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

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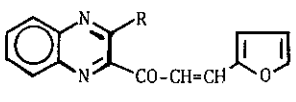
2-(2-Furfurylidene)acetyl-quinoxaline(1a) and its 3-methyl derivative (1b) gave quantitatively 1-furfuryl-pyrrolo[1,2-a]quinoxalin-3-ol(2a) and its 4-methyl analogue(2c), respectively, by treating with hydrochloric acid in ethanol. 2c was treated with bromine in carbon tetrachloride to give dibromide(3a).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

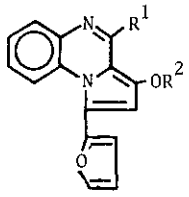
Several systems of diazasteroid were synthesized in our laboratory. Robinson reported the synthesis of steroid skeleton starting with 2-(2-furfurylidene)acetyl-6-methoxy-naphthalene, which afforded 1,4-diketone derivative by treating with hydrochloric acid in ethanol[1]. According to this procedure, synthesis of 6,9-diazasteroid system was tried starting with 2-(2-furfurylidene)acetyl-quinoxaline(1a), which was prepared from 2-acetyl-quinoxaline[2] 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 δ6.9 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 δ2.83 and 4.02 ppm due to two methyl protons, AB type signals at δ6.58 and 6.68 ppm (J=3 Hz), and symmetrical multiplet signals from δ6.8 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 δ6.69 ppm and triplet signals at δ7.69 ppm (J=1.5 Hz),

disappeared from the nmr spectrum of 2d. Both 2d (mp 160∿162°) and 2e (enol acetate of 2c, mp 174∿176°, which was obtained by treating 2c 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 2a to 3b were suggested as shown in the following chart.



1 a: R = H
b: R = CH_3



a: R^1= H, R^2= H
b: R^1= H, R^2= CH_3
c: R^1= CH_3, R^2= H
d: R^1= CH_3, R^2= CH_3
e: R^1= CH_3, R^2= $COCH_3$

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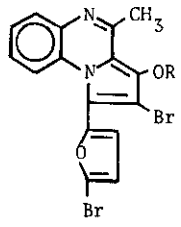

a: R = H
b: R = CH_3

3

The C^{13} nmr spectrum[3] of 2d supported this structure. A similar synthesis of indolizine derivatives from 2-acetyl-pyridine was reported[4]. It is interesting that the furan ring in the substrate (1a or 1b) 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 C^{13} nmr spectrum, the authors want to express their thanks to Dr. M.Hanaoka and Dr. T.Imanishi, Faculty of Pharmaceutical Sciences in Kanazawa University.
4) F.W.Krock and F.Krohnke, Chem.Ber., 1971, 104, 1629.
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Received, 22th January, 1980