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Stereoselective Total Synthesis of (±)-Samin, the General Furofuran Lignan Precursor

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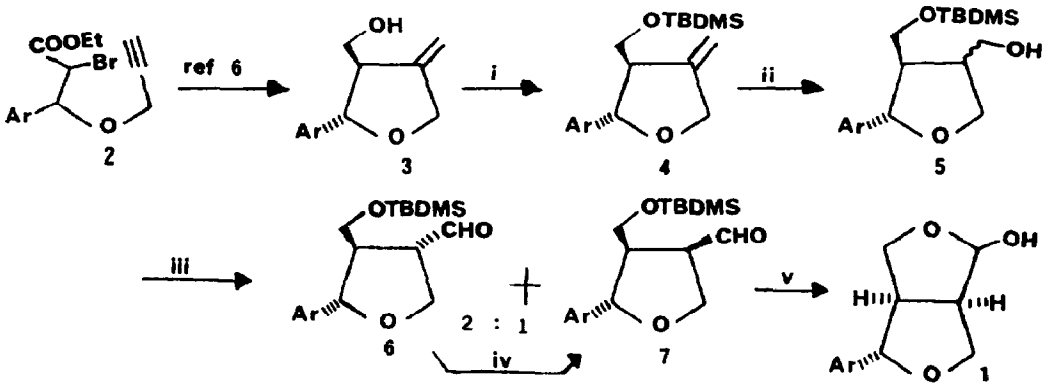
Abstract : A concise stereoselective synthesis of the general furofuran lignan precursor (±)-Samin 1 has been achieved through a radical annulation reaction in good overall yield.

The furofuran lignans are one of the largest groups of naturally occurring lignans[1], whose members show a variety of biological activities[2]. Although interesting syntheses[3] providing these natural products have been developed, the tin-hydride mediated radical cyclisation reaction is still unexplored. We report here a stereoselective synthesis of racemic Samin 1[4] through radical annulation route in good overall yield. Samin 1 has been shown[5] to be a suitable precursor for both symmetrical and unsymmetrical types of the furofuran lignans, such as Acuminatolide, Sesamolin and Sesamin.

Recently we reported[6] the synthesis of racemic Paulownin and Isogmelinol using radical cyclisation of the bromoester 2 as a key step. The present synthesis consists of only four steps starting from the easily accessible alcohol 3[6] (Scheme)



Ar=3,4-Methylenedioxyphenyl

Scheme. Reagents and Conditions : i, TBDMS-Cl, Et_3N, 4-DMAP (cat), imidazole (cat)., CH_2Cl_2, 12h at rt; ii, B_2H_6, 0 °C, 1.5h then 3N NaOH, H_2O_2 (30%), r.t.; iii, $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2, -78 °C to r.t., 5h; iv, NaOMe, MeOH, 10h, r.t.; v, excess $Bu_4NF.3H_2O$, THF, 6h, r.t.

without employing any difficult procedure. Thus, treatment of the alcohol 3 with TBDMS-Cl and

Et_3N in presence of 4-DMAP (cat) afforded the olefin 4[7] in 85% yield. Hydroboration of the olefin 4 followed by oxidation with alkaline H_2O_2 (30%) furnished the alcohol 5 in about 70% yield. It was not possible to predit in this stage (^1H NMR) whether 5 was a mixture of stereoisomers or not. But this was immediately realised when the crude alcohol 5 was subjected to Swern oxidation to give the isomeric mixture of the aldehyde 6 and 7 in a ratio of 2:1 (^1H NMR). The crude mixture of the aldehydes 6 and 7 was treated with methanolic NaOMe to afford quantitatively the thermodynamically more stable cis-aldehyde 7. On treatment with excess of $Bu_4NF.3H_2O$ in THF at room temperature, aldehyde 7 furnished Samin 1[8,9] in 76% yield as a crystalline solid, m.p. 108-109°C (lit.[4b] m.p. 106°C). Surprisingly, under identical reaction condition, the crude mixture of aldehydes 6 and 7 also afforded exclusively Samin 1 in 80% yield. Probably the fluoride ion from Bu_4NF present in the reaction mixture was responsible for in situ isomerisation finally leading to Samin 1 as the sole product.

In conclusion, a stereoselective synthesis of the versatile furofurano lignan precursor Samin in racemic form has been accomplished through radical cyclisation reaction.

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7. All compounds reported here gave satisfactory spectral and analytical data consistant with assigned structures.
8. Selected spectral data for 1 : IR (KBr) : 3420 (br), 2940, 2900, 1510, 1500, 1450, 1350, 1270, 1250, 1220, 1100, 1070, 1030 cm^{-1}; ^1H NMR ($CDCl_3$) : δ 2.81-2.95 (m, 1H), 3.0-3.12 (m, 1H), 3.25 (brs, 1H), 3.55 (dd, J = 9 and 7.7 Hz, 1H), 3.91 (dd, J = 9 and 1 Hz, 1H), 4.15 (dd, J = 9 and 6.2 Hz, 1H), 4.35-4.45 (m, 2H), 5.38 (s, 1H), 5.95 (s, 2H), 6.75-6.95 (m, 3H); ^{13}C NMR ($CDCl_3$): δ 52.7, 53.6, 69.4, 71.1, 86.8, 100.9, 102.2, 106.5, 108.1, 119.5, 134.7, 147.2, 148.0.
9. IR, ^1H NMR and ^{13}C NMR spectra are quite identical with the spectra kindly provided by Professor K. Ogasawara, Tohoku University, Japan and Dr. D.W. Knight, University Park, Nottingham. We are grateful to them.

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