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An Unexpected Degradation Pathway of a 1,2,4-Triazolo[4,3-*a*]pyridine Derivative:  
The Formation of Two Cationic Pseudodimers of an 11 $\beta$ -Hydroxysteroid  
Dehydrogenase Type 1 Inhibitor Drug Candidate in a Stressed Capsule Formulation

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**An Unexpected Degradation Pathway of a 1,2,4-Triazolo[4,3-*a*]pyridine Derivative: The Formation of Two Cationic Pseudodimers of an 11 $\beta$ -Hydroxysteroid Dehydrogenase Type 1 Inhibitor Drug Candidate in a Stressed Capsule Formulation**

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**Abstract**

Degradation of an active pharmaceutical ingredient (API), a 2-(3-(1-(4-chlorophenyl)cyclopropyl)-[1,2,4]triazolo[4,3-*a*]pyridin-8-yl)propan-2-ol hydrochloride salt, was observed in a capsule formulation stressed at 50°C or 40°C/75% relative humidity conditions for one month. Two unknown degradants were identified as cationic pseudodimers of the API via accurate mass liquid chromatography-mass spectrometry and one- and two-dimensional NMR analyses. A plausible degradation pathway of the API was postulated which led to the identification of two key N-oxide degradants in the stressed capsule formulation at trace levels. It was hypothesized that the N-oxide degradants could be protonated and undergo further transformation so as to react with another API free base to form pseudodimeric N-oxide intermediates, followed by protonation/dehydration to yield the cationic pseudodimers of the API. The proposed degradation pathway was further supported by formulation screening studies: (1)

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