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A NOVEL REARRANGEMENT OF THE LATIFOLIN SKELETON

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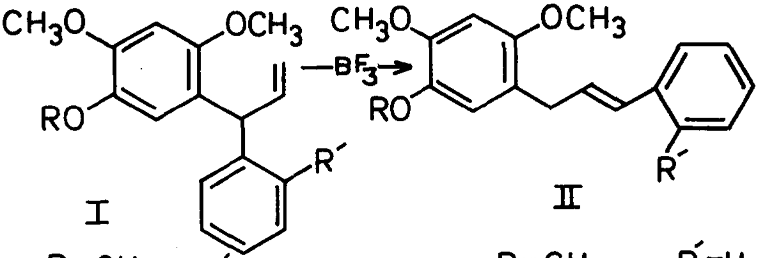
Latifolin (Id) is an important member of the neoflavanoid group of compounds. As recently described[1] its synthesis involves an ionic coupling of trimethoxy benzene (C_6) and o-methoxy cinnamyl cation (C_9), the latter being generated from o-methoxy cinnamyl chloride by a Lewis acid. As a preliminary to this, it was important to know the stability of the latifolin skeleton towards different Lewis acids under mild conditions. For this purpose, latifolin dimethyl ether (Ia) was kept with excess of anhydrous aluminium chloride, anhydrous zinc chloride and borontrifluoride in dry ether solution at room temperature and the product examined from time to time. It was observed that while other Lewis acids did not have any appreciable effect, boron trifluoride caused a complete change of the molecule; the change was slow and complete conversion took about four days. The new product, isolated by column chromatography, was identified as the isomeric benzyl styrene (IIa), m.p.56-57°, λ_{max}^{EtOH} 250 mμ (4.23), 260 mμ (4.15) and 295 mμ (4.03) (Found: C, 73.1; H, 7.3%. $C_{19}H_{22}O_4$ requires C, 72.6; H, 7.0%);

mixed m.p. with authentic sample[1] was undepressed.



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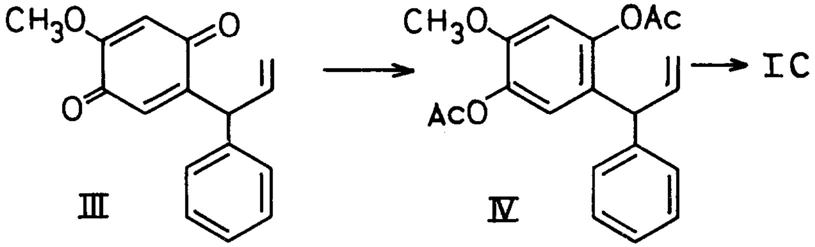
a, $R=CH_3$; $R'=OCH_3$. c, $R=CH_3$; $R'=H$.

b, $R=C_2H_5$; $R'=OC_2H_5$. d, $R=H$; $R'=OH$.

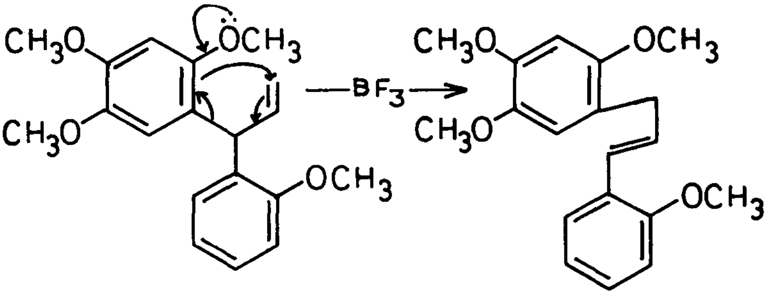
Since isomerisation of this type is novel, some details about the structural requirements and scope were investigated with the help of suitable models and the results are reported in this communication.

It was observed that BF_3 is a specific catalyst in this isomerisation and conversion does not take place with $AlCl_3$, $ZnCl_2$ and also with dry HCl in ether solution. Attempt to accelerate the change by carrying out the reaction at higher temperature has not been fruitful, as it promotes other side reactions and isolation of a pure product becomes difficult. Dihydrolatifolin dimethyl ether is stable to BF_3 showing that the allyl double bond is involved in the isomerisation. The reaction takes place with latifolin diethyl ether[2] (Ib) also and it undergoes similar change giving the benzyl styrene (IIb) as a semi-solid (T.L.C. pure); λ_{max}^{EtOH} 252 mμ and 295 mμ.

It appeared that the ease of this isomerisation was associated with the number and position of methoxyl groups of ring A. Activation from one methoxyl is not enough as 3(2-methoxy phenyl)-3-phenyl propene[3] was stable to BF_3. As a suitable and easily available model compound, 3(2,4,5-trimethoxy phenyl)-3-phenyl propene (Ic) was chosen. It was prepared from 4-methoxydalbergenone m.p.115-116° (III) in two stages: (1) reductive acetylation to 3(2:5-diacetoxy-4-methoxy phenyl)-3-phenyl propene (IV), m.p. 71.5-72.5°; λ_{max}^{EtOH} 278 mμ (3.4) (Found: C, 70.3; H, 6.0. calculated for $C_{20}H_{20}O_5$: C, 70.6; H, 5.9%); (2) methylation of the quinol acetate (IV) by methyl sulphate in aqueous alcoholic sodium hydroxide yielding (Ic) m.p. 55-56°, λ_{max}^{EtOH} 292 mμ (3.7) (Found: C, 75.6; H, 7.5; $C_{18}H_{20}O_3$ requires: C, 76.0; H,7.0%).



Isomerisation of (Ic) with BF_3 was very slow and was almost complete in 10 days. The benzyl styrene (IIc), isolated by chromatography on silver nitrate-silica gel column, crystallised from methanol, m.p. 53-54°, λ_{max}^{EtOH} 273 mμ (4.2), 248 mμ (4.3) and 285 mμ (3.9); (Found: C,76.4; H, 7.3. calculated for $C_{18}H_{20}O_3$: C, 76.0; H, 7.0%). This experiment proves the importance of nucleophilic action of ring A. As already mentioned latifolin dimethyl ether and diethyl ether undergo the isomerisation with greater facility this could be attributed to the additional methoxyl or ethoxyl in the 2'-position; the primary factor may be the degree of nucleophilic activity of ring A. The following mechanism is suggested for this isomerisation.



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