Proc. Indian Acad. Sci., Vol. 87 A (Chemical Sciences-5), No. 10, October 1978, pp. 389–394,

The Claisen rearrangement of 7-cinnamyloxy derivatives of 3-methoxyflavone, 4-methylcoumarin and isoflavone*

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MS received 16 February 1978

Abstract. The Claisen rearrangement of 7-cinnamyloxy derivatives of 3-methoxyflavone (2), 4-methylcoumarin (7) and isoflavone (13) yield 8-(1-phenyl-2-propenyl)-7-hydroxy-3-methoxyflavone (3), 4-methyl-8-(1-phenyl-1-propenyl)-7-hydroxycoumarin (9) and 8-(1-phenyl-1-propenyl)-7-hydroxyisoflavone (14) respectively. The compound 3 represents the normal rearranged product and further has structural features similar to those present in some natural neoflavonoids; whereas other products (9 and 14) are abnormal ones formed by further allylic rearrangement of the normal ones (say 8).

Keywords. 8-(1-phenyl-2-propenyl)-7-hydroxy-3-methoxy-flavone, 4-methyl-8-(1-phenyl-1-propenyl)-7-hydroxycoumarin and 8-(1-phenyl-1-propenyl)-7-hydroxyisoflavone.

1. Introduction

In continuation of our work on the Claisen rearrangement of cinnamyl ethers of complex polyphenols (Jain and Gupta 1974, 1975), the rearrangement of 7-cinnamyloxy derivatives (2, 7 and 13) of 3-methoxyflavone, 4-methylcoumarin and isoflavone respectively has been studied by refluxing them in *NN*-dimethylaniline. In each case, only one product has been isolated. The products are different from those reported earlier (Jain and Gupta 1974, 1975) and one of them (3) has a similar feature as is present in some natural neoflavonoids, such as latifolin.

2. Results and discussion

2.1. *The Claisen rearrangement of 7-cinnamyloxy-3-methoxyflavone* (2)

7-Cinnamyloxy-3-methoxyflavone (2) was prepared from 7-hydroxy-3-methoxyflavone (1) (Allan and Robinson 1924) by refluxing with cinnamyl bromide in the presence of potassium carbonate and acetone and its structure confirmed by its NMR spectrum which showed signals of one cinnamyloxy group (δ 4·75, d, J=5Hz, 2H, $-OCH_2-$, 6·10—6·50 m, 2H, $-CH=CH-$, 7·16 — 8·00 m, C_6H_5-) besides signals of the parent compound. The cinnamyloxyflavone (2) when reflxued with *N*, *N*-dimethylaniline gave a crystalline product whose elemental analysis indicated

A preliminary note on some of the results was published in 1977 *Curr. Sci.* **46** 839

it to be an isomeric product. Its NMR spectrum identified it to be 8-(1-phenyl-2-propenyl)-7-hydroxy-3-methoxyflavone (3). Thus its 60 MHz NMR spectrum in DMSO-d_6 showed resonance signals of one methoxy and the side chain phenyl group and in addition signals of ABCX pattern at δ 5·19 (1H, m, $CH_2{=}CH{-}\underline{C}H{-}Ar_2$), 5·30–5·65 (2H, m, $C\underline{H}_2{=}CH{-}$), 6·23–6·83 (octect, 1H, $-\underline{C}H{=}CH_2$), 7·17–7·36 (5H, m, $C_6\underline{H}_5{-}$) and of only two aromatic protons of the ring A which were placed *ortho* to each other (7·08, 7·89, 2d, J = 10Hz, H_6 and H_5 respectively). In agreement with the structure, the rearranged product formed monoacetate and monomethyl ether whose NMR spectra agreed with structures 4 and 5.

2.2. *The Claisen rearrangement of* 4-*methyl*-7-*cinnamyloxycoumarin* (7)

4-Methyl-7-cinnamyloxy coumarin (7), prepared similarly from 4-methyl-7-hydroxycoumarin (6) (Pechman and Duisberg 1883) and identified by its NMR spectrum, on rearrangement in *NN*-dimethylaniline alslo gave only one crystalline product, and again its elemental analysis indicated it to be an isomeric product. But the following resonance signals in its NMR spectrum established that it is not the normal rearranged product (8) but 4-methyl-8- (1-phenyl-1-propenyl)-7-hydroxycoumarin (9): δ 1·68 (3H, d, J = 7Hz, $C\underline{H}_3{-}CH{=}$), 6·68 $\left(1H, q, J = 7Hz, = C\begin{matrix}\underline{H}\\ \diagdown\\ \diagup\\ CH_3\end{matrix}\right)$. Further the rearrangement occurred in the 8 position because there were resonance signals of only two *ortho* coupled aromatic protons at δ 7·00 and 7·55 (2d, J = 9 Hz, 2H). In conformity with this structure, it formed a monoacetate and a monomethyl ether whose NMR spectra agreed with the structures 10 and 11. The formation of the product (9) can be explained by further allylic rearrangement of the normal Claisen rearrangement product (8).

2.3. *The Claisen rearrangement of* 7-*cinnamyloxyisoflavone* (13)

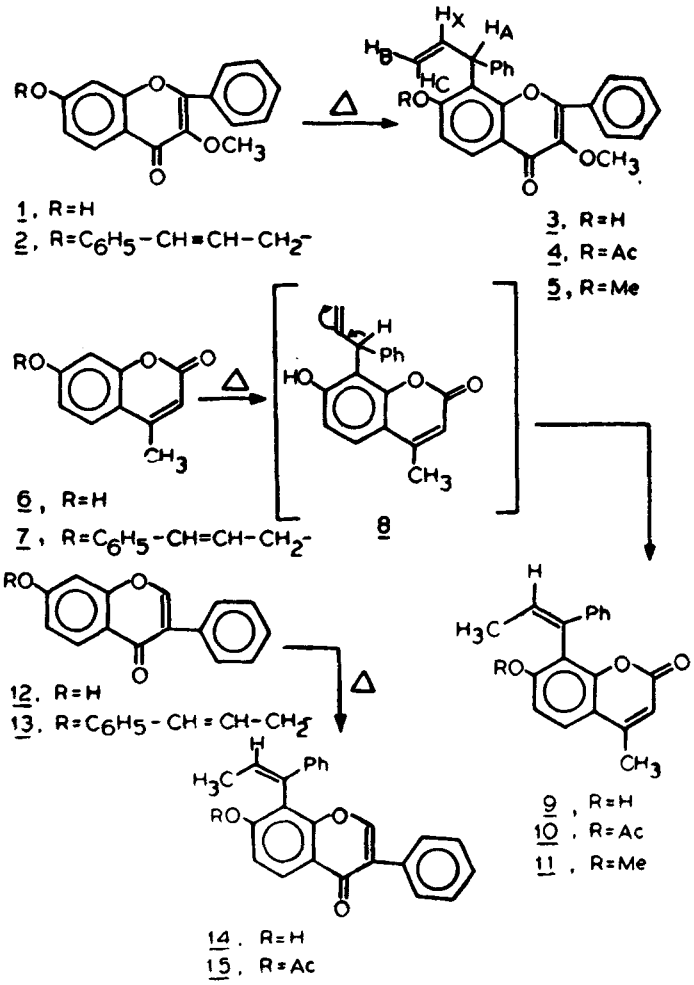
7-Cinnamyloxyisoflavone (13) also yielded a Claisen rearrangement product similar to the above. Thus it formed 8-(1-phenyl-1-propenyl)–7-hydroxyisoflavone (14) having important NMR signals at δ 1·70 of an olefinic methyl group, 6·61 of an olefinic proton and 7·02, 8·16 (J = 9Hz) of two *ortho* coupled aromatic protons of the ring A. This structure was further confirmed by preparation of its acetate which showed the desired NMR spectrum.

The above results indicate that the Claisen rearrangement of 7-cinnamyloxy derivatives of coumarin, flavone and isoflavone yields either the normal rearranged product or its further allylic rearrangement product and further the rearrangement takes place only in 8 position; 6 position remains unaffected. This preferential migration may be explained on the basis of the greater reactivity of the *peri* position as in β-naphthol derivatives.

3. Experimental

All melting points taken at an altitude of~2000M are uncorrected. The following spectrometers were used for spectral measurements; UV Unicam SP 8000; IR Perkin-Elmer 137; NMR BS 487c (80 MHz) and varian A60D (60 MHz). UV data were

taken in MeOH; λ_{max} values are in nm and values in parentheses are log ϵ. IR values are recorded in cm^{-1} using nujol film. NMR data were recorded in different



solvents using TMS as an internal standard and chemical shifts are reported in δ values (ppm). Silica gel G was used for TLC and silica gel for column chromatography. Light petroleum used had a boiling range 60–80°C. R_f values are those recorded on TLC plates which were sprayed with 10% aqueous H_2SO_4. The solvent systems for TLC were: (A) benzene: ethyl acetate (17:3); (B) benzene: ethyl acetate (9:1); (C) benzene: ethyl acetate (4:1); (D) benzene alone.

3.1. *7-Cinnamyloxy-3-methoxyflavone* (2)

To an acetone solution of 7-hydroxy-3-methoxyflavone (1, 2·5 g) was added cinnamyl bromide (1·84 ml, 1·1 mole equiv.) and anhydrous K_2CO_3 (8 g). The resulting solution was refluxed for 3 h, acetone distilled off and water (200 ml) added to the residue. The solid was collected and crystallized from methanol when it gave 2 as colourless crystals (2·8 g); m.p. 121–22°C; R_f 0·61 (solvent A); IR 1710 (C=0); λ_{max} 219, 259

and 314 (4·00, 4·45 and 4·26 respectively); 60 MHz NMR ($CDCl_3$): 3·90, (3H, s, $-OC\underline{H}_3$), 4·75 (2H, d, J = 5Hz, $-OC\underline{H}_2$), 6·10–6·50 (2H, m, $-C\underline{H}=C\underline{H}-$), 6·73 (1H, br s, H-8), 6·96 (1H, dd, J = 10Hz and 3Hz, H-6), 7·16–8·00 (10H, m, 2X $C_6\underline{H}_5$) and 8·14 (1H, d, J = 10Hz, H-5) (Found: C, 78·5; H, 5·4. $C_{25}H_{20}O_4$ requires: C, 78·1; H, 5·2%).

3.2. *The Claisen rearrangement of 7-cinnamyloxy-3-methoxyflavone [Formation of 8-(1-phenyl-2-propenyl)-7-hydroxy-3-methoxyflavone* (3)]

7-Cinnamyloxy-3-methoxyflavone (2, 1·8 g) was refluxed in *N N*-dimethylaniline (35 ml) for 4 h and then treated with ice-cold dil. HCl (100 ml., 1:1). The solid collected was dried and crystallized from benzene when 3 was obtained as colourless crystals (1·1 g), m.p. 209–10°C; R_f 0·25 (solvent B); λ_{max} 221, 256 and 316 (4·4, 4·39 and 4·37 respectively); 60 MHz NMR (DMSO-d_6): 3·78 (3H, s, $-OC\underline{H}_3$), 5·19 (1H, m, CH_2 = CH—C<u>H</u> Ar_2), 5·30–5·65 (2H, m, $C\underline{H}_2$=CH), 6·23–6·83 (1H, octet, $-C\underline{H}=CH_2$), 7·08 (1H, d, J = 10Hz, H-6), 7·17—7·36 (10H, m, 2X $C_6\underline{H}_5$) and 7·89 (1H, d, J = 10 Hz, H-5) (Found: C, 78·5; H, 5·6. $C_{25}H_{20}O_4$ requires: C, 78·1; H, 5·2%).

Its acetate prepared by the Ac_2 O-pyridine method crystallised from benzene-light petroleum mixture as colourless needles, m.p. 160–61°C; R_f 0·4 (solvent D); 60 MHz NMR ($CDCl_3$): 2·12 (3H, s, $-OCOC\underline{H}_3$)., 3·85 (3H, s, $OC\underline{H}_3$), 5·13 (1H, m, J_{AX} = 8·0 Hz, $J_{AB}=J_{AC}$ = 1·6 Hz, $CH_2=C\underline{H}-C\underline{H}-Ar_2$), 5·43 (2H, m, $C\underline{H}_2=CH-$), 6·38 (1H, m, $CH_2=C\underline{H}-CH\ Ar_2$), 7·13 (1H, d, J = 9Hz, H-6), 7·18—7·71 (10H, m, 2X $C_6\underline{H}_5$) and 8·20 (1H, d, J = 9Hz, H-5) (Found: C, 76·2; H, 5·1. $C_{27}H_{22}O_5$ requires: C, 76·0; H, 5·2%).

3.3. 8-(1-*Phenyl-2-propenyl*)-3, 7-*dimethoxyflavone* (5)

An acetone solution of 3 (100 mg) was refluxed with Me_2SO_4 (0·028 ml) and K_2CO_3 (1 g) for 3 h. The solvent was distilled off and water added to the residue. The dimethylether 5 crystallized from methanol as colourless crystals (80 mg); m.p. 188°C; R_f 0·6 (solvent B); ν_{max} 1675 (C = 0); λ_{max} 276 and 222 (4·30 and 4·23 respectively); 80 MHz NMR ($CDCl_3$): 3·83, 3·90 (6H, 2s, 2X—$OC\underline{H}_3$), 5·08 (1H, m, CH_2=CH—C<u>H</u> Ar_2), 5·15–5·62 (2H, m, $C\underline{H}_2$ = CH—), 6·10–6·48 (1H, m, CH—C<u>H</u>= CH_2), 7·05 (1H, d, J = 10Hz, H-6), 7·12—7·46 (10H, m, 2X—$C_6\underline{H}_5$) and 8·9 (1H, d, J = 10Hz, H-5) (Found: C, 78·0; H, 5·8. $C_{26}H_{22}O_4$ requires; C, 78·4; H, 5·6%).

3.4. 4-*Methyl-7-cinnamyloxycoumarin* (7)

An acetone solution of 4-methyl-7-hydroxycoumarin (6, 2 g) was refluxed with cinnamyl bromide (1·12 ml., 1·1 mole) and anhydrous K_2CO_3 (10 g) for 5 hr. 4-Methyl-7-cinnamyloxycoumarin (7) crystallized from ethyl acetate as colourless crystals (1·8 g); m.p. 178–79°C; R_f 0·45 (solvent B); λ_{max} 219, 253 and 320 (4·52, 4·57 and 4·46 respectively); 60 MHz NMR (DMSO-d_6): 2·45 (3H, d, J = 1Hz, $-C\underline{H}_3$), 4·82 (2H, d, J = 5Hz, O—$C\underline{H}_2$—), 6·15 (1H, q, J = 1Hz, H-3), 6·40–6·64 (2H, m, Ar—C<u>H</u>=C<u>H</u>—), 6·70 (1H, d, J = 2·5Hz, H-8), 6·95 (1H, dd, J = 10Hz and 2·5 Hz,

H-6), 7·30 (5H, d, J = 1·5Hz, C_6H_5) and 7·60 (1H, d, J = 10Hz, H-5) (Found: C, 78·4; H, 5·5. $C_{19}H_{16}O_3$ requires: C, 78·1; H, 5·5%).

3.5. *The Claisen rearrangement of* 7 [*(Formation of 4-methyl-8-(1-phenyl-1-propenyl)-7-hydroxycoumarin* (9)]

The above cinnamyloxycoumarin (7, 1·2 g) was refluxed in *NN*-dimethylaniline 20 ml) for 4 hr and the reaction worked up as in the previous case. The rearranged coumarin (9) crystallized from ethyl acetate as colourless needles (700 mg); m.p. 222-23°C; R_f 0·6 (solvent A); λ_{max} 220, 250 and 323 (4·54, 4·53 and 4·46 respectively); 60 MHz NMR ($CDCl_3$): 1·68 (3H, d, J = 7Hz, CH_3—CH=), 2·42 (3H, d, J = 1Hz, —CH_3 in 4 position), 6·10 (1H, d, J = 1Hz, H-3), 6·68 (1H, q, J=7Hz, $=C\langle^{H}_{CH_3}$), 7·00 (1H, d, J = 9Hz, H-6), 7·28 (5H, s, —C_6H_5) and 7·55 (1H, d, J = 9Hz, H-5) (Found: C, 78·0; H, 5·4. $C_{19}H_{16}O_3$ requires: C, 78·1; H, 5·5%).

It formed an acetate (10) (Ac_2 O-pyridine method) which crystallized from ethanol as colourless crystals, m.p. 139-40°C; R_f 0·75 (solvent B); 60 MHz NMR ($CDCl_3$): 1·64 (3H, d, J = 7Hz, =CH(CH_3), 2·06 (3H, s, O—CO—CH_3), 2·56 (3H, d, J = 1·5Hz, —CH_3 at C_4), 6·25 (1H, q, J=1·5Hz, H_3), 6·35 (1H, q, J=7Hz, $=C\langle^{H}_{CH_3}$), 7·20 (1H, d, J = 10Hz, H_6), 7·25, (5H, s, C_6H_5) and 7·50 (1H, d, J = 10Hz, H-5) (Found: C, 75·1; H, 5·8. $C_{21}H_{18}O_4$ requires: C, 75·4; H, 5·4%).

3.6. *4-Methyl-8 (1-phenyl-1-propenyl)-7-methoxycoumarin* (11)

An acetone solution of 9 (100 mg) was refluxed with Me_2SO_4 (0·6, 1·1 mole equiv.) and anhydrous K_2CO_3 (1 g) for 3 h. 11 crystallized from methanol as colourless crystals (70 mg); m.p. 165°C; R_f 0·78 (solvent B); λ_{max} 220, 250 and 321 (4·20, 4·18 and 4·14 respectively); 60 MHz NMR ($CDCl_3$): 1·61 (3H, d, J = 7Hz, CH_3—CH=), 2·42 (3H, d, J = 1·5Hz, CH_3 in 4 position), 3·83 (3H, s, O—CH_3), 6·11 (1H, q, J = 1·5 Hz, H-3), 6·42 (1H, m, $=C\langle^{H}_{CH_3}$), 6·92 (1H, d, J = 9Hz, H-6), 7·18 (5H, s, —C_6H_5) and 7·56 (1H, d, J = 9Hz, H-5) (Found: C, 78·2; H, 5·9. $C_{20}H_{18}O_3$ requires: C, 78·4; H, 5·9%).

3.7. *7-Cinnamyloxyisoflavone* (13)

An acetone solution of 7-hydroxyisoflavone (Iyer *et al* 1951) (12, 1·5 g) was refluxed with cinnamyl bromide (0·81 ml, 1·1 mole) and anhydrous K_2CO_3) for 5 h. 7-Cinnamyloxyisoflavone (13) crystallized from ethyl acetate as colourless crystals (800 mg); m.p. 152-53°C; R_f 0·75 (solvent A); 80 MHz NMR ($CDCl_3$); 4·62 (2H, d, J = 5Hz, O—CH_2), 6·20 (2H, m, —CH=CH), 6·80 (1H, d, J = 2·5Hz, H-8), 6·95 (1H, dd, J_{meta} = 2·5Hz, J_{ortho} = 9Hz, H-6), 7·32 (10H, m, 2X C_6H_5), 7·76 (1H, s, H-2) and 8·1 (1H, d, J = 9Hz, H-5) (Found: C, 81·6; H, 5·2. $C_{24}H_{18}O_3$ requires: C, 81·3; H, 5·1%).

3.8. *The Claisen rearrangement of 7-cinnamyloxyisoflavone* (13) [*Formation of 8-(1-phenyl-1-propenyl)-7-hydroxyisoflavone* (14)]

7-Cinnamyloxyisoflavone (13, 0·7 g) was refluxed with *NN*-dimethylaniline (10 ml)

for 8h. 8-(1-Phenyl-1-propenyl)-7-hydroxy-isoflavone (14) crystallized from methanol as colourless crystals (0·5 g); m.p. 192-93°C; R_f 0·5 (solvent A); λ_{max} 218 and 251 (4·42 and 4·64 respectively); 60 MHz NMR ($CDCl_3$): 1·70 (3H, d, J = 7Hz, $C\underline{H}_3-CH=$), 6·61 (1H, q, $\underline{H}-C-CH_3$), 7·02 (1H, d, J = 9Hz, $\underline{H}$-6), 7·21 (5H, s, $-C_6\underline{H}_5$), 7·40 (5H, m, $-C_6\underline{H}_5$), 7·71 (1H, s, $\underline{H}$-2) and 8·16 (1H, d, J = 9Hz, $\underline{H}$-5) (Found: C, 81·4; H, 5·2. $C_{24}H_{18}O_3$ requires: C, 81·3, H, 5·1%).

The monoacetate (15) prepared by the acetic anhydride-pyridine method crystallized as colourless flakes, m.p. 142-43°C; R_f 0·6 (solvent A); λ_{max} 218 and 250 (4·53 and 4·73 respectively); 60 MHz NMR ($CDCl_3$): 1·63 (3H, d, J = 7Hz, $C\underline{H}_3-CH=$) 2·03 (3H, s, $O-CO-C\underline{H}_3$), 6·48 (1H, q, $-C\underline{H}-CH_3$), 7·20 (5H, s, $C_6\underline{H}_5$), 7·30 (5H, m, $C_6\underline{H}_5$), 7·38 (1H, d, J = 9Hz, $\underline{H}$-6), 7·85 (1H, s, $\underline{H}$-2), and 8·33 ppm (1H, d, J = 9Hz, $\underline{H}$-5) (Found: C, 79·5; H, 5·2. $C_{25}H_{20}O_4$ requires: C, 79·7; H, 5·1%).

Acknowledgements

The authors express their sincere gratitude to UGC, New Delhi for award of fellowship to AK and to CSIR New Delhi for a fellowship to DKT.

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