the glycerol chain, giving rise to \( \alpha \)-hydroxy-\( \alpha \)-(o-toloyl)propionic acid and, to a much lesser extent to o-toloylacetonic acid. The analogous metabolites are, hence, expected to be isolated from GGE. Results of further studies of urinary excretion and metabolites of GGE will be reported.

Tetsuzo Kato and Yutaka Yamamoto\(^{a,b}\): Studies on Ketene and Its Derivatives. XVIII,\(^{a,2}\) Reaction of Diketene with Acridine.

(Pharmaceutical Institute, Tohoku University School of Medicine\(^{a,2}\))

(Received December 3, 1966)

In the previous papers\(^1\) of this series, we have reported reaction of diketene with the C=N double bond in the aromatic heterocycles such as quinoline or phenanthridine to give the Wollenberg’s type compound (I).\(^3\) Also, we have reported that diketene reacted with the C=N double bond of the Schiff base to give the alkylidene acetoacetamide (II).\(^3\) The continuous study was undertaken to see if diketene could react with the C=N double bond of acridine in a similar fashion as described above. In the present paper we wish to report reaction of diketene with acridine proceeded in a different manner from the case of quinoline or phenanthridine, affording 9-substituted acridan.

![Chart 1.](image)

When acridine was treated with an excess of diketene, colorless needles of m.p. 140–141\(^\circ\), C\(_{12}\)H\(_{13}\)ON (III), were obtained. The ultraviolet spectrum of this compound showed only one maximum absorption at 281 m\(\mu\), on the other hand, in the case of acridine 9-acridylacetone (IV) two maximum peaks appeared at 249, 357 m\(\mu\), and 252, 360 m\(\mu\), respectively. The infrared spectrum of III in chloroform exhibited a characteristic peak at 1710 cm\(^{-1}\)(C=O) and the NH absorption band at 3448 cm\(^{-1}\). In the nuclear magnetic resonance (NMR) spectrum signals of methyl protons (3H, 1.83 p.p.m., singlet),

\(^{a1}\) Kita-4, Sendai (工藤俊三, 山本 豊).
\(^{a2}\) Part XVII. T. Kato, Y. Yamamoto: This Bulletin, 15, 1334 (1967).
methylene protons (2H, 2.58 p.p.m., doublet, J=6.66 c.p.s.), a methine proton (1H, 4.51 p.p.m., triplet, J=6.66 c.p.s.) and an NH proton (1H, 6.07 p.p.m., broad) were observed.

Although the details of the experimental have not been reported yet, Hayashi described that the oxidation of III, which was obtained from the reaction of acridine with acetone, with chloranil gave IV. When II was oxidized with chloranil in benzene according to Hayashi's method, 9-acridylacetone (IV) was obtained in 68.7% yield.

From these results, compound III must have the structure of 9-acridanylacetone (III).

Concerning this reaction, Procter and Taylor reported the reaction of acridine or 9-methylacrindle with dimethylketene to give acridan compounds (V or VI, VII) as shown in Chart 3. Although these reactions are not always same with ours, high activity of 9-position of acridine would be expected, and we propose a likely pathway as shown in Chart 4. Though none of compounds listed in the blanket are isolated, the intermediate of this reaction would be A or B, and the subsequent stage might well involve the hydrolysis giving γ-(9-acridanyl)acetoacetic acid (C) or α-(9-acridanyl)acetoacetic acid (D), followed by decarboxylation giving III.

Experimental

Reaction of Diketene with Acridine—Acridine (3 g.) was dissolved in diketene (6 ml.), and allowed to stand at room temperature for 5 days. The solution was condensed under reduced pressure and the residue was dissolved in ether. The ether solution was passed through an alumina column. The eluent was condensed, and the residue was purified again by chromatography using petroleum ether and ether (10:1) as a solvent. From the first eluent starting material, acridine, was recovered. The subsequent eluent was condensed to give III. The analytical sample, m.p. 140~141°, was secured after recrystallization from petroleum ether—ether, colorless needles. Yield, 0.5 g. (13%). Anal. Calcd. for C_{14}H_{15}ON (II): C, 80.98; H, 6.37; N, 5.90. Found: C, 80.75; H, 6.50; N, 5.84.

9-Acridylacetone (IV)—Acridanylacetone (III) (0.11 g.) was dissolved in benzene (5 ml.) and a solution of chloranil (0.114 g.) in benzene (5 ml.) was added. The solution was refluxed for 2 hr. After cooling, conc. NH_{4}OH was added to the reaction mixture. The benzene layer was washed with water, dried over K_{2}CO_{3}, and filtered. The filtrate was condensed to give a semi-solid, which was purified by crystallization from ether to give yellow needles, m.p. 144°. Yield, 0.075 g. (68.7%). Anal. Calcd. for C_{14}H_{13}ON (V): C, 81.68; H, 5.57; N, 5.95. Found: C, 81.56; H, 5.57; N, 5.54. NMR p.p.m. (in CDCl_{3}, TMS as internal standard at 60 Mc.) 2.13 (3H, singlet), 4.67 (2H, singlet), 7.4~8.4 (8H, ring protons).