To a solution of **1** (3.0 g, 8×10^{-3} mole) in AcOH (60 ml), AcOH solution (30 ml) containing CrO_3 (2.4 g, 2.4×10^{-2} mole) was added under cooling, and the solution was stirred for 40 hr at room temperature. H_2O (200 ml) was added to the reaction mixture and separated material was extracted several times with $CHCl_3$ (300 ml). $CHCl_3$ solution was extracted with saturated $NaHCO_3$ (200 ml), washed with H_2O, dried over Na_2SO_4, and evaporated. Recrystallization of the residue from EtOH afforded 1-acetyldioxindole-3-(α-phthalimido) propionic acid lactone (**6**), as colorless crystals, mp 228—233° (decomp.). Yield, 620 mg (20%). The first fraction of chromatography (on silica gel–$CHCl_3$) afforded colorless fine needles (**6a**), mp 250° (decomp.) (from $CHCl_3$–EtOH). *Anal.* Calcd. for $C_{21}H_{14}O_6N_2$: C, 64.61; H, 3.62; N, 7.18. Found: C, 64.35; H, 3.63; N, 7.04. IR ν_{max}^{KBr} cm^{-1}: 1800, 1775, 1725.

The second fraction afforded colorless prisms (**6b**), mp 235° (decomp.) (from $CHCl_3$–EtOH). *Anal.* Calcd. for $C_{21}H_{14}O_6N_2$: C, 64.61; H, 3.62; N, 7.18. Found: C, 65.10; H, 3.71; N, 7.49. IR ν_{max}^{KBr} cm^{-1}: 1800, 1775, 1725.

The $NaHCO_3$ solution was acidified with 5% HCl, resulting white crystals were collected, and the filtrate was extracted with $CHCl_3$ (100 ml). The extract was washed with H_2O, dried over Na_2SO_4, and evaporated to afford white crystals. Recrystallization of the combined white crystals from MeOH afforded Nα-phthaloyl-N-acetylkynurenine (**4**) as colorless prisms, mp 237—238° (decomp.) Yield, 1.05 g (35%). *Anal.* Calcd. for $C_{20}H_{16}O_6N_2$: C, 63.15; H, 4.24; N, 7.35. Found: C, 63.14; H, 4.55; N,7.32. UV λ_{max}^{EtOH} mμ: 228, 260, 268. IR ν_{max}^{KBr} cm^{-1}: 3000—2200, 1720, 1650, 785, 760, 720.

Kynurenine (5)——A solution of AcOH (5 ml) and conc. HCl (2 ml) containing **4** (500 mg, 1.3×10^{-3} mole) was left for 2 hr in a boiling water bath. Conc. HCl (2 ml) was added and further warmed under the same condition for 2 hr. After the solvent was evaporated *in vacuo*, the residue was extracted with a small quantity of H_2O and conc. H_2SO_4 (100 mg) was added to the H_2O extract. The extract was evaporated to dryness *in vacuo*. Recrystal lization of the residual white solid from EtOH containing one drop of conc. H_2SO_4 afforded colorless needles, mp 170° (yield, 170 mg, 40%), which was identified through IR spectra, UV spectra, and admixture with the sample prepared from N-acetyltryptophan.[12b]

Hydrolysis of 6a and 6b——A solution of AcOH (10 ml) and 5% HCl (4 ml) containing **6a** (60 mg) was left for 1 hr in a boiling water bath. The solvent was evaporated *in vacuo* and recrystallization of the residual white crystals fom MeOH afforded dioxindole-3-(α-phthalimido) propionic acid lactone (**8a**) as needles, mp 265—268° (decomp.). Yield, 40 mg (75%). *Anal.* Calcd. for $C_{19}H_{12}O_5N_2\cdot1/2H_2O$: C, 63.87; H, 3.67; N, 7.84. Found: C, 63.78; H, 3,86; N, 7.88. Mass Spectrum (Table I) *m/e*: 348.0708 (M^+) (Calcd. for $C_{19}H_{12}O_5N_2$; 348.0746). IR ν_{max}^{KBr} cm^{-1}: 3650, 1800, 1775, 1750, 1710. 1625. TLC (on alumina-$CHCl_3$): *Rf* 0.45.

By the procedure described above, colorless needles, mp 220—262° (decomp.) (from MeOH), were obtained quantitatively from **6b**. *Anal.* Calcd. for $C_{19}H_{12}O_5N_2\cdot1/2H_2O$:C, 63.87; H, 3.67; N, 7.84. Found: C, 63.70; H, 3.90; 7.70. This compounds showed two spots (*Rf* 0.45 and 0.33) containing **8a** and **8b** by thin-layer chromatography (on alumina–$CHCl_3$) and epimerized to **8a** completely on heating for 5 hr in a solution of AcOH and 5% HCl, since the obtained material was identified with **8a** through TLC, IR spectra, NMR spectra, and admixture.

Reaction of N-Phthaloyltryptophan (7) with 2 Moles of NBS——To a solution of **7** (334 mg, 10^{-3} mole) in *tert*-BuOH (30 ml), NBS (356 mg, 2×10^{-3} mole) was gradually added under stirring in a stream of N_2 and stirring was continued during 1.5 hr. The solvent was evaporated *in vacuo* at roomtemperature and the viscous residual oil was dissolved in EtOAc (30 ml). The EtOAc extract was washed with saturated $NaHCO_3$ (30 ml) and H_2O, dried over Na_2SO_4, and evaporated. Recrystallization of the residue from MeOH afforded colorless crystals (**8**), mp 240—265° (decomp.). Yield,316 mg (89%).

Acetylation of **8** (190 mg) with Ac_2O (3 ml) gave **6**, mp 245—250°(decomp.) (from $CHCl_3$–MeOH).

21) All melting points are uncorrected.

Yield, 192 mg (90%). **6** was separated into **6a** and **6b** by the method described above, and were respectivcly identified with the oxidation products of **1** through IR spectra, NMR spectra, and admixture.

Reaction of 7 with 1 Mole of NBS——By the procedure described above, **8**, mp 240—266° (yield, 164 mg, 16%), and oxindole-3-(α-phthalimido) propionic acid (**9**) were obtained from **7** (1.0 g, 3.0×10^{-3} mole) and NBS (530 mg, 3.0×10^{-3} mole). **9** occurs as colorless needles, mp 137—142° (from MeOH). Yield, 532 mg *Anal.* Calcd. for $C_{19}H_{14}O_5N_2\cdot2H_2O$: C, 59.06; H, 4.70; N, 7.25. Found: C, 59.49; H, 4.48; (51%). N, 7. 35. Mass Spectrum *m/e*: 350 (M^+). IR ν_{max}^{KBr} cm^{-1}: 1720 (broad). NMR (d_6-Me_2CO) τ:7. 4-6.7 (multiplet, 2H), 6.32 (quartet, 1H), 3.4—2.6 (multiplet, 4H), 0.59 (singlet, 1H).

Bromination of 8——To a solution of **8** (mp 253—263°, 380 mg, 1.1×10^{-3} mole) in AcOH (20 ml), a solution of Br_2 (600 mg, 3.7×10^{-3} mole) in AcOH (10 ml) was added during 1 hr (solid appeared). After stirring for 1 hr at room temperature, N_2 gas was passed in the solution for 1 hr for removal of HBr produced and H_2C was added. Separated solid was collected, washed with H_2O, and dried. Recrystalelization from MeOH–$CHCl_3$ afforded 5-bromodioxindole-3-(α-phthalimido) propionic acid lactone (**10**) as colorless prisms,mp 285—296° (decomp.). Yield, 420 mg (90%). *Anal.* Calcd. for $C_{19}H_{11}O_5N_2Br$: C, 53. 42; H, 2.60; N, 6.56. Found: C, 52.74; H, 2.46; N, 6.29. IR ν_{max}^{KBr} cm^{-1}: 1810, 1810. 1725 (strong). NMR (d_6-DMSO) **6**.98 (quartet, 2H), 4.51 (triplet,1H), 3.05 (doublet, $J=8$ cps, IH) 2.43 (singlet, IH), 2.37 (doublet-doublet, $J=8$ cps, $J=1$ cps,IH), 2.01 (broad singlet, 4H, pthalimide), —2.1 (broad singlet, IH).

Reaction of 9 with 1 Mole of NBS——By the procedure described above, **8** and **10** were obtained from **9** (350 mg, 10^{-3} mole) and NBS (178 mg, 10^{-3} mole) and were separated by their fractional crystallization from MeOH. **8**, mp 262—263° (decomp.). Yield, 215 mg (62%). **10**, mp 280—292° (decomp.). Yield, 51 mg (12%).

Hydrogenation of 8——A solution of **8** (mp 263—267°, 200 mg, 5.8×10^{-3} mole) in AcOH (4 ml) was hydrogenated at atmospheric pressure in the presence of 10% Pd-C for 10 hr. The catalyst was removed by filtration and the filtrate was evaporated *in vauo*. The residue was dissolved in EtOAc (30 ml) and this solution was extracted with 10% $NaHCO_3$ (10 ml). The crystals that separated out when the alkaline solution was acidified with 5% HCl were extracted with EtOAc (50 ml). The extract solution was washed with H_2O, dried over Na_2SO_4, and evaporated. Recrystallization of the residue from MeOH afforded **9**, mp 137—143° (yield, 15 mg, 7.5%), which was identified with an authentic sample through IR spectra and admixture. The starting material was recovered from the EtOAc extract (150 mg, 75%).

1-Acetyl-3-(1-acetyloxyethylidene)-2-indolinone (11)——A mixture of **9** (370 mg, 1.1×10^{-3}mole), Ac_2O (5 ml), and AcONa (200 mg) was refluxed for 3 hr. When cooled, ice water was added and the separated solid was extracted with EtOAc (50 ml). The extract was washed with 10% $NaHCO_3$ and H_2O, dried over Na_2SO_4, and evaporated. Recrystallization of the residue from MeOH afforded colorless needles, mp 139° (yield, 20%), which was identified with the authentic sample through IR sepctra and admixture. *Anal.* Calcd. for $C_{14}H_{13}O_4N$: C, 64.86; H, 5.05; N, 5.40. Found: C, 65.35; H, 5.25; N, 5.18. IR ν_{max}^{KBr} cm^{-1}: 1776, 1748, 1706. UV λ_{max}^{EtOH} mμ: 251, 259, 2,93. NMR ($CDCl_3$) τ: 7.60 (singlet, 3H), 7.32 (singlet, 3H), 7.30 (siglet, 3H).

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