

## Indoles – New Reactions and Synthesis

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The word indole is derived from the word India: a blue dye imported from India was known as 'indigo' in the sixteenth century. Chemical degradation of the dye gave rise to oxygenated indoles that were named indoxyl and oxindole; indole itself was first prepared in 1866 by zinc dust distillation of oxindole. Since then, it is arguable that indole has been the most studied of any of the aromatic heterocycles, prompted early on by interest in the synthesis of the many and varied structures found amongst the thousands of indole alkaloids, and latterly also by medicinal chemical interest in indole-containing biologically active substances – ondansetron (Zofran) (anti-emetic), Sumatriptan (migraine treatment), and indomethacin (Indocin) (rheumatoid arthritis treatment) are examples. The notorious LSD was chanced upon during one such medicinal chemistry project.

Given the long history of indole chemistry, one might expect little new to be emerging – this is far from the truth. For example, the venerable Fischer indole synthesis (1883), though still used frequently in its original form, now has several modern extensions. The most significant of the many recently described routes for the ring synthesis of indoles will be covered.

Ring metallations play a major role in indole manipulation and will be covered in some detail, though these very significant methodologies will also be discussed in another of the short courses, given by Professor Gribble. Transition metal-catalysed cross-couplings are also very significant and will also be dealt with but, again, such processes are also covered in Professor Gribble's course. The traditional susceptibility of indoles to electrophilic substitution still has a major role in the synthesis of particular indole compounds and the reagents that can now be used have become refined over the years and will be described. The chemistry of indole *N*-anions and the participation of the indole 2,3-double bond in electrocyclic processes will also be described.