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PREPARATION OF TETRAHYDROBENZ[*cd*]INDOLES FROM 1-TETRALONES

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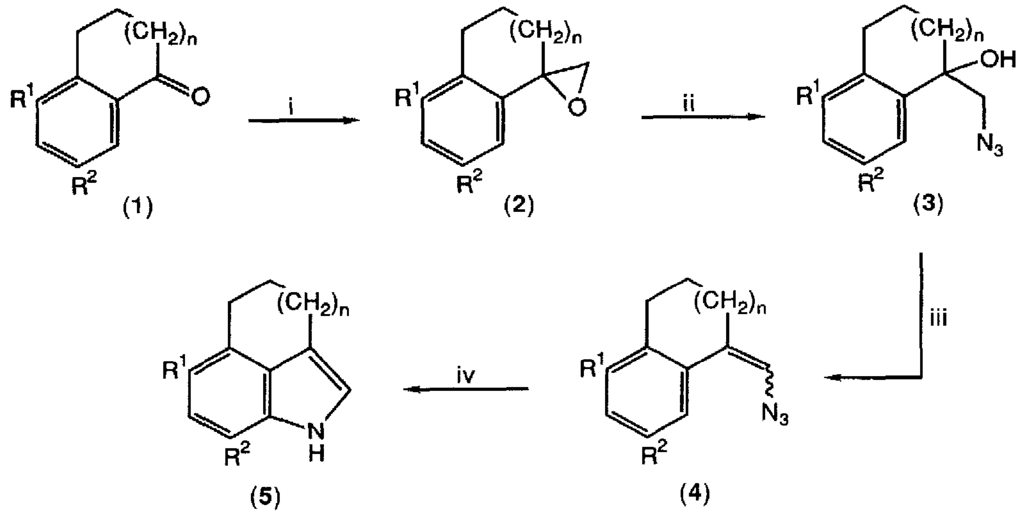
Summary: 3,4-Bridged indoles (5) are prepared from readily available aromatic ketones (1) by conversion into epoxides, ring opening with azide ion, dehydration, and thermolysis of the resulting vinyl azides.

The tetrahydrobenz[*cd*]indole ring system is a key structural feature in a number of naturally occurring indoles, such as the well known ergot alkaloids,[1] α-cyclopiazonic acid,[2] and the more recently isolated hapalindoles.[3] Since many of these indoles possess important pharmacological properties, new routes to them are of interest,[4] and therefore we now report a novel approach to this ring system which starts from readily available 1-tetralones.

The route is based on cyclisation reactions of vinylnitrenes,[5] and stems from our use of such reactions in the synthesis of the left-hand unit of the antitumour antibiotic CC-1065.[6] The required vinyl azides (4a-c) were prepared from the commercially available 1-tetralones (1a-c) by conversion into the corresponding epoxides (2), ring opening with azide ion, and dehydration of the resulting azido-alcohols (3). Thus reaction of 1-tetralone (1a) with dimethylsulphoxonium methylide in dimethyl sulphoxide (DMSO) gave the known epoxide (2a) (65%) which was converted into the azido-alcohol (3a) (53%) by reaction with sodium azide and lithium chloride in dimethylformamide (DMF). Dehydration of the azido-alcohol (3a) using thionyl chloride in pyridine gave the vinyl azide (4a) (56%), together with the alternative dehydration product with an endocyclic double bond (15%). The vinyl azides (4b,c) were prepared similarly from the corresponding methoxy tetralones, and the azide (4d) was prepared from 1-benzosuberone (**1d**) (Scheme).

On heating in boiling mesitylene (b.p. 162-164°C), the azides (4) were converted into the 3,4-bridged indoles (5) in good yield [(5a) 67%, m.p. 54-56°C (lit.,[7] 55-56°C); (5b) 70%, m.p. 94-95°C; (5c) 67%, m.p. 70-71°C (lit.,[4] 71-72°C); (5d) 72%, m.p. 65-67°C]. Thus the current work represents a new approach to tetrahydrobenz[*cd*]indoles and related compounds in that the pyrrole ring is built onto a readily available bicyclic aromatic ketone.



	R^1	R^2	n
a	H	H	1
b	OMe	H	1
c	H	OMe	1
d	H	H	2

Scheme. *Reagents and Conditions:* i, $Me_2S^+OCH_2^-$, DMSO, 55°C; ii, NaN_3, LiCl, DMF, 65°C; iii, $SOCl_2$, pyridine, room temperature; iv, mesitylene, reflux.

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