SYNTHESIS OF NATURAL 4′-METHOXY-6″, 6″-DIMETHYLPYRANO (2″,3″ ; 7,8) ISOFLAVONE AND ITS LOWER ANALOGUE

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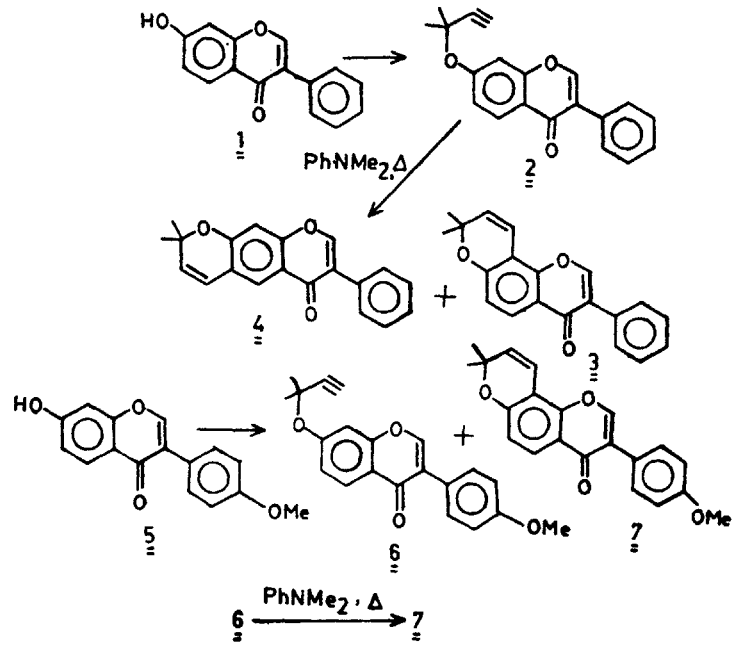
Reaction of 7-hydroxyisoflavone (**1**) with 2-chloro-2-methyl-3-butyne in the presence of K_2CO_3, KI and Me_2 CO for 80 h gave the corresponding 1,1-dimethylpropargyl ether (**2**) which on heating in *N, N*-dimethylaniline afforded 6″, 6″-dimethylpyrano (2″, 3″: 7,8) isoflavone (**3**) and its linear isomer (**4**) in 4 : 1 ratio. However, 1,1-dimethylpropargylation of 7-hydroxy-4′-methoxyisoflavone (**5**) in the presence of the above reagents and a few drops of DMF converted the whole amount of the substrate in 30 h to give a mixture of the 1,1-dimethylpropargyl ether (**6**) and the naturally occurring 4′-methoxy-6″, 6″-dimethylpyrano (2″, 3″ : 7, 8) isoflavone (**7**). Further thermal rearrangement of **6** gave **7** as the sole product.

INTRODUCTION

FROM *Calopogonium mucunoides*, a new isoflavone was isolated by Vilain and Jadot (1975) who gave it the structure of 4′-methoxy-6″, 6″-dimethylpyrano (2″, 3″ : 7, 8) isoflavone (**7**) mainly on the basis of its NMR, UV, IR and MS spectra. This constitution is now supported by its synthesis using the general method of Hlubucek *et al.* (1971) which is generally known to give angular pyrano derivatives.

Before the synthesis of the natural isoflavone itself, the synthesis of its lower analogue 6″, 6″-dimethylpyrano (2″, 3″ ; 7, 8) isoflavone (**3**) was projected. 7-Hydroxyisoflavone (Iyer *et al.*, 1951) (**1**) when heated with 2-chloro-2-methyl-3-butyne in the presence of K_2CO_3, KI and acetone gave the corresponding 1,1-dimethylpropargyl ether (**2**). In accordance with the structure, its NMR spectrum showed two characteristic singlets, one at δ 1.76 due to a *gem* dimethyl group and the other at δ 2.10 due to an acetylenic hydrogen besides the signals of the starting isoflavone. The above propargyl ether when refluxed in *N, N*-dimethylaniline gave rise to a mixture of two products in the ratio of 4 : 1 which could be separated by column chromatography. The major product proved to be the angular chromene (**3**) and the minor one the linear chromene (**4**). The structures were further supported by the identity of the two samples prepared earlier by Jain *et al.* (1972) by another route.

In order to synthesize the natural chromene, 7-hydroxy-4′-methoxyisoflavone (Kagal *et al.*, 1956) was reacted with 2-chloro-2-methyl-3-butyne in nearly the same way as in the case of (**1**) with the difference that a few drops of DMF were also added to expedite the reaction. In fact, it was observed that the starting material is completely changed in 30 h. However, the use of DMF gave a mixture of two products formed in the ratio of 5 : 2. The major amount was identified as the corresponding 1, 1-dimethylpropargyl ether by its NMR spectrum and the minor fraction was found to



be identical with the natural isoflavone in all its properties mp, TLC, UV and NMR data.

The 1, 1-dimethylpropargyl ether (**6**) on heating with *N, N*-dimethylaniline gave angular chromene (**7**) as the sole product.

The main difference in the above two experiments is that 7-hydroxy isoflavone gave both linear and angular chromenes, whereas 7-hydroxy-4'-methoxy isoflavone yielded only the angular chromene. It appears that the substitution makes the difference.

Experimental

All melting points are uncorrected (unless otherwise stated). UV spectrawere recorded in methanol; IR spectra were determined on a Perkin-Elmer model 137-B nujol mull; PMR spectra were determined on BS 487C spectrometer (80 MHz) in deuteriochloroform with reference to tetramethylsilane as an internal standard; the chemical shifts are given in δ values; light petroleum ether used had boiling range 60–80 ° ; silica gel was used for column chromatography and silica gel G for TLC; R_F values recorded are on T×C plates using one of the following solvent systems ; (A) benzene; ethyl acetate (9 : 1), (B) toluene : acetone (19 ; 1); spraying was carried out with 10% aq. H_2SO_4 and/or 1% alcoholic ferric chloride.

7-(1,1-Dimethylpropargyloxy) isoflavone (**2**)—A mixture of 7-hydroxyisoflavone (Iyer *et al.* 1951) (**1**, 2 g) in acetone (100 ml), 2-chloro-2-methyl-3-butyne (1.01 ml), anhydrous potassium carbonate (10 g) and potassium iodide (3 g) was refluxed for 80h. The solvent was removed and water added to the residue. The solid thus collected

crystallized from benzene-light petroleum mixture to afford 7-(1,1-dimethylpropargyloxy) isoflavone (**2**) as colourless needles (1.8 g), mp 124–5 °C; R_F 0.45 (solvent A); IR ; 1540 (> C=0); PMR : 1.76 (s, 6, $2CH_3$), 2.70 (s, 1, C≡ CH)$_1$, 7.20 (2d, J_0 = 9Hz, *Jm* = 3Hz, 2, H–6 and 8), 7.34–7.57 (m, 5, C_6H_5), 7.95 (m, 1, H-2) and 8.19 (d, J = 9Hz, 1, H–5); λ_{max} 250 (log ϵ 4.48), 301 (4.08). Found ; C, 78.8; H, 5.4. $C_{20}H_{16}O_3$ requires : C, 78.9; H, 5.3%.

Thermal rearrangement of 7-(1, 1-dimethylpropargyloxy) – isoflavone (**2**) *and formation of pyrano isoflavones* (**3** *and* **4**)—The above isoflavone (**2**, 1.2 g) was refluxed in *N, N*-dimethylaniline (20 ml) for 3 h at 210–20 °C and the resulting solution was poured on ice-cold dilute HCl. The solid product thus obtained found to be a mixture of two compounds. Fractional crystallization from methanol (mother liquor A) gave a solid which on crystallization from benzene-light petroleum mixture afforded 6″, 6″-dimethylpyrano (2″, 3″ ; 7, 8) isoflavone (**3**) as shining plates (0.2 g), mp 180–81 °C (cf. Jain *et al.*, 1972, mp 179–80 °C).

The mother liquor A yielded a solid which on crystallization from methanol afforded 6″, 6″-dimethylpyrano (2″, 3″ : 7,6) isoflavone (4, 0.5 g) as colourless crystals, m.p. 166–67 °C (cf. Jain *et al.*, 1972, mp 168 °C).

1, 1-Dimethylpropargylation of 7-hydroxy-4′-methoxyisoflavone (**5**) (*Formation of* **6** *and* **7**)—A solution of 7-hydroxy-4′-methoxy-isoflavone (Kagal *et al.*, 1956) (**5**, 100 mg) in acetone (30 ml) was refluxed with 2-chloro-2-methyl-3-butyne (0.1 ml), potassium iodide (0.5 g), potassium carbonate (1 g) and a few drops of DMF for 30 h. The product was found to be a mixture of two compounds. It was therefore subjected to column chromatography and careful elution with benzene ; light petroleum (1 ; 4) gave two fractions A and B.

Fraction A when crystallized from benzene-light petroleum yielded 6″, 6″-dimethylpyrano (2″, 3″ ; 7,8)-4′-methoxy isoflavone (**7**) as light yellow crystals (20 mg), mp 142–44 °C (Vilain & Jadot, 1975; mp 144–45 °C); R_F 0.7 (solvent B); PMR; 1.50 (s, 6, $2CH_3$), 3.85 (s, 3, OCH_3), 5.70 (d, *J* = 10Hz, 1, H-5″), 6.80 (d, *J* = 10Hz, 1, H–4″), 6.83 (d, *J* = 9Hz, 1,H–6), 6.94 (d, *J* = 9Hz, 2, H–3′, 5′), 7.50 (d, *J* = 9Hz, (2, H–2′-6′), 7.95 (s, 1H, H–2) and 8.05 (d, *J* = 9Hz, 1, H–5); λ_{max} 234 (log ϵ 4.39), 257 (4.62). Found : C, 75.1; H, 5.2. Calculated for $C_{21}H_{18}O_4$ C, 75.45; H, 5.4%. It agrees in all these properties with those described for natural sample.

Fraction B on crystallization from benzene-light petroleum mixture gave 7-(1, 1-dimethylpropargyloxy)-4′-methoxyisoflavone (**6**) as colourless crystals (50 mg), mp 128–29 °C; R_F 0.43 (solvent A); PMR : 1.64 (s, 6, $2CH_3$), 2.55 (s, 1, C ≡ CH), 3.87 (s, 3H, OCH_3), 6.80 (d, J_m = 3Hz, 1, H–8), 6.90 (dd, J_0 = 9Hz, J_m = 3Hz, 1, H–6), 7.20 (d, *J* = 10Hz, 2, H–3′ and 5′), 7.45 (d, *J* = 10Hz, 2, H–2′ and 6′), 7.87 (s, 1, H–2) and 8.17 (d, *J* = 9Hz, 1, H–5); λ_{max} 252 (log ϵ 4.26), 298 (3.96). Found ; C, 75.3; H, 5.5. $C_{21}H_{18}O_4$ requires C, 75.4; H, 5.4%.

Conversion of Compound **6** *into* **7** — 4′-Methoxy-7-(1, 1-dimethylpropargyloxy) isoflavone (**6**, 50 mg) was refluxed in *N, N*-dimethylaniline (6 ml) for 3h at 215–20 °C. The brown coloured liquid was poured into ice-cold dilute HCl. The solid was filtered, dried and crystallized from benzene-light petroleum when **7** formed light yellow crystals (40 mg), mp and mmp with the sample prepared above 142–44 °C.

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