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Development of a novel and efficient route to the tropomyosin-related kinase (Trk) inhibitor larotrectinib (LOXO-101)

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Larotrectinib (LOXO-101) is a small-molecule ATP-competitive oral inhibitor of the tropomyosin-related kinase (Trk) family of receptor kinases, including Trk-A, Trk-B and Trk-C kinases. Herein, a novel and efficient route for the synthesis of Larotrectinib using starting materials that are commercially available has been achieved. The procedure employed mild reaction conditions and avoided the use of expensive reagents compared to the original synthetic route reported by Array Biopharma. More importantly, gram scale synthesis was accomplished, and this protocol could be valid in the synthesis of similar drugs.

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