

ORIGINAL RESEARCH ARTICLES

A NOVEL SYNTHETIC ROUTE TO RACEMIC SOLRIAMFETOL: ADVANCING THERAPIES FOR NARCOLEPSY

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ABSTRACT

Narcolepsy is a chronic neurological disorder marked by excessive daytime sleepiness (EDS) and sudden muscle weakness (cataplexy), severely affecting the quality of life. It involves dysregulation of sleep-wake cycles, often linked to loss of orexin-producing neurons. Current treatments manage symptoms but require improvement. Solriamfetol, a wake-promoting agent, selectively inhibits dopamine and norepinephrine reuptake, enhancing alertness with fewer cardiovascular side effects than traditional stimulants. This study presents a novel, efficient synthesis of racemic solriamfetol, starting with phenylmagnesium bromide reacting with allyl bromide to form allyl benzene, followed by dihydroxylation to yield 3-phenylpropane-1,2-diol. Selective hydroxyl protection enables a Mitsunobu reaction to invert stereochemistry, with subsequent deprotection forming 2-amino-3-phenylpropanol. Final carbamylation produces solriamfetol with high purity and yield. This streamlined synthetic route offers scalability, cost reduction, safer reagents and enhanced control over stereochemistry, improving solriamfetol accessibility for narcolepsy treatment and advancing therapeutic options for this debilitating disorder.

Keywords: Orphan drugs, rare diseases, narcolepsy, solriamfetol