Stereoselective Introduction of the Methoxycarbonyl Group into a Tetrahydrofluorenone

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Summary Stereoselective introduction of the methoxy-carbonyl group into the tetrahydrofluoren-9-one (1) giving the 9β -methoxycarbonyl derivative (5) has been achieved in high yield.

MUCH attention has been focused on the synthesis of hydrofluorenone derivatives which may serve as important intermediates in the total synthesis of gibberellins, $^{1-4}$ Introduction of the methoxycarbonyl group into hydrofluorenones has also been studied. 3,4 We report here a stereoselective and efficient synthesis of the 9β -methoxycarbonyltetrahydrofluorene (5), which has a similar functionality to that of ring B in gibberellins, starting from the tetrahydrofluorenone (1a).

Reaction of the trimethylsilyl ether (1b), m.p. 164°, with dimethylsulphonium methylide in anhydrous tetrahydrofuran(THF)-hexamethylphosphoric triamide (-20 °C; 30 min) afforded stereoselectively the β -epoxide (2b) \dagger [m.p. 168 °C, δ (CDCl₃) 2·87 (1H, d, J 4·3 Hz, Hb), 3·41 (1H, s, 9a-H), 3.66 (1H, d, J 4.3 Hz, Ha)] in 90% yield as the sole product, while an epimeric mixture (3:1) of the β - (2b) and α -epoxide (3b) [m.p. 155°, δ (CDCl₃) 3·13 (1H, d, J 4·0 Hz, Ha), 3·37 (1H, s, 9a-H), and 3·49 (1H, d, J 4·0 Hz, Hb)] was obtained in 60% yield when the reaction was carried out in anhydrous Et₂O-THF. Similar reactions of the acetate (1c) and the tetrahydropyranyl ether (1d) in anhydrous Et₂O-THF afforded a 1:1 epimeric mixture (30% yield) of (2c), m.p. 173-175°, and (3c), m.p. 205-208°, and a 3:2 mixture (60% yield) of (2d), m.p. $151-154^{\circ}$, and (3d), m.p. 175-176°, respectively. The stereochemistry of the oxiran rings was assigned on the basis of NOE measurement.

Rearrangement of the β -epoxide (2b) with BF₃-Et₂O in anhydrous THF at -20° afforded exclusively the β -aldehyde (4b) [m.p. 149°, δ (CDCl₃) 9·85 (1H, d, J 2·2 Hz)] in

90% yield. A similar reaction of the acetate (2c) also gave the corresponding β -aldehyde (4c), m.p. 143°, in 70% yield; however, an epimeric mixture (6:1) of (4c) and its isomer was obtained (84%) when the reaction was carried out in anhydrous Et₂O. A similar stereoselectivity was observed for the α -epoxide (3c): treatment of (3c) with BF₃-Et₂O in THF gave only the β -aldehyde (4c) (65%), although reaction in Et₂O gave a 1:1 epimeric mixture of the aldehydes.

† Satisfactory elemental analyses were obtained for all new compounds, and spectroscopic data obtained were in agreement with the structures shown. The product ratios indicated were estimated by n.m.r. spectroscopy.

Mild Jones oxidation (0°; 30 s) of the β -aldehyde (4b), and subsequent methylation and treatment with toluene-psulphonic acid yielded the 9β -methoxycarbonyl derivative (5a) [m.p. 145°, m/e 332 (M^+), $\nu_{\rm max}$ (CHCl₃) 3600, 1775, and 1745 cm⁻¹, δ (CDCl₃) 3·49 (1H, d, J 9·2 Hz), 3·85 (3H, s), 3·88 (3H, s), and 3.88 (1H, d, J 9.2 Hz)] in 90% overall yield.

We thank Professor K. Nakanishi, Columbia University, for helpful advice, and Dr. S. Sato, Nichiden Varian Ltd., for NOE measurements.

(Received, 1st April 1974; Com. 373.)

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