A NEW SYNTHETIC METHOD OF 5-, 6-, and/or 7-ALKYL-SUBSTITUTED INDOLES

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Variously substituted pyrrole derivatives 4 were prepared in moderate yields by reaction of suitably alkylated 1-trimethylsilyloxy-1,3-butadiene compounds 3 with an endoperoxide 2 derived from 1-methoxycarbonylpyrrole 1, according to our established procedure, which has been hitherto applied to the synthesis of 4-alkylindoles as well as ergot and related alkaloids. Formation of 5-, 6-, and/or 7-alkyl-substituted indoles 6 was readily achieved by treatment of 4 with a catalytic amount of p-TsOH in boiling benzene to produce 5 in high yields, which was hydrolyzed quite easily with a diluted alkali to afford 6 in almost quantitative yield.

Using the above novel cyclization reaction, naturally occurring 6-(3-methyl-2-butenyl)indole 9 and 7-(3-methyl-2-butenyl)indole 8 were readily synthesized from 7, which was prepared from 1 and 3 (R^1=R^2=H, R^3=isoprenyl) in 28% yield. On treatment of 7 with p-TsOH and subsequent alkaline hydrolysis, 8 was obtained in 40% yield, whereas on exposure of 7 to trimethylsilyl trifluoromethanesulfonate, 9 was isolated in 35% yield after hydrolysis of the cyclization product.

Furthermore, a model synthetic study of teleocidins B was carried out. A pyrrole derivative 10 [≡ 4 (R^1=H, R^2, R^3 = -$(CH_2)_4$-], was oxidized to 11 with sodium chlorite and 11 was converted to an amide 12. Cyclization to the indole derivative 13 was attained with $POCl_3$-PCl_3 (5:1) in 66% yield.