G. W. MULLER\*, W. E. KONNECKE, A. M. SMITH, V. D. KHETANI (CELGENE CORPORATION, WARREN, USA)

A Concise Two-Step Synthesis of Thalidomide

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## **Concise and Scalable Synthesis of Thalidomide**

## Previous synthesis:

**Significance:** Thalidomide is a widely used drug in clinics for its immunomodulating and anti-inflammatory properties. Previously, thalidomide was synthesized with three steps, but the last step is a high-temperature melt reaction to afford crude thalidomide that needs to be purified with multiple recrystallizations. The authors aim to develop a more efficient and convenient synthesis to aid further research into thalidomide's biological activities and mode of action.

**Comment:** The synthesis starts with readily available L-glutamine. Treatment of L-glutamine with Na<sub>2</sub>CO<sub>3</sub> in water, followed by the addition of *N*-carbethoxyphthalimide yields a white solid that does not need purification. Thalidomide crystallizes out of the cyclization-reaction mixture during the reflux. Then thalidomide is filtered out as a white solid, generally of greater than 99% purity.

Category

Innovative Drug Discovery and Development

## Key words

thalidomide crystallization gram scale



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