

NOVEL RING-OPENING TRANSFORMATIONS OF VINCA ALKALOIDS

Sh.M. Adizov¹, M.M. Mirzayeva², S.F Aripova¹, Tashkhodjaev¹

¹ S.Y. Yunusov Institute of the Chemistry of Plant Substances, 77, Mirzo-Ulugbek Str.,
Tashkent, 100170, Uzbekistan, E-mail: adizovsh@gmail.com

² Tashkent pharmaceutical institute, 100015, A. Aybek street 45, Tashkent, Uzbekistan

Alkaloids constitute a structurally diverse class of natural products and represent valuable scaffolds for the development of biologically active compounds. Among them, indole alkaloids are of particular interest because of their pronounced structural complexity and broad range of biological activities. In this work, we investigated the chemical reactivity of vincanine **1** and explored a previously unreported pathway for the transformation of its indole framework.

Vincanine (**1**) contains a highly reactive α,β -unsaturated aldehyde moiety. Reaction with hydroxylamine afforded the corresponding oxime, which, upon standing in an aqueous alcoholic medium, underwent an intramolecular rearrangement accompanied by hydration of the double bond to give 2-hydroxy-16-cyano-2,16-dehydrovincanine. Subsequent treatment with hydrogen chloride in an alcoholic medium promoted dehydration across the C2–C16 bond, affording 16-cyanovincanine hydrochloride.

Notably, the resulting hydrochloride exhibited high stability under standard conditions. In contrast, heating with phenylhydrazine hydrochloride on a water bath triggered a pronounced structural rearrangement involving selective cleavage of the N1–C2 bond of the indole ring. This transformation proceeded quantitatively and furnished the corresponding pyrazoline derivatives (**2**). Under milder conditions, **1** reacted with phenylhydrazine predominantly through condensation at the aldehyde group, giving the corresponding phenylhydrazone (**5**).

A distinct reactivity pattern was observed when vincanine hydrochloride was treated with thiourea under reflux in an alcoholic hydrochloric acid medium. Under these more forcing conditions, N1–C2 cleavage of the indole ring occurred, leading to previously inaccessible, structurally complex vincanine-derived products incorporating heterocyclic motifs, including a thiourea-derived thiopirimidine-type ring (**4**) and a hydroxythiamine-derived oxazoline ring-**5**.

Overall, these findings establish that the indole framework of vincanine can undergo controlled ring-opening under appropriate reaction conditions. The observed transformations provide a concise entry to structurally novel alkaloid-derived heterocycles and highlight the potential of indole-ring cleavage as a strategy for expanding the chemical space of biologically relevant natural-product scaffolds.

