A New Regioselective Synthesis of Pterocarpans

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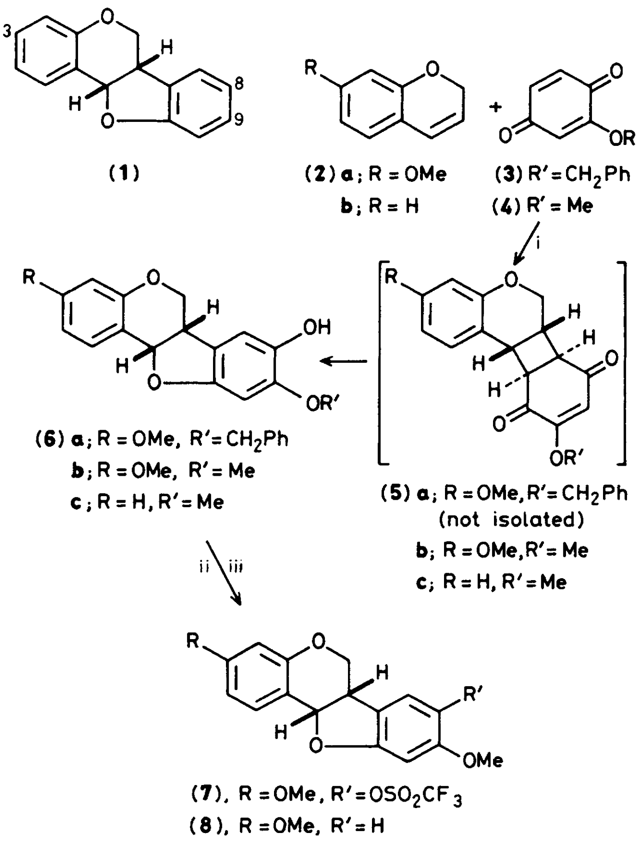
Pterocarpans are formed directly and efficiently *via* titanium(IV) catalysed reactions of 2*H*-chromenes and 2-alkoxy-1,4-benzoquinones.

Many naturally occurring phytoalexins which display important biological activity contain the pterocarpan ring system (**1**) or one of its various oxidised forms.[1,2] There has been considerable interest recently in synthesis of these plant products, a significant number of which incorporate oxygen functionality at the C-3, C-8, and/or C-9 positions.[3] We now report a new, direct, and regioselective method for the preparation of oxygenated pterocarpans.

The method utilises a regioselective Lewis acid catalysed 2 + 2 cycloaddition of 2*H*-chromenes with 2-alkoxy-1,4-benzoquinones to give cyclobutane adducts which can undergo *in situ* reorganisation to the pterocarpan nucleus.[4] Thus, titanium(IV) catalysed reaction of 2*H*-chromene (**2a**)[5] with 2-benzyloxy-1,4-benzoquinone (**3**) for 5—10 h at −78 °C to −25 °C produces pterocarpan (**6a**) in 93% yield.† In a similar manner, chromene (**2a**) and 2-methoxy-1,4-benzoquinone (**4**) produce (**6b**) in 59% yield. However, if the reaction of (**2a**) and (**4**) is kept at low temperature (−78 °C; 10 h), a ~1 : 8 mixture of (**6b**) and cyclobutane (**5b**) is isolated in 90% yield. With chromene (**2b**), 2 + 2 adduct (**5c**) is the major product (84%) upon Ti^{IV} catalysed reaction with (**4**) under the optimum conditions found thus far [1 : 1 $TiCl_4$/$Ti(OiPr)_4$, CH_2Cl_2, −78 °C, 3 h]. Treatment of (**5b**) and (**5c**) with a protic acid (p-$MeC_6H_4SO_3H$ or H_2SO_4, CH_2Cl_2, room temp.) yields (**6b**) (80%) and (**6c**) (71%). The stereochemical assignments of the ring junctures in (**5b—c**) and (**6a—c**) are based on ^1H n.m.r. nuclear Overhauser enhancement experiments.[6] Phenol (**6b**) can be deoxygenated to (**8**) (homopterocarpin)[8] in 78% overall yield *via* palladium catalysed triethylammonium formate reduction of triflate (**7**).[7]

Of particular note in the preparation of (**6a**) is that the method produces a pterocarpan nucleus with differentiated oxygen functionality at positions C-3, -8, and -9. Thus, (**6a**) should be a useful intermediate in the synthesis of a variety of antimicrobial phytoalexins. We are currently investigating the



Scheme 1. *Reagents and conditions:* i, 1 : 1 $TiCl_4$/$Ti(OiPr)_4$ (2 equiv.), CH_2Cl_2, −78 °C or −78 to −25 °C, see text; ii, $(CF_3SO_2)_2O$, pyridine, CH_2Cl_2, −70 °C to room temp., 87%; iii, $Et_3NH^{+}\,{}^{-}O_2CH$, $Pd(OAc)_2$, (0.21 equiv.), 1,1'-bis(diphenylphosphino)ferrocene (0.53 equiv.), dimethylformamide, 74 °C, 92%.

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† All new compounds exhibited satisfactory spectra (^1H and ^{13}C n.m.r., i.r., and mass), elemental analysis and/or exact mass.

generality and other applications of this new one-step synthesis of pterocarpans.

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