165. Photodecomposition of Lysergic Acid Diethylamide (LSD)

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It has already been known that lysergic acid diethylamide (LSD) and ergot alkaloids are easily decomposed by photoirradiation. Stoll et al. have found that lumi-LSD is obtained by photoirradiation of LSD in acetic acid solution, and Hellberg also has verified that lumi-ergot alkaloids are obtained as photoproducts of ergot alkaloids. Genest et al. have identified LSD by thin-layer chromatography after photoirradiation of the sample spotted on thin layer utilizing that LSD is photodecomposed to give several spots of photoproducts on the chromatograms but other narcotics are not. Andersen has reported that photoproducts of LSD in chloroform are distinctly different from those of ergot alkaloids by thin-layer chromatography and this fact could be successfully applied to identify LSD and ergot alkaloids. However, correlation between photodecomposition of LSD and irradiation time, and photoproducts except lumi-LSD have not been clarified yet.

In the present work, time courses of photodecomposition of LSD in five kinds of organic solvents, acid and alkaline solution are measured, and photoproducts are separated by thin-layer chromatography.

Experimental Materials. LSD was synthesized from d-lysergic acid (Sigma Co.) by Garbrecht's method and organic solvents were distilled.

Irradiation. Fifty µg of LSD was dissolved in 1 ml of solvent in 10 ml of round flask and irradiated by low-pressure mercury lamp (253.7 mµ) at the distance 10 cm from surface of the solution to the lamp in a certain time. The quantity of the light used for irradiation was $1.14 \times 10^{-9}$ einstein/sec by ferrioxalate actinometry.

Thin-layer chromatography. The plates for thin-layer chromatography were prepared with Silica Gel G (Merck) at a thickness of 250 µ and for developing solvent (1) methanol–chloroform–n-hexane (1:4:2), (2) methanol–chloroform (1:4), and (3) acetone–chloroform (4:1) were used. Spots were detected under U. V. light (3650 Å) and then by spraying with Van Urk reagent.

Determination of the amounts of unchanged LSD. After the
irradiation the solvent was evaporated in vacuo and residue obtained was dissolved in 100 µl of ethanol. Of 10 µl was applied to thin-layer chromatography. The amount of unchanged LSD which was separated on thin-layer chromatogram was determined by in situ fluorometry described previously by the authors.\(^7\)

Results and discussion. Time course of photodecomposition of LSD. Photodecomposition curves of LSD were remarkably depending upon the solvent as shown in Fig. 1.

The irradiation time for decomposition of 50% of LSD in ethanol, dioxane, 0.1 N NH\(_3\), ethylacetate, 0.1 N HCl and CHCl\(_3\) were 175,
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85, 70, 58, 12 and 6 minutes, respectively. In case of benzene solution, 87% of LSD was still unchanged by the irradiation for 15 hours. It was considered that a large percentage of photon was absorbed by benzene molecules and photodecomposition of LSD occurred hardly, since benzene has a strong absorption at 254 m\( \mu \). On the other hand, LSD in chloroform solution was most rapidly decomposed and not detected by the irradiation for only 45 minutes. Moreover, when LSD was dissolved in chloroform which was irradiated preliminarily under the same condition for 30 and 60 minutes and left to stand in the dark place, diminish of LSD was observed as shown in Fig. 2.

It was suggested that such intermediate photoproducts of chloroform as \( \text{Cl}_3\text{COOH} \) participated to photodecomposition of LSD.

As control experiment, each solution of LSD was left to stand in the dark place and unchanged LSD was determined in the same
manner as mentioned above. In any solvent, 95% and 90% of LSD were survived by the leaving for 8 and 15 hours, respectively.

**Photodecomposition products of LSD.** Thin-layer chromatograms of photoproducts obtained at the time when 50% of LSD was decomposed in each solvent except benzene were shown in Fig. 3. In case of benzene solution the irradiation was performed for 15 hours and chromatographed.

The numbers of photoproducts detected on thin-layer chromatograms were as follows: in ethanol solution 10, 0.1 N HCl 9, CHCl₃ 8, 0.1 N NH₃ 7, benzene 6, and dioxane 4. It was suggested that the complicated photoreaction of LSD was induced by the solvent effect.

The product B, which was main product in acid solution and also detected in ethanol, chloroform and alkaline solution, was isolated by band thin-layer chromatography. The product showed positive color reaction with Van Urk reagent and maximum ultraviolet absorption at 285 mμ, but had no fluorescence under U.V. light. The mass spectrum of the product showed the peaks at m/e 223, 222, 221, 167, 154 which were induced from lysergic acid skelton⁹⁻¹¹) and by high resolution mass spectrometry the molecular ion peak was observed at m/e 341.212 for the calculated value 341.210 C₂₀H₂₇N₃O₂ (lumi-LSD). From these facts the product B was identical with lumi-LSD. Other products are now under investigation.

**References**