

ACID CATALYZED ISOMERIZATION OF 2-(2-FURFURYLIDENE)ACETYL-QUINOXALINE
AND ITS 3-METHYL DERIVATIVE

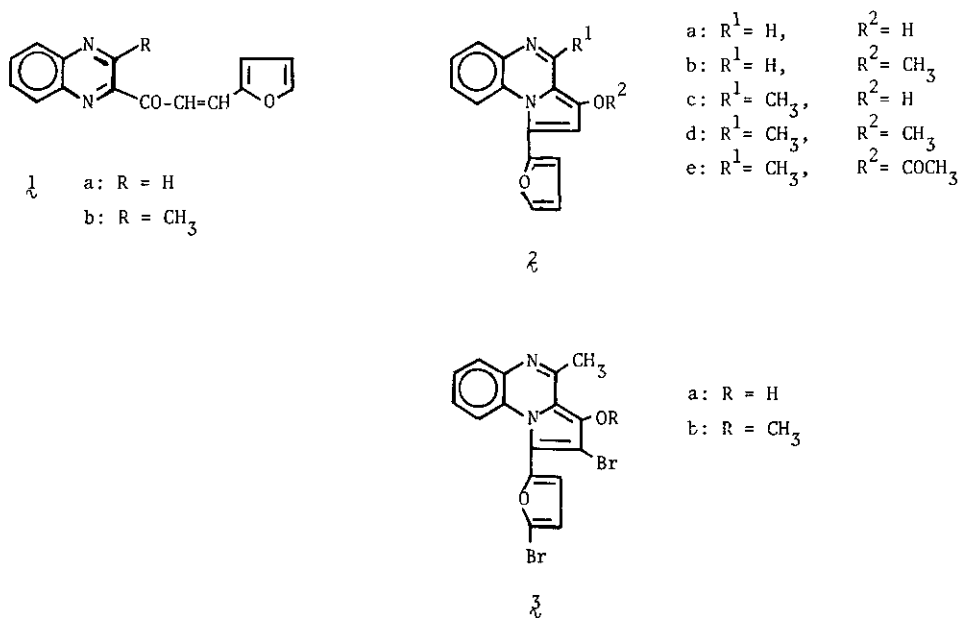
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2-(2-Furfurylidene)acetyl-quinoxaline($1a$) and its 3-methyl derivative ($1b$) gave quantitatively 1-furfuryl-pyrrolo[1,2-a]quinoxalin-3-ol($2a$) and its 4-methyl analogue($2c$), respectively, by treating with hydrochloric acid in ethanol. $2c$ was treated with bromine in carbon tetrachloride to give dibromide($3a$). $2d$ (methyl ether of $2c$) and $2e$ (enol acetate of $2c$) afforded 1 to 2 adducts with dimethyl acetylenedicarboxylate.

Several systems of diazasteroid were synthesized in our laboratory. Robinson reported the synthesis of steroid skeleton starting with 2-(2-furfurylidene)acetyl-6-methoxy-naphthalene, which afforded 1,4-diketone derivative by treating with hydrochloric acid in ethanol¹. According to this procedure, synthesis of 6,9-diazasteroid system was tried starting with 2-(2-furfurylidene)acetyl-quinoxaline($1a$), which was prepared from 2-acetyl-quinoxaline² and 2-furfurylaldehyde. To an ethanolic solution of $1a$ (0.9g), concentrated hydrochloric acid (4.5 ml) was added and the mixture was refluxed overnight to give quantitatively yellow brown crystalline compound($2a$), which was an isomer of $1a$ and exhibited signals only at lower field than δ 6.9 ppm in the nmr spectrum measured in trifluoroacetic acid solution. The ferric chloride test for $2a$ was positive but weak. This enolic product was treated with diazomethane in ether and methanol to give the corresponding methyl ether($2b$, mp 141~142°). In a similar fashion, 2-(2-furfurylidene)acetyl-3-methyl-quinoxaline($1b$) also gave quantitatively an enolic product($2c$) by treating with hydrochloric acid in ethanol. $2c$ had similar properties to $2a$. $2c$ was treated with an excess of bromine in carbon tetrachloride to give quantitatively dibromide($3a$), which was methylated to afford a dibromide methyl ether($3b$, mp 83~85°), which exhibited in the nmr spectrum, two singlet signals at δ 2.83 and 4.02 ppm due to two methyl protons, AB type signals at δ 6.58 and 6.68 ppm ($J=3$ Hz), and symmetrical multiplet signals from δ 6.8 ppm to 7.9 ppm associated with four protons. When this spectrum was compared with that of $2d$, it was revealed that two signals, singlet signal at δ 6.69 ppm and triplet signals at δ 7.69 ppm ($J=1.5$ Hz),

disappeared from the nmr spectrum of λ_d . Both λ_d (mp 160~162°) and λ_e (enol acetate of λ_c , mp 174~176°, which was obtained by treating λ_c with acetic anhydride) afforded 1 to 2 adducts with dimethyl acetylenedicarboxylate. The formulas of these adducts were established by means of mass spectra and elemental analyses.

From the above experimental and physical data, the structures of λ_a to λ_b were suggested as shown in the following chart.



The C¹³ nmr spectrum³⁾ of λ_d supported this structure. A similar synthesis of indolizine derivatives from 2-acetyl-pyridine was reported⁴⁾. It is interesting that the furan ring in the substrate (λ_a or λ_b) is quite stable under these conditions. On the other hand, Popp et al., reported that 2-(2-furfurylidene)acetyl-quinoline gave rise to methyl 2-quinolinecarboxylate under the similar conditions.⁵⁾ Further studies must be done on the structures of the adducts by dimethyl acetylenedicarboxylate.

References

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- 3) For the measurement of this C¹³ nmr spectrum, the authors want to express their thanks to Dr. M.Hanaoka and Dr. T.Imanishi, Faculty of Pharmaceutical Sciences in Kanazawa University.
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