

REACTIONS AND SYNTHETIC APPLICATIONS OF β -KETOSULFOXIDES. VII.

A NOVEL SYNTHESIS OF PYRANOCARBAZOLE ALKALOIDS, GIRINIMBINE AND MURRAYACINE

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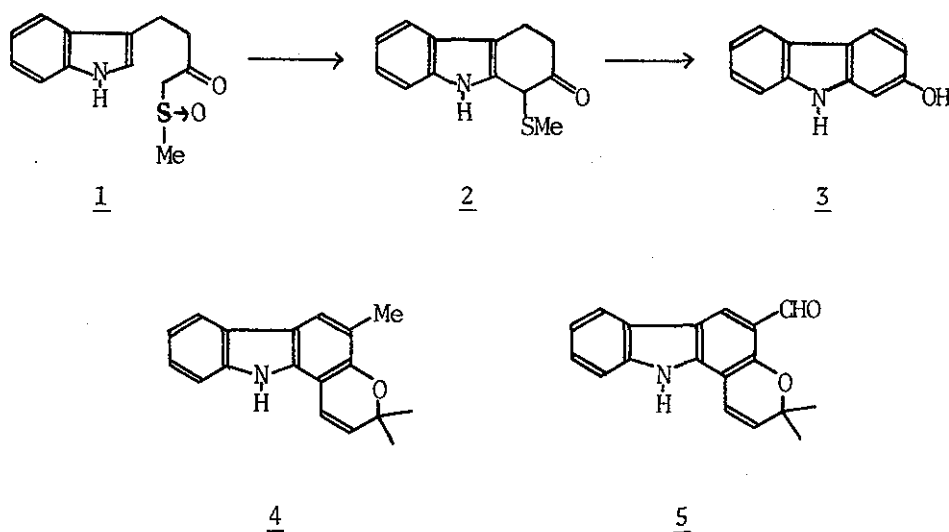
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On treatment with *p*-toluenesulfonic acid in acetonitrile, 1-(3-indolylmethyl)ethyl 4-methyl-1-methylsulfinyl-3-pentenyl ketone (6a) prepared from methyl indoleisobutyrate (8) with sodium methylsulfinylmethide followed by prenylation gave dihydrogirinimbine (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 cycloheptaphylline (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 $\rightarrow$ 2 $\rightarrow$ 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

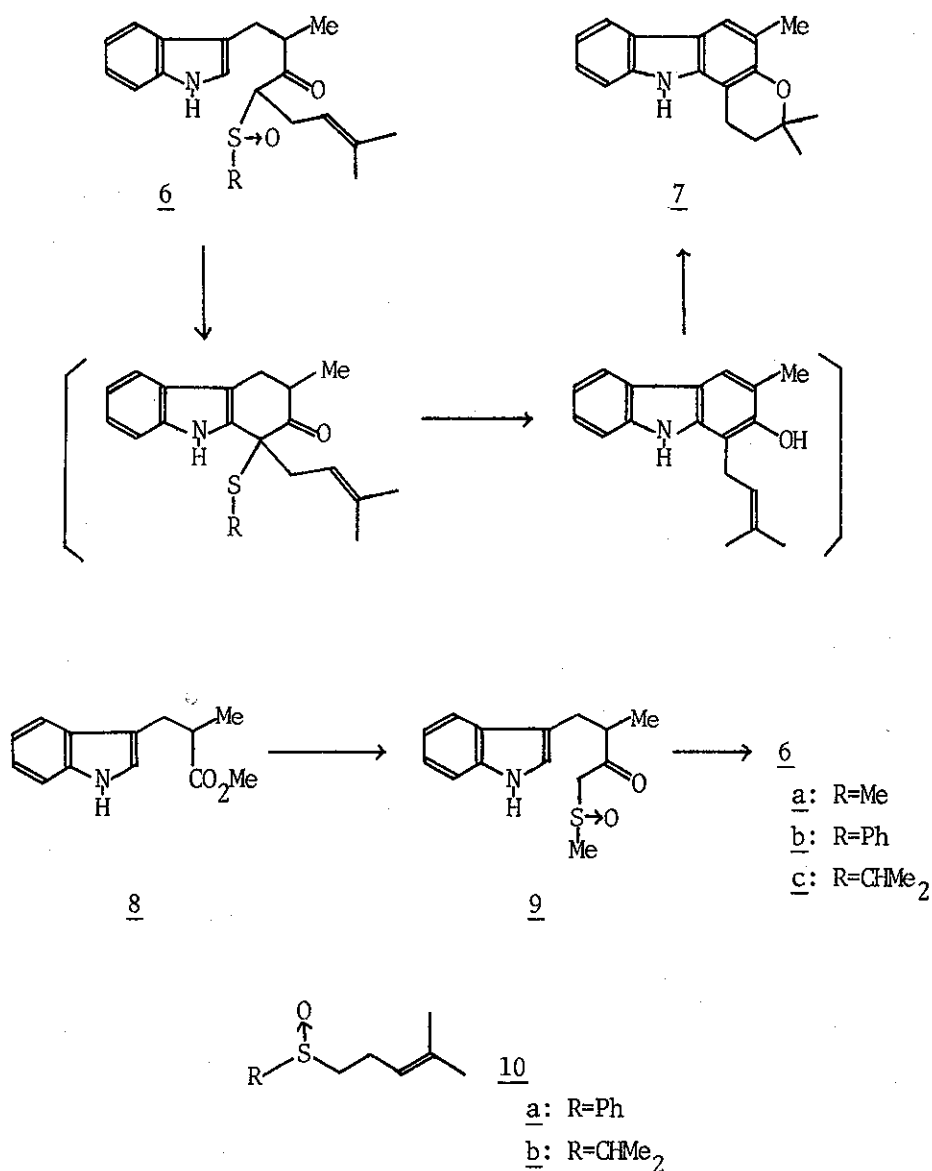
As another example showing the utility of the synthetic method we report here a novel synthesis of the pyranocarbazole alkaloids girinimbine (4) and murrayacine (5), which were isolated from *Murraya koenigii* Spreng³ and synthesized by several methods.⁴



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 way⁵ 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.

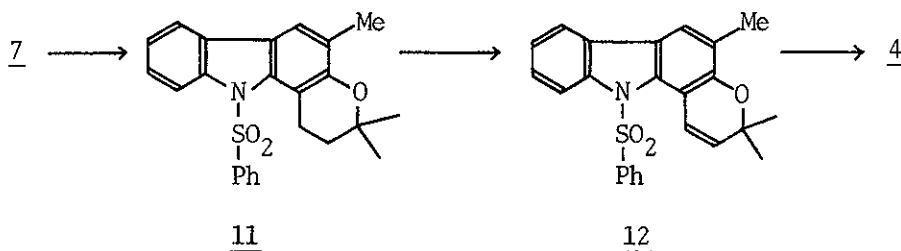
On treatment with 10a prepared from methylphenylsulfoxide and prenyl bromide in the presence of lithium diisopropylamide, 8 was directly converted into 6b [oil; m/e 267 ($M^+ - \text{PhSOH}$), 218 (PhSSPh); ν (neat) 3300, 1700, 1620, 1600, 1580, 1040 cm^{-1}] in 70 % yield. Similarly, 6c was synthesized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



and 10b in 40 % yield [$\underline{m/e}$ 267 ($M^+ - Me_2CHSOH$); $\underline{\nu}$ (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) [$\underline{mp}$ 174.5-176° (cyclohexane); lit.⁶ $\underline{mp}$ 176°; $\underline{m/e}$ 265 (M^+), 209 (base peak); $\underline{\lambda}_{max}$ (EtOH) 240, 257 (sh), 300, 316 (sh), 330 (sh) nm; $\underline{\delta}$ ($CDCl_3$) 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.

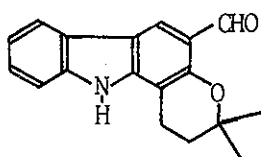
Since all attempts to dehydrogenate 7 into girinimbine (4) without side reactions were unsuccessful, 7 was first converted into a phenylsulfonamide (11) [84 %; $\underline{mp}$ 181.5-182.5° (EtOH); $\underline{m/e}$ 405 (M^+), 264 ($M^+ - PhSO_2$, base peak); $\underline{\nu}$ (Nujol) 1610, 1590, 1360, 1180 cm^{-1} ; $\underline{\lambda}_{max}$ (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 %; $\underline{mp}$, 164-166° (EtOH); $\underline{m/e}$ 403 (M^+), 388, 362, 247 (base peak); $\underline{\nu}$ (neat) 1630, 1585, 1360, 1185 cm^{-1} ; $\underline{\lambda}_{max}$ (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 [$\underline{mp}$ 170-172° (cyclohexane); lit.⁷ $\underline{mp}$ 175°;



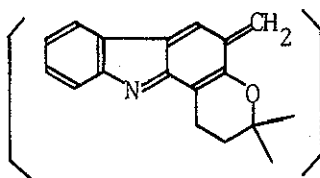
m/e 263 (M^+), 248 (base peak)].

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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