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Novel synthesis and structural characterization of Venetoclax impurities *via* [2,3] Meisenheimer rearrangement

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Venetoclax 1, a BCL-2 inhibitor, is extensively used in the treatment of chronic lymphocytic leukemia, small lymphocytic lymphoma, and acute myeloid leukemia. In this study, is reported the synthesis of a novel Venetoclax impurity, VHA **3**, *via* a [2,3] Meisenheimer rearrangement of VNO **2**. Upon heating, VHA **3** undergoes further rearrangement, resulting in the formation of [1,2] Meisenheimer rearranged product VHA **4**. The structures of these impurities have been confirmed using ^{1}H and ^{13}C NMR, HPLC, and mass spectrometry. This synthetic approach provides an efficient method for synthesising Venetoclax impurities VHA **3** and VHA **4**.

Keywords: Meisenheimer rearrangement, VNO (Venetoclax N-Oxide), VHA (Venetoclax hydroxylamine), *m*-CPBA