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INDOLIZINO[3,4,5,6-cde]QUINOXALINE

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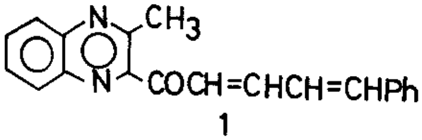
Abstract — 4-Methyl-3-oxo-1-styrylpyrrolo[1,2-a]quinoxalin-10-ium chloride(4) and 3-hydroxy-4-methyl-1-styrylpyrrolo[1,2-a]quinoxaline(3a) hydrochloride were cyclized exclusively to 2-hydroxy-3-methyl-8-phenylindolizino-[3,4,5,6-cde]quinoxaline(6a) and its 8,9-dihydro compound (5a), respectively, by the irradiation of high pressure mercury lamp.

In our previous paper,[1,2] we reported an interesting cyclization reaction of the chalcones and vinylogous chalcones derived from 2-acetyl-3-methylquinoxaline or 2-acetyl-3-methylquinoxaline 4-oxide; 3-methyl-2-quinoxalyl 4-phenyl-1,3-butadienyl ketone(1) and 3-methyl-4-oxido-2-quinoxalyl 4-phenyl-1,3-butadienyl ketone (2) were converted into 3-hydroxy-4-methyl-1-styrylpyrrolo[1,2-a]quinoxaline(3a) hydrochloride and 4-methyl-3-oxo-1-styryl-3H-pyrrolo[1,2-a]quinoxalin-10-ium chloride(4), respectively, by treatment with hydrochloric acid in refluxing ethanol. In this paper, we want to report the result obtained in the photochemical cyclization reactions on 3a and 4. A methanolic solution of 3a-hydrochloride was irradiated with 200 W high pressure mercury lamp for 2h, and then the residue obtained after neutralization was fractionated by a silica-gel column chromatography to give two products as crude materials. The major product exhibited in the ^{1}H-nmr spectrum a characteristic ABX-type signals at δ 3.29, 3.55, and 4.40, and singlet signals at δ 2.88(3H) and 6.37(1H). The mass spectrum suggested that the product was an isomer of 3a. From these physical data, the product was considered to be 2-hydroxy-3-methyl-8-phenyl-8,9-dihydroindolizino[3,4,5,6-cde]-quinoxaline(5a), which was converted into the corresponding methyl ether(5b, mp 152-154°C) and acetate(5c, mp 180-183°C) by the treatment with an excess of diazomethane and acetic anhydride in pyridine, respectively. Compound 5c exhibited in the ^{13}C-nmr spectrum a triplet and doublet signals at δ 30.3 and 41.4 due to the C_9 and C_8, respectively.



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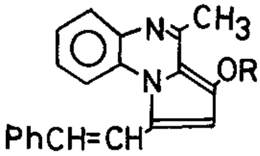

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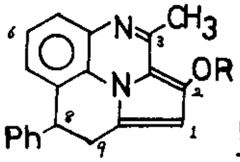

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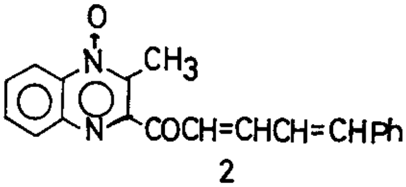

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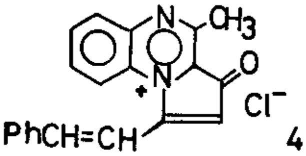

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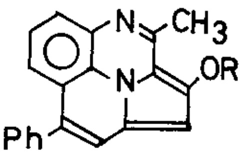

6

a: R=H, b: R=Me, c: R=Ac

The nmr spectrum of the minor product exhibited no characteristic signals except the vinylic methyl and vinylic proton. The mass spectrum suggested the formulas to be $C_{20}H_{14}N_2O$, dehydrogenated compound of 5a. Thus the product was considered to be 2-hydroxy-3-methyl-8-phenylindolizino[3,4,5,6-cde]quinoxaline(6a), which was also methylated to its methyl ether(6b, mp 210-212°C). Formation of compound 6a may occur via photochemical oxidation on 5a. The overall yield of 5b and 6b from 3a were 67.4 and 12.0%, respectively.

The photochemical cyclization reaction did not occur on the neutralized, methylated, or acetylated materials(3a, 3b, or 3c, respectively).

A methanolic solution of 4 was irradiated under the similar conditions to give quantitatively one product, which was identified with 6a by derivation to the methyl ether(6b).

These photochemical cyclization reactions were interesting ones and could be applied to the synthesis of a hitherto unknown indolizino[3,4,5,6-cde]quinoxaline ring system, which is expected to have anticancer activity because of its molecular-flatness to intercalate into nucleic acid.[3]

REFERENCES

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2) K. Matoba, T. Terada, M. Sugiura, and T. Yamazaki, Heterocycles, in press.

3) S. D. Phillips and R. N. Castle, J. Heterocyclic Chem., 1980, 17, 1489, and references cited therein.

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