REACTION OF CHROMONE EPOXIDES. I REACTION OF 2,3-EPOXYISOFLAVONE WITH ALKYLAMINES Ichiro Yokoe^{*a}, Kumiko Nakamura^a, Kyoko Higuchi^a, Yoshiaki Shirataki^a, Manki Komatsu^a, and Hiroshi Miyamae^b Faculty of Pharmaceutical Sciences^a and Faculty of Sciences^b, Josai University, Keyakidai, Sakado, Saitama 350-02, Japan <u>Abstract</u>—— The reaction of 2,3-epoxyisoflavone (1) with primary alkylamines gave 2'-hydroxy-[1-phenyl-1-(N-formyl)alkylamino]acetophenones (22d), whose structures were determined on the basis of spectroscopic properties and X-ray crystallographic analysis for N-propyl derivative (2c).

Donnely¹ reported the facile synthesis of chromone epoxides and their acid-catalysed rearrangement reaction. These epoxides can also be regarded as being attacked by other nucleophiles². In this communication we report the formation of unexpected products on the formal 1,2-shift of CHO group rearrangement reaction of 2,3-epoxy-isoflavone (1) with primary alkylamines.

To a solution of 2,3-epoxyisoflavone (1) in CH_2Cl_2 was added an excess 40% MeNH₂ solution and the mixture was stirred for 2 h at room temperature to give compound 2a as colorless needles, mp 89-91°, in ca. 30% yield. The IR spectrum of 2a showed \widetilde{W} the presence of chelated hydroxyl and carbonyl groups (3400 and 1650 cm⁻¹) and N-formyl group (1680 cm⁻¹). The UV spectrum of 2a in MeOH has maxima at 259 and 332 nm ($\varepsilon = 9.45 \times 10^3$ and 4.20 x 10^3) and these were shifted to 379 nm ($\varepsilon = 5.40 \times 10^3$) by the addition of KOH solution. The ¹H-NMR spectrum of 2a showed the signals due to N-methyl proton at δ 2.86 (s, 3H), N-formyl proton at δ 8.26 (s, 1H), chelated hydroxyl proton at δ 11.96 (s, 1H; disappeared by the addition of D₂O), and nine aromatic and one benzylic protons at δ 6.64-7.61 (m, 10H) ppm. In addition to these signals some small peaks due to the rotational isomer of the amide group were observed. The molecular composition was determined as $C_{16}H_{15}NO_3$ by high resolution mass spectrometry and elemental analysis³.

Other reaction products (2b-d) (Table 1) also had similar spectral properties to 2a. To determine the structure of 2, X-ray crystallographic analysis of 2c (R=n-propyl) was undertaken.

The crystal used for X-ray analysis had a dimension of ca. 0.18 x 0.15 x 0.15 mm.

Crystal data are : $C_{18}H_{19}NO_3=297.34$, monoclinic, space group $B_{2/b}$, a=26.884(3), b=22.640(5), c=9.465(2) Å, γ =33.69(6)°, Z=8, Dx=1.236. A total of 2375 unique reflections having Fo > 30(Fo) were measured on Rigaku AFC-5 diffractometer using graphite-monochromated Cu-Ka radiation. The structure was solved by the direct method and by using MULTAN system⁴. The refinement of atomic parameters were carried out by block-diagonal least squares calculations⁵. The final R value was 0.0715. The molecular structure of 2c and the yields of 2 were shown in Fig. 1

From this structure, it is clear that the abnormal low field shift of benzyl proton is due to the anisotropic effect of N-formyl group which is in close proximity. The tentative mechanism of the formation of 2 was shown in Chart 1. The epoxide (1) was attacked by alkylamines at α -position (3-position on chromone ring) and opened to give (A)⁶, followed by the rearrangement to 2 through the intermediate (B).

Table 1. Yields and mp of 2.

2	R	Yield (%)	mp (°C)
а	снз	32.7 7	89-91
b	с ₂ н ₅	67.4	93
с	n-C3H7	64.0	106
d	cyclohexyl	68.9	162-163



Fig.1.



Chart1.

REFERENCES AND NOTES

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- 3. ¹³C-NMR of 2a in CDCl₃, δ (ppm); 32.89(q), 60.37(d), 118.65(d), 119.10(d), 119.26 (s), 129.0(d), 129.35(d), 129.69(d), 130.62(d), 133.67(s), 136.78(d), 162.96(d),

163.02(d), 201.97(s). MS of 2a; m/z 269(M⁺), 148(base peak, M⁺-121), 121, 120.

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- 6. It has been reported that the nucleophilic substitution of α,β-epoxyketones occured at α-position: M.Tomoeda, M.Inuzuka, T.Furuta and M.Shinozuka, <u>Tetrahedron</u>, 1968, <u>24</u>, 959; M.A.Tobias, J.G.Strong and R.P.Napier, <u>J.Org.Chem</u>., 1970, <u>35</u>, 1709; A.G.Schultz, W.Y.Fu, R.D.Lucci, B.G.Kurr, K.M.Lo and M.Boxer, <u>J.Am.Chem.Soc.</u>, 1978, <u>100</u>, 2140; We also found in other experiments that epoxyisoflavones were attacked at the 3-position of chromone ring by other nucleophiles, such as thiols and halides.

7. In addition to 2a, another crystalline product (mp 99°) was obtained and the structure is under investigation.

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