Total synthesis of apigenin 7,4′-di-O-β-glucopyranoside, a component of blue flower pigment of Salvia patens, and seven chiral analogues

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Abstract—We have succeeded in the first total synthesis of apigenin 7,4′-di-O-β-D-glucopyranoside (1a), a component of blue pigment, protodelphin, from naringenin (2). Glycosylation of 2 according to Koenigs–Knorr reaction provided a monoglucoside 4a in 80% yield, and this was followed by DDQ oxidation to give apigenin 7-O-glucoside (12a). Further glycosylation of 4′-OH of 12a with 2,3,4,6-tetra-O-acetyl-α-D-glucopyranosyl fluoride (5a) was achieved using a Lewis acid-and-base promotion system (BF3·Et2O, 2,6-di-tert-butyl-4-methylpyridine, and 1,1,3,3-tetramethylguanidine) in 70% yield, and subsequent deprotection produced 1a. Synthesis of three other chiral isomers of 1a, with replacement of D-glucose at 7 and/or 4′-OH by L-glucose (1b–d), and four chiral isomers of apigenin 7-O-β-glucosides (6a,b) and 4′-O-β-glucosides (7a,b) also proved possible.

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