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# REACTION OF CHROMONE EPOXIDES. I

## REACTION OF 2,3-EPOXYISOFLAVONE WITH ALKYLAMINES

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Abstract—— The reaction of 2,3-epoxyisoflavone (**1**) with primary alkylamines gave 2'-hydroxy-[1-phenyl-1-(N-formyl)alkylamino]acetophenones (**2a**-**d**), whose structures were determined on the basis of spectroscopic properties and X-ray crystallographic analysis for N-propyl derivative (**2c**).

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

To a solution of 2,3-epoxyisoflavone (**1**) in $CH_2Cl_2$ was added an excess 40% $MeNH_2$ 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 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 $4.20 \times 10^3$) 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 protons at $\delta$ 2.86 (s, 3H), N-formyl proton at $\delta$ 8.26 (s, 1H), chelated hydroxyl proton at $\delta$ 11.96 (s, 1H; disappeared by the addition of $D_2O$), and nine aromatic and one benzylic protons at $\delta$ 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 analysis[3].

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 > 3σ(Fo) were measured on Rigaku AFC-5 diffractometer using graphite-monochromated Cu-Kα radiation. The structure was solved by the direct method and by using MULTAN system[4]. The refinement of atomic parameters were carried out by block-diagonal least squares calculations[5]. The final R value was 0.0715. The molecular structure of **2c** and the yields of **2** were shown in Fig. 1 and Table 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) |
|---|---|---|---|
| a | $CH_3$ | 32.7[7] | 89-91 |
| b | $C_2H_5$ | 67.4 | 93 |
| c | n-$C_3H_7$ | 64.0 | 106 |
| d | cyclohexyl | 68.9 | 162-163 |

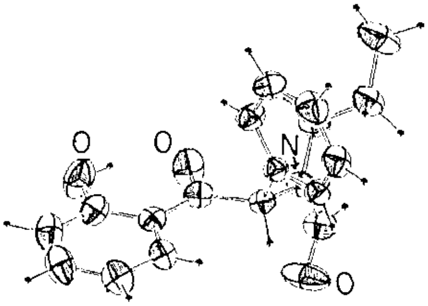

Fig.1.

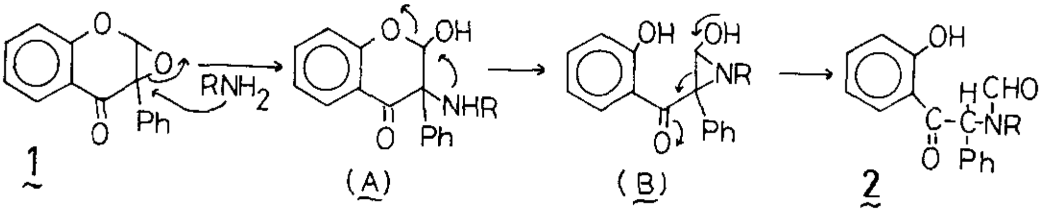

Chart 1.

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2. A.H.Haines in 'Comprehensive Organic Chemistry', ed. by D.H.R.Barton and W.D.Ollis, Pergamon, Oxford, 1979, Vol. 1, Section 4.4 ; J.March,'Advanced Organic Chemistry' 2nd ed., McGraw-Hill, 1977, 381.

3. $^{13}$C-NMR of **2a** in $CDCl_3$, 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.

4. P.Main, S.E.Hull, L.Lessinger, G.Germain, J.P.Declercq and M.M.Woofson (1978), MULTAN 78. A system of computer programs for the automatic solution of crystal structures for X-ray diffraction data, Univ. of York, England and Louvain, Belgium.
5. UNICS system; T.Sakurai and K.Kobayashi, Rikagaku Kenkyusho Hokkoku (Rep. of Inst. Phys. Chem. Res., in Japanese), 1978, **55**, 69.
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, *Tetrahedron*, 1968, **24**, 959; M.A.Tobias, J.G.Strong and R.P.Napier, *J.Org.Chem.*, 1970, **35**, 1709; A.G.Schultz, W.Y.Fu, R.D.Lucci, B.G.Kurr, K.M.Lo and M.Boxer, *J.Am.Chem.Soc.*, 1978, **100**, 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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