Category

Innovative Drug Discovery and Development

Key words

ketamines

anesthetic drug rearrangement



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Amino Ketone Rearrangements. IV. Thermal Rearrangements of α-Amino Methyl Ketones J. Org. Chem. **1965**, 30, 2967–2972, DOI: 10.1021/jo01020a019.

Synthesis of Anesthetic Ketamine



Significance: Ketamine is an anesthetic drug used both in human and veterinary medicine. It acts primarily as a noncompetitive antagonist of the NMDA receptor, but also shows an activating effect on AMPA receptors. Besides its use as a sedative or pain management drug, ketamine has been shown to be a potent short-acting antidepressant. It induces effects similar to phencyclidine (PCP) with reduced behavioral toxicity. **Comment:** The key methodology for the synthesis of ketamine is a thermal rearrangement of α -hydroxy imines to α -amino ketones. This was developed by Stevens and co-workers, who also reported on a series of analogs in a patent (US patent 3254124), which included ketamine. Although synthesized as a racemic mixture, the two enantiomers have remarkably different pharmacologies, with (S)-ketamine being a more potent anesthetic and (*R*)-ketamine being a more potent antidepressant.

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