REACTIONS AND SYNTHETIC APPLICATIONS OF β-KETOSULFOXIDES. VII. A NOVEL SYNTHESIS OF PYRANOCARBAZOLE ALKALOIDS, GIRINIMBINE AND MURRAYACINE

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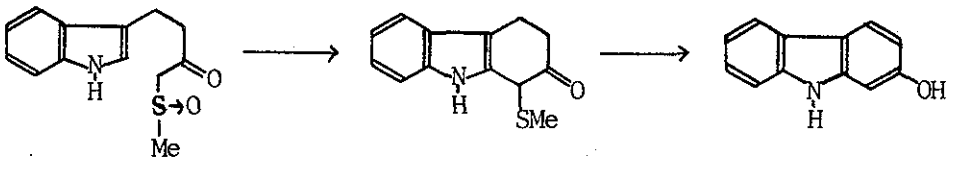
On treatment with p-toluenesulfonic acid in acetonitrile, 1-(3-indolylmethyl)ethyl 4-methyl-1-methylsulfinyl-3-pentenyl ketone (6a) prepared from methyl indoleisobutyrate (8) with sodium methylsulfinylmethide followed by prenylation gave dihydrogirinimbine (7) through three consecutive acid-catalyzed reactions. Compound (7) was converted into N-phenylsulfonamide (11), which was dehydrogenated with N-bromosuccinimide in the presence of azobisisobutyronitrile to afford N-phenylsulfonyl-girinimbine (12). Lithium aluminium hydride reduction of 12 gave girinimbine (4). Oxidation of 4 with DDQ furnished murrayacine (5). Under similar conditions, 7 gave cyclohepta-phylline (13). The results in this communication may provide a shortcut and convenient method for the synthesis of pyranocarbazole alkaloids.

We recently reported that acid-catalyzed cyclization of β-ketosulfoxides afforded a new synthesis of condensed aromatic and heteroaromatic compounds,[1] e.g. 1 → 2 → 3, and this method was applied to the synthesis of the pyrido-

[4,3-b]carbazoles olivacine and ellipticine through compounds of type 2.[2]

As another example showing the utility of the synthetic method we report here a novel synthesis of the pyranocarbazole alkaloids girinimbine (4) and murrayacine (5), which were isolated from Murraya koenigii Spreng[3] and synthesized by several methods.[4]



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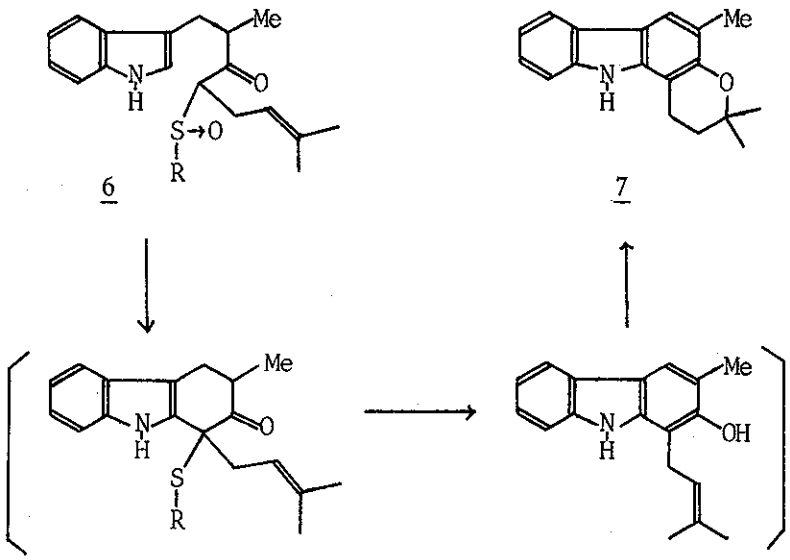
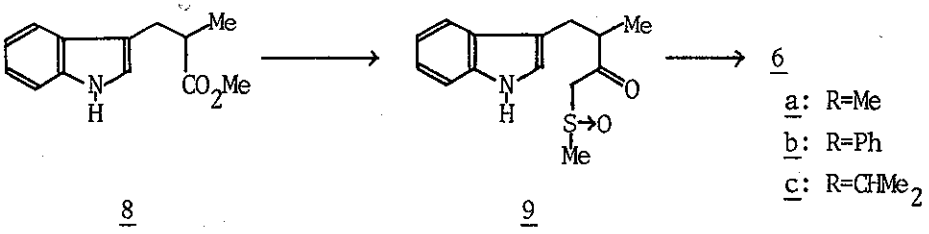
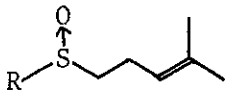
It was presumed that β-ketosulfoxides of type 6 on treatment with an acid would undergo three consecutive acid-catalyzed reactions, cyclization, aromatization and recyclization, to give dihydrogirinimbine (7) and this method might provide a shortcut and convenient general way for the synthesis of pyranocarbazole alkaloids.

The ester (8) was treated with sodium methylsulfinylmethide in the usual way[5] to give quantitatively a ketosulfoxide (9).[1c] Alkylation of 9 with prenyl bromide in the presence of potassium hydride gave 6a [oil; m/e 267 (M^+ - MeSOH); ν (neat) 3375, 3250, 1705, 1620, 1040 cm^{-1}] in 71 % yield.

On treatment with 10a prepared from methylphenylsulfoxide and prenyl bromide in the presence of lithium diisopropylamide, 8 was directly converted into 6b [oil; m/e 267 (M^+ - PhSOH), 218 (PhSSPh); ν (neat) 3300, 1700, 1620, 1600, 1580, 1040 cm^{-1}] in 70 % yield. Similarly, 6c was synthesized from 8



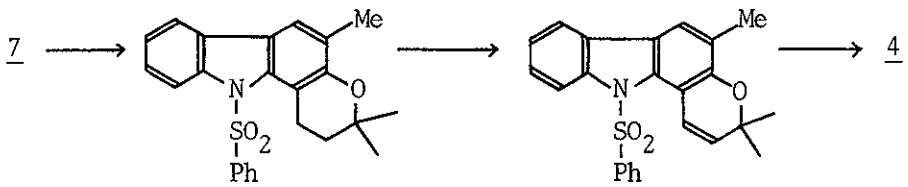




and 10b in 40 % yield [oil; m/e 267 (M^+ - Me_2CHSOH); ν (neat) 3400, 3275, 1705, 1600, 1050 cm^{-1}].

When 6a was heated with p-toluenesulfonic acid in boiling acetonitrile for 3 hr, the expected acid-catalyzed reactions occurred to afford dihydrogirinimbine (7) [mp 174.5-176° (cyclohexane); lit.[6] mp 176°; m/e 265 (M^+), 209 (base peak); λ_{max} (EtOH) 240, 257 (sh), 300, 316 (sh), 330 (sh) nm; δ ($CDCl_3$) 1.36 (6H, s), 1.87 (2H, t, J = 6 Hz), 2.30 (3H, s), 2.80 (2H, t, J = 6 Hz), 7.1-7.3 (3H, m), 7.60 (1H, broad), 7.8-7.95 (1H, m)] in 23 % yield. Treatment of 6b and 6c with the same acid did not improve the yield of 7.

Since all attempts to dehydrogenate 7 into girinimbine (4) without side reactions were unsuccessful, 7 was first converted into a phenylsulfonamide (11) [84 %; mp 181.5-182.5° (EtOH); m/e 405 (M^+), 264 (M^+ - $PhSO_2$, base peak); ν (Nujol) 1610, 1590, 1360, 1180 cm^{-1}; λ_{max} (EtOH) 220, 268 (sh), 273, 295, 303 (sh) nm], which on treatment with N-bromosuccinimide in the presence of azobisisobutyronitrile in boiling carbon tetrachloride for 25 min was smoothly dehydrogenated to give N-phenylsulfonylgirinimbine (12) [35 %; mp, 164-166° (EtOH); m/e 403 (M^+), 388, 362, 247 (base peak); ν (neat) 1630, 1585, 1360, 1185 cm^{-1}; λ_{max} (EtOH) 221, 232, 266, 296 (sh), 310 (sh), 346 (sh) nm]. Lithium aluminium hydride reduction of 12 in ether gave girinimbine (4) in 70 % yield [mp 170-172° (cyclohexane); lit.[7] mp 175°;



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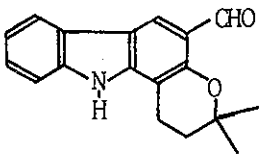
m/e 263 (M^+), 248 (base peak)].

p-Cresol is known to be converted into p-hydroxybenzaldehyde by the treatment with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ).[8] This reaction was applied to the oxidation of 4 and 7. Oxidation of 4 in methanol with DDQ at room temperature for 20 min furnished murrayacine (5) [81 %; mp 237-240°(sublimation); lit.[6] mp 242-244°; m/e 277 (M^+), 262 (base peak)], which was identical spectroscopically (IR, UV, Mass) with the natural product.[6]

Similarly, 7 was converted into cycloheptaphylline (dihydromurrayacine) (13) in 80 % yield [mp 246-247° (MeOH); lit.[9] mp 250°] probably via a dehydrogenated intermediate (14).



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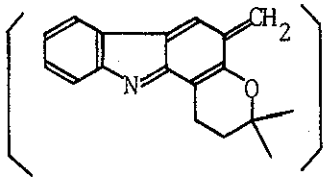

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