Tetrahedron Vol. 35, pp. 697-699
0040-4020/79/0301-0697/$02.00/0

CLAISEN REARRANGEMENTS—IX[1]

SYNTHESIS OF THE COUMARIN, FUROPINNARIN

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(*Received in UK 22 September 1978*)

Abstract—The first example of a successful *para*-Claisen rearrangement of a 1,1-dimethylallyl aryl ether has been realised. The rearrangement product, a natural coumarin, on methylation gave another natural coumarin, furopinnarin.

In 1970, two new coumarins, pinnarin (1) and furopinnarin (2) were isolated from the roots of *Ruta pinnata*,[2] the structure of the latter being assigned primarily from spectroscopic evidence. More recently, the phenol (3) corresponding to 2 was isolated from the aerial parts of *Peucedanum stenocarpum*.[3] The 1,1-dimethylallyl group at C_8 in pinnarin (1) was introduced synthetically[4] by the regiospecific *ortho*-Claisen rearrangement of the 3,3-dimethylallyl aryl ether (4). However, the presence of the furan ring precluded a similar approach for the synthesis of 2 and 3. Consequently it was believed that if the 1,1-dimethylallyl ether (5) could be prepared, its pyrolysis should result in a *para*-Claisen rearrangement to 2 with a double inversion and hence net retention of the ends of attachment of the allyl group.

The pyrolysis of 1,1-dimethylallyl ethers of phenols possessing a vacant *ortho* position has been shown to be a convenient method for the introduction of a prenyl moiety *ortho* to a phenol.[5] Although *para*-Claisen rearrangements of 3,3-dimethylallyl aryl ethers are well known,[6] no report has yet been recorded of the successful *para*-Claisen rearrangement of a 1,1-dimethylallyl aryl ether. Indeed, the 1,1-dimethylallyl ether (8), which, having both *ortho* positions in the aryl moiety blocked and the *para* position vacant, was expected to rearrange to 9, remarkably underwent rearrangement[7] solely to the *ortho* position yielding the stable *ortho*-dienone (10). Surprisingly, no trace of the anticipated *para*-rearrangement product (9) could be detected, even on prolonged pyrolysis of 10. It is indeed unusual for an *ortho*-dienone to be the stable product of a Claisen rearrangement especially when *para*-rearrangement and rearomatisation is possible.[6] Consequently it was of considerable interest to prepare 5 and to study its behaviour towards pyrolysis.

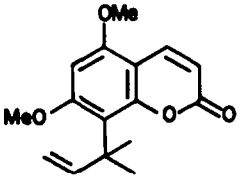
The established method for preparing 1,1-dimethylallyl aryl ethers is by semi-hydrogenation of the corresponding 1,1-dimethylpropargyl ether.[5] Bergaptol[8] (6), on etherification with 3-chloro-3-methylbutyne, gave two products, the required 1,1-dimethylpropargyl ether (7; 30%) and the corresponding C,O-bisalkylated analogue (11, 9%), but unreacted bergaptol remained even after prolonged reaction. It is interesting that no trace of the C-alkylated phenol (12) could be detected. This anomaly, namely that when C-alkylation of the phenol occurs the product is more readily etherified than the starting material has previously been observed[7] but not yet rationalised. Semi-hydrogenation of 7 proceeded cleanly over 5% Pd–$BaSO_4$ to give 5 (95%). This 1,1-dimethylallyl ether was stable to silica[7] but rearranged smoothly at 120° to give one product (56%) apart from some cleavage (32%) to bergaptol. The product, which was phenolic (UV base shift), was isomeric with the starting material and differed only in its NMR spectrum in that the sole benzenoid proton in 5 was absent and a C-1,1-dimethylallyl group was present. This clearly indicated that a *para*-Claisen rearrangement had taken place. The spectral data of the compound are in complete agreement with those reported[3] for the phenol (3) from *P. stenocarpum*. Treatment of 3 with ethereal diazomethane afforded the corresponding methyl ether (2), the spectral properties of which were in complete accord with those quoted for natural furopinnarin.[2] Since bergaptol has been synthesised,[8] this sequence constitutes a total synthesis of furopinnarin and its phenolic analogue.

It is not immediately apparent why the 1,1-dimethylallyl ether (5) should undergo the *para*-rearrangement and show no trace of an intermediate *ortho*-dienone while the structurally closely related coumarin (8) behaved in such an anomalous manner. Efforts to resolve these questions are currently in progress.

EXPERIMENTAL

M.ps were determined with a Kofler hot stage apparatus. Microanalyses were performed by Mrs. W. Harkness and her staff. IR spectra were recorded on a Perkin Elmer 225 spectrophotometer by Mrs. F. Lawrie and her staff. ^{1}H NMR spectra of solns in $CDCl_3$ with TMS as internal standard were recorded on a Varian T-60 spectrometer. Mass spectra were recorded by Mr. A. Ritchie with an AEI-GEC MS12 mass spectrometer. UV spectra of MeOH solns were recorded on a Unicam SP800 spectrophotometer. Kieselgel GF_{254} (Merck) was used for preparative tlc. Light petroleum refers to the fraction of b.p. 60–80°.

5-O-(1,1-Dimethylpropargyl)bergaptol (7). K_2CO_3 (4.4 g) and KI (0.51 g) were added to a stirred soln of 6 (3 g) in aqueous acetone (2% v/v; 250 ml) and stirred for 1 hr at room temp. 3-Chloro-3-methylbut-1-yne (4.4 g) was added and the mixture refluxed for 20 hr. K_2CO_3 (4.4 g) and 3-chloro-3-methylbut-1-yne (4.4 g) were then added and refluxing continued for a further 4 hr. Work up, by filtration and evaporation and extraction into EtOAc, gave, on evaporation of solvent, a brown gum. Purification by tlc ($CHCl_3$) gave a yellow oily solid (2.03 g). Trituration with ether/light petroleum followed by crystallisation of the solid residue from $CHCl_3$ afforded 5-O-(1,1-*dimethylpropargyl*)*bergaptol* (7) as yellow needles, m.p. 111–112° (1.25 g, 30%) (Found: C, 71.8; H, 4.6. $C_{16}H_{12}O_4$ requires: C, 71.65; H, 4.45%); NMR signals at δ 1.75 (6H, s), 2.50 (1H, s), 6.30 (1H, d, J = 9.5 Hz), 6.68 (1H, d, J = 2 Hz), 7.33 (1H, s), 7.56 (1H, d,



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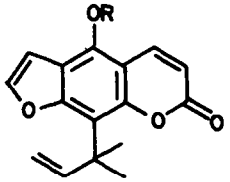
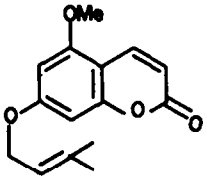


2: R = Me
3: R = H



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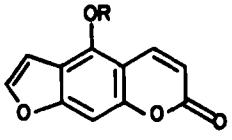
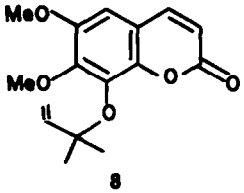


5: R = $CMe_2CH{=}CH_2$
6: R = H
7: R = $CMe_2C{\equiv}CH$



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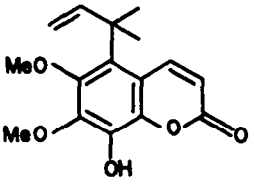

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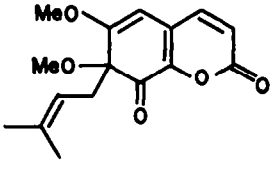

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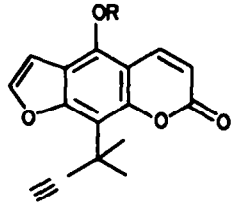

11: R = $CMe_2C{\equiv}CH$
12: R = H

J = 2 Hz) and 8.17 (1H, d, J = 9.5 Hz); mass spectral peaks at *m/e* 268 (M^+, 15%), 202 (100), 174 (42) and 145 (21); ν_{max}^{KBr} 3290, 3130, 2100, 1730 and 1625 cm^{-1}. Evaporation of the mother liquors of trituration gave a yellow oil (0.61 g) which, after preparative tlc ($CHCl_3$) and crystallisation from EtOAc–light petroleum, afforded 5 - O - 7 - *bis*(1,1 - *dimethylpropargyl*)*bergaptol* (11) as yellow needles, m.p. 92–95° (0.41 g, 9%); NMR signals at δ 2.01 (12H, s), 2.31 (1H, s), 6.32 (1H, d, J = 9.5 Hz); 6.68 and 7.56 (each 1H, d, J = 2 Hz) and 8.19 (1H, d, J = 9.5 Hz); mass spectral peaks at *m/e* 334 (M^+, 14%), 268 (95), 253 (100), 202 (92) and 174 (38).

5 - O - (1,1 - *Dimethylallyl*)*bergaptol* (5). 5% Pd-$BaSO_4$ (40 mg) was added to a soln of 7 (165 mg) in EtOAc (50 ml). After hydrogenation at room temp. for 30 min the uptake of H_2 was 1 mole. Filtration through celite followed by evaporation of solvent gave 5 as a yellow solid, m.p. 115–116° (160 mg, 95%); NMR signals at δ 1.48 (6H, s), 4.98 (2H, AB part of ABX), 6.12 (1H, X part of ABX), 6.23 (1H, d, J = 9.5 Hz), 6.70 (1H, d, J = 2 Hz), 7.15 (1H, s), 7.58 (1H, d, J = 2 Hz) and 8.10 (1H, d, J = 9.5 Hz).

para-*Claisen rearrangement*. The ether (5, 160 mg) was heated in a sublimation block at 120° for 1 hr. On cooling, the yellow solid residue was purified by tlc (EtOAc–light petroleum; 7:3) to give 6 (44 mg, 32%) and 3 which crystallised from EtOAc–light petroleum as yellow needles, m.p. 231–235° (lit.[3] 213–215°) (89 mg, 56%) (Found: C, 71.0; H, 5.3. Calc. for $C_{16}H_{14}O_4$: C, 71.1; H, 5.2%); NMR signals at δ 1.73 (6H, s). 4.87 (2H, AB part of ABX), 6.10 (1H, d, J = 9.5 Hz), 6.31 (1H, X part of ABX), 7.05 and 7.70 (each 1H, d, J = 2 Hz) and 8.23 (1H, d, J = 9.5 Hz); mass spectral peaks at *m/e* 270 (M^+, 82%), 255 (100), 227 (79), 215 (71) and 199 (44); ν_{max}^{KBr} 3150, 1690 and 1610 cm^{-1}; λ_{max} 253, 267 (sh), 274, 292 and 315 nm (log ϵ 4.01, 4.22, 4.26, 4.02 and 3.95), λ_{max} (in base) 237, 262 (sh), 291, 332 and 402 nm (log ϵ 4.05, 3.91, 4.31, 3.85 and 3.53).

Furopinnarin (2). A soln of 3 (200 mg) in ether (100 ml) was kept with a 10-fold excess of ethereal diazomethane for 24 hr. Evaporation of the solvent and purification of the residue by tlc (EtOAc–light petroleum; 1:1) afforded 2 which crystallised from benzene–hexane as yellow needles, m.p. 124–127° (lit.[2] 124–125°) (182 mg, 90%) (Found: C, 71.85; H, 5.4. Calc. for $C_{17}H_{16}O_4$: C, 71.85; H, 5.65%); NMR signals at δ 1.78 (6H, s), 4.17 (3H, s), 5.00 (2H, AB part of ABX), 6.20 (1H, d, J = 9.5 Hz), 6.43 (1H, X part of ABX), 6.96 and 7.49 (each 1H, d, J = 2 Hz) and 8.10 (1H, d, J = 9.5 Hz); mass spectral peaks at *m/e* 284 (M^+, 95%), 269 (100), 241 (30), 229 (63), 202 (96) and 174 (61); $\nu_{max}^{CCl_4}$ 2998, 1743, 1622 and 1478 cm^{-1}; λ_{max} 227, 254, 270 and 315 nm (log ϵ 4.11, 3.94, 3.96 and 3.79).

Acknowledgement—We are grateful to the S.R.C. for a maintenance award (to K.W.M.L.).

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