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Quinoid derivatives of the nevirapine metabolites 2-hydroxy- and 3-hydroxy-nevirapine: activation pathway to amino acid adducts

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Electronic Supplementary Information

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Figure S3: A. Tandem mass chromatogram and mass spectrum of the *m/z* 415 ion, corresponding to the protonated molecule of adduct **25**, formed upon nucleophilic attack of lysine to quinone **12**. **B.** Proposed ESI-MS/MS fragmentation mechanisms for the *m/z* 415 ion.

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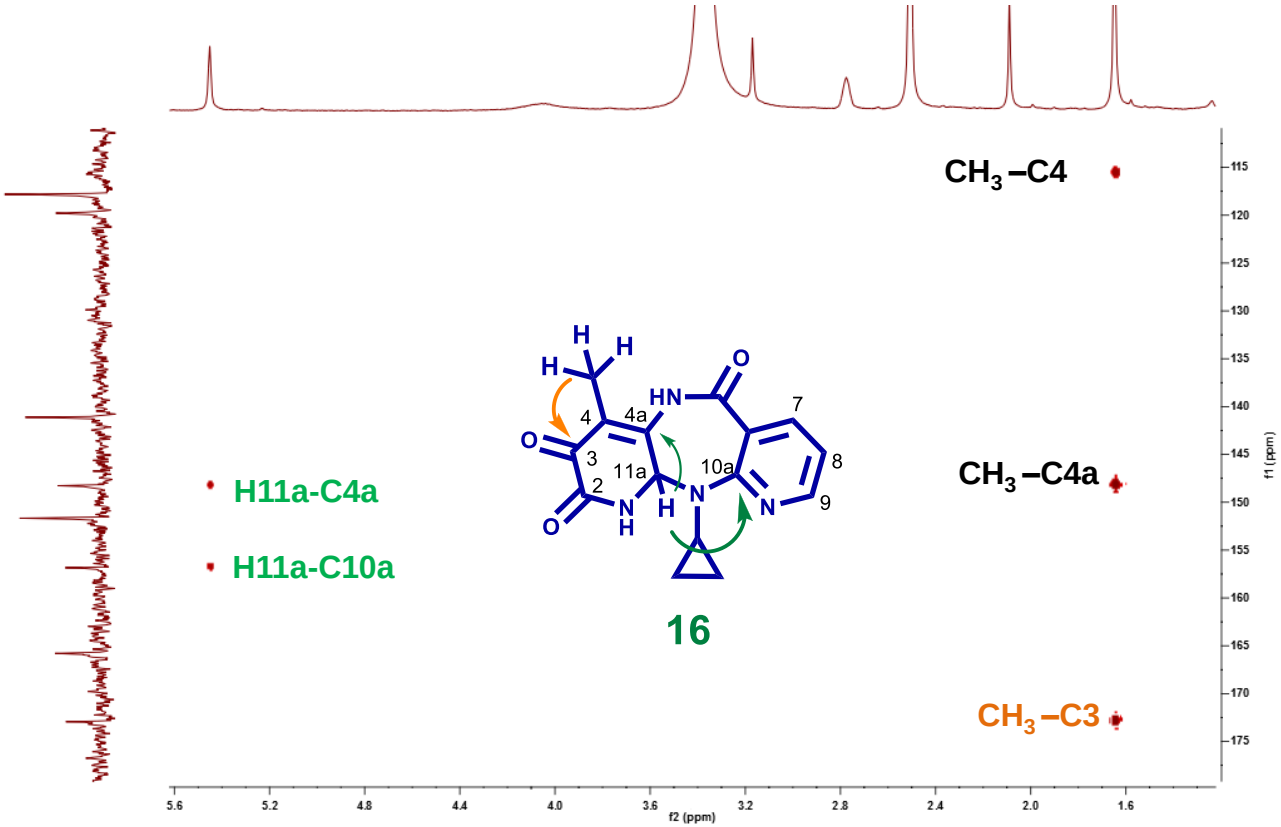
Scheme S1. Proposed mechanism for the formation of the maleimide **13**, involving the transient generation of 2,3-NVP-quinone (**12**). The quinone was generated by oxidation with Frémy's salt, as indicated, and also in the presence of tyrosinase and myeloperoxidase.

Scheme S2. Proposed ESI-MS/MS fragmentation mechanisms for the protonated molecule of adduct **23**.

Scheme S3. Reversible nucleophilic attack of *N*-acetylcysteine (NAC) to the quinoid intermediates **10** and **12**. Also shown is the formation of adduct **26** by reaction of **13** with NAC. RSH represents a generic sulfhydryl nucleophile. The R group is specified for NAC under the structure of adduct **26**.



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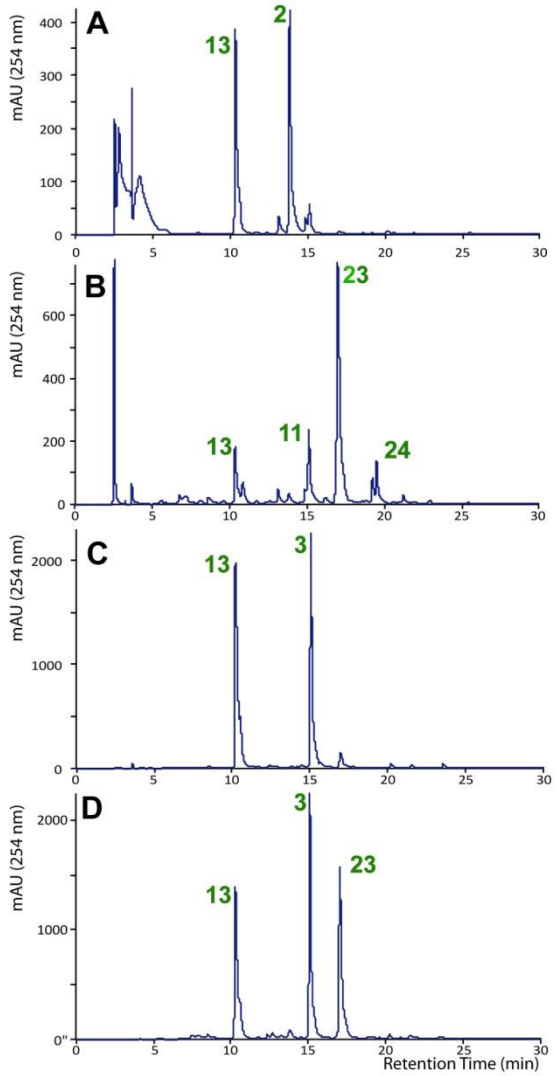

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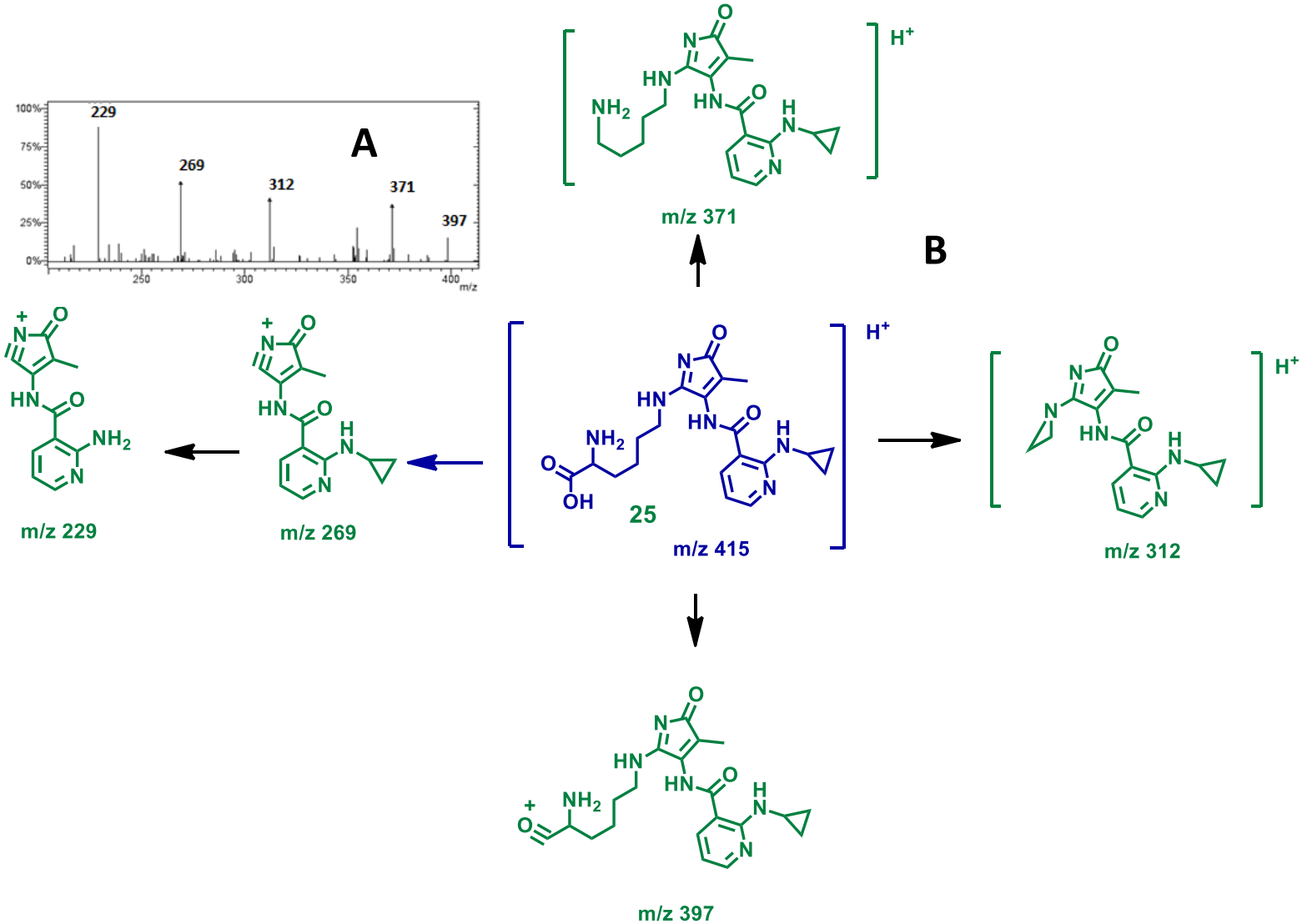

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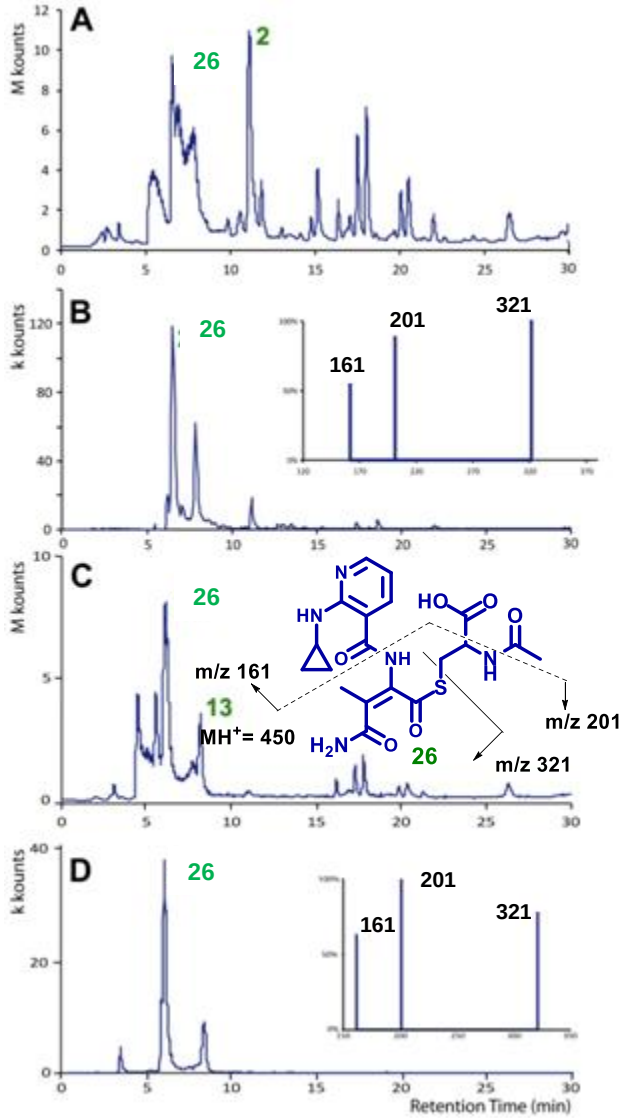

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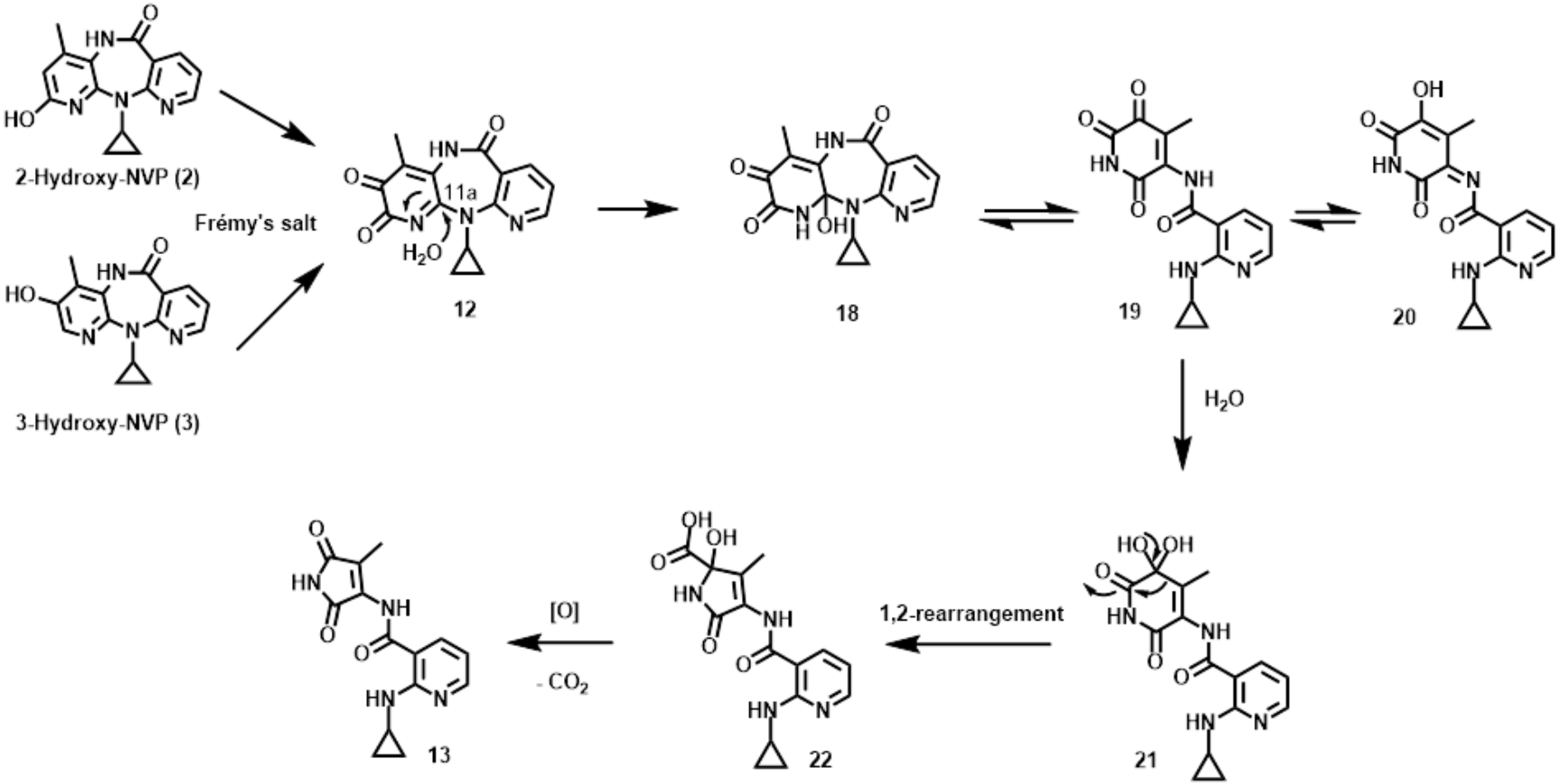

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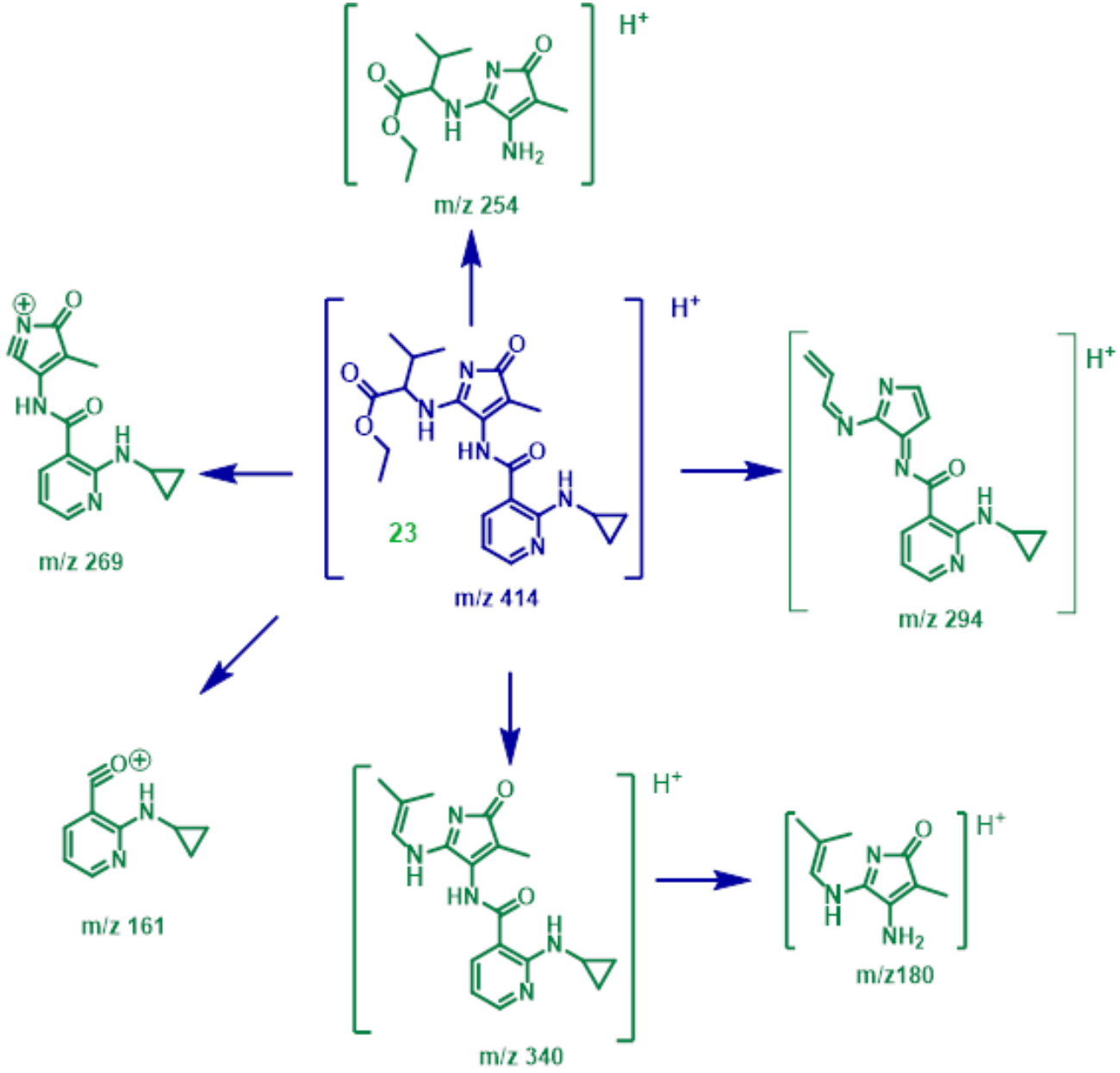

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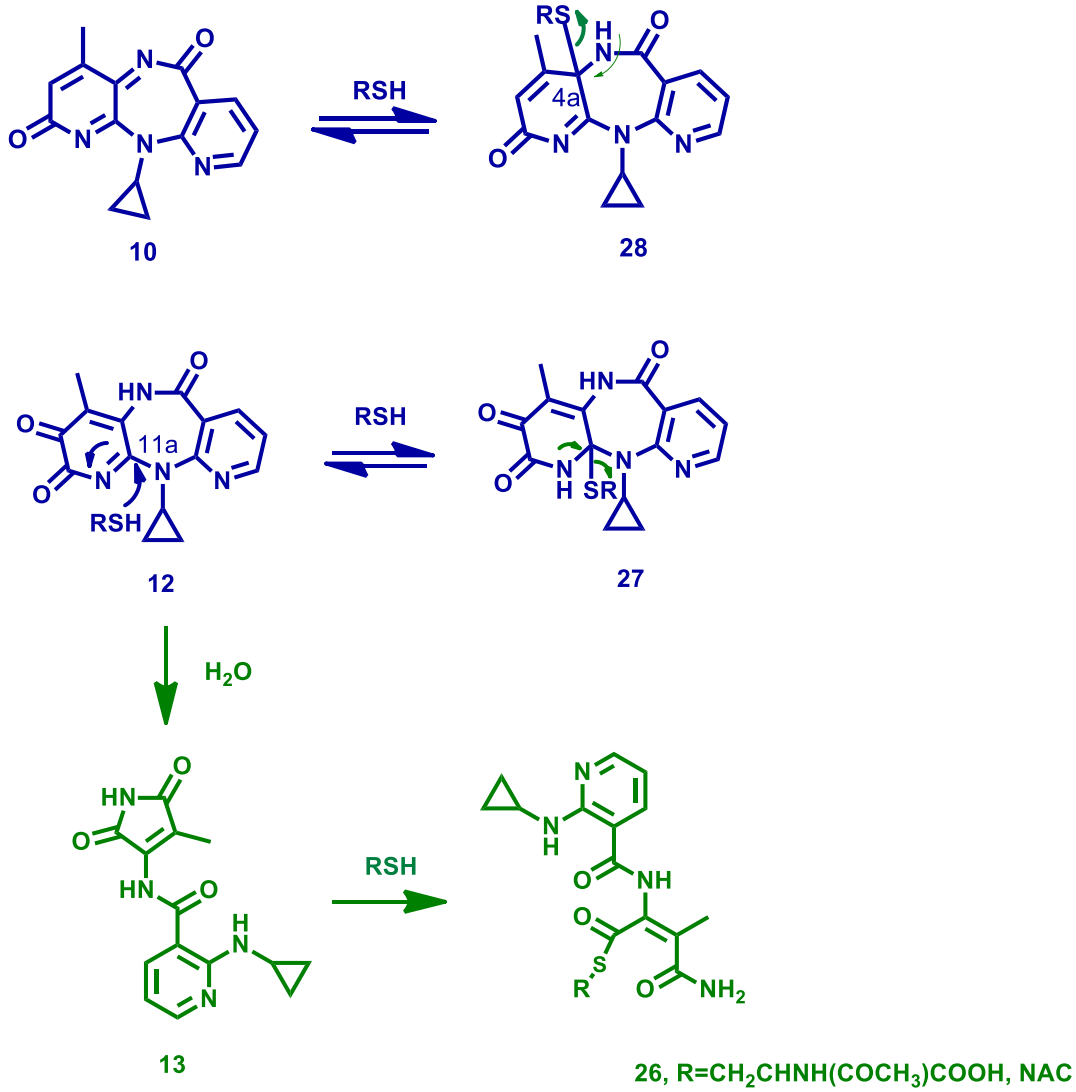

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