Tetrahedron Letters, Vol. 33, No. 40, pp. 6025-6026, 1992.
Printed in Great Britain

0040-4039/92 $5.00 + .00
Pergamon Press Ltd

# Stereoselective Radical Annulation Route to the Synthesis of (±)-Paulownin and (±)-Isogmelinol

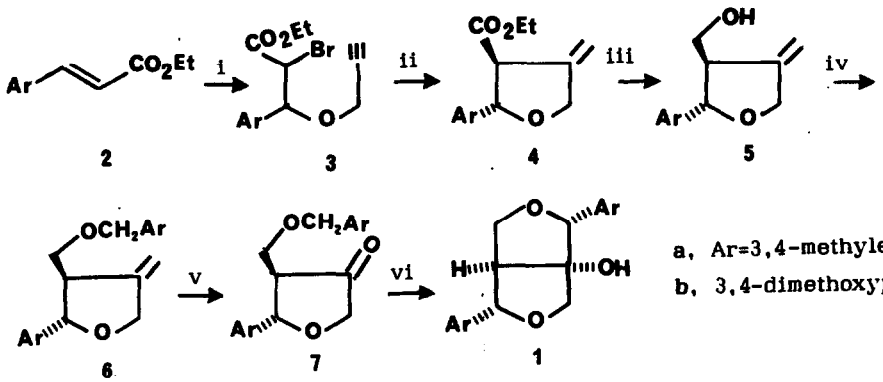
Sankar Adhikari and Subhas Roy*

Department of Organic Chemistry, Indian Association for the Cultivation of Science, Jadavpur, Calcutta - 700 032, India.

**Abstract** : A highly stereocontrolled synthesis of (±)-paulownin (**1a**) and (±)-isogmelinol (**1b**) is reported involving intramolecular radical cyclisation reaction as a key step.

Due to the widespread occurance in nature and broad range of biological activities, Lignans have attracted a considerable attention to organic chemists over the years. Though, several syntheses have been reported,[1] the radical cyclisation reactions, which witnessed a renaissance recently leading to the preparation of complex natural products,[2] remained unexplored. We now report a radical annulation strategy for the stereoselective synthesis of **1a**[3] and **1b**[4] in racemic form in good overall yield.

Cinnamic ester **2**, on treatment with N-bromosuccinimide and propargyl alcohol in $CH_2Cl_2$[5] afforded the bromoester **3**[6] in about 78-80% yield (3b, m.p. 80-81°C). Intramolecular radical cyclisation of **3** was successfully achieved with n-$Bu_3SnH$ and AIBN (cat.) in refluxing benzene (0.02M) producing exclusively,[7] the ester **4** in about




a, Ar=3,4-methylenedioxophenyl
b, 3,4-dimethoxyphenyl

**Scheme**; Reagents and conditions : i, NBS, propargyl alcohol (excess), $CH_2Cl_2$, -15°C to rt, overnight; ii, n-$Bu_3SnH$, AIBN (cat.), benzene, reflux, 4 h; iii, $LiAlH_4$, $Et_2O$, reflux, 3 h; iv, NaH, DME, $ArCH_2Cl$, reflux, 20 h; v, $O_3$, $CH_2Cl_2$, -78°C, 15 min for **6a**; $OsO_4$, $NaIO_4$, $Et_2O$, $H_2O$, rt, overnight for **6b**; vi, $h\nu$, benzene, 45 min for **7b**.

80-82% yield. Reduction of ester **4** with $LiAlH_4$ in refluxing $Et_2O$ furnished **5** in almost quantitative yield. Alcohol **5**, on reflux with NaH and the corresponding benzyl chloride in DME produced the protected alcohol **6** in 75-76% yield. Oxidation of **6a** to the ketone **7a** was performed by ozonolysis at -78°C in $CH_2Cl_2$ in about 79% yield. Since, the conversion of **7a** to **1a** has already been done,[1b] we report here a formal synthesis of **1a**. Ozonolysis of **6b** under identical condition gave an intractable mass. **6b** underwent smooth oxidation to the ketone **7b** with $OsO_4$ and $NaIO_4$ in aqueous $Et_2O$[8] in about 90% yield. **7b** on irradiation with 450W Hanovia medium pressure mercury lamp for 45 min, in benzene in a quartz vessel afforded **1b**[9] in 72% yield, m.p. 150-151°C (conversion 90%, GC).

In conclusion, the stereoselective radical annulation strategy has been demonstrated by total synthesis of racemic paulownin and isogmelinol in only six steps from cinnamic ester.

**References and Notes**


1. (a) Ward, R.S. Chem. Soc. Rev. **1992**, 75 and references cited therein. (b) Kraus, G.A.; Li Chen J. Am. Chem. Soc. **1990**, 112, 3464 and references cited therein. (c) Jansen J.F.G.A.; Feringa, B.L. Tetrahedron Lett. **1991**, 32, 3239.

2. (a) Giese, B. 'Radicals in Organic Synthesis, Formation of Carbon-Carbon Bonds'. Pergamon Press, Oxford, **1986**. (b) Ramaiah, M. Tetrahedron **1987**, 43, 3541. (c) Srikrishna, A. Current Science **1987**, 56, 392. (d) Curran, D.P. Synthesis, **1988**, 417 and 489.

3. Takahashi, K.; Nakagawa, N. Chem. Pharm. Bull. **1966**, 14, 641.

4. Tasukamoto, H.; Hisada, S.; Nishibe, S. Chem. Pharm. Bull. **1984**, 32, 2730 and 4482.

5. Okabe, M.; Abe, M.; Tada, M. J. Org. Chem. **1982**, 47, 1775.

6. All compounds reported here gave satisfactory spectral and analytical data consistant with assigned structures.

7. No reduced product was formed. 9.9 Hz coupling constant in $^1H$ NMR for the benzylic methine proton in **4** indicated that the aryl and the carbethoxy groups are trans (ref. 1b).

8. Charlton, A.P.; Morris, G.A.; Sutherland, J.K. J. Chem. Soc. Perkin Trans.1 **1991**, 1205.

9. Selected spectral data for **1b** : IR (KBr) 3370, 1590, 1510, 1415, 1265, 1240, 1140 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) 1.56 (s, 1H), 3.07-3.17 (m, 1H), 3.80-3.92 (m, 14H with three singlets at 3.86, 3.88 and 3.90), 4.05 (d, 1H, J = 9.3 Hz), 4.54 (t, 1H, J = 8.4 Hz), 4.85 (s, 1H), 4.87 (d, 1H, J = 4.8 Hz), 6.82-7.0 (m, 6H).


(Received in UK 21 July 1992)