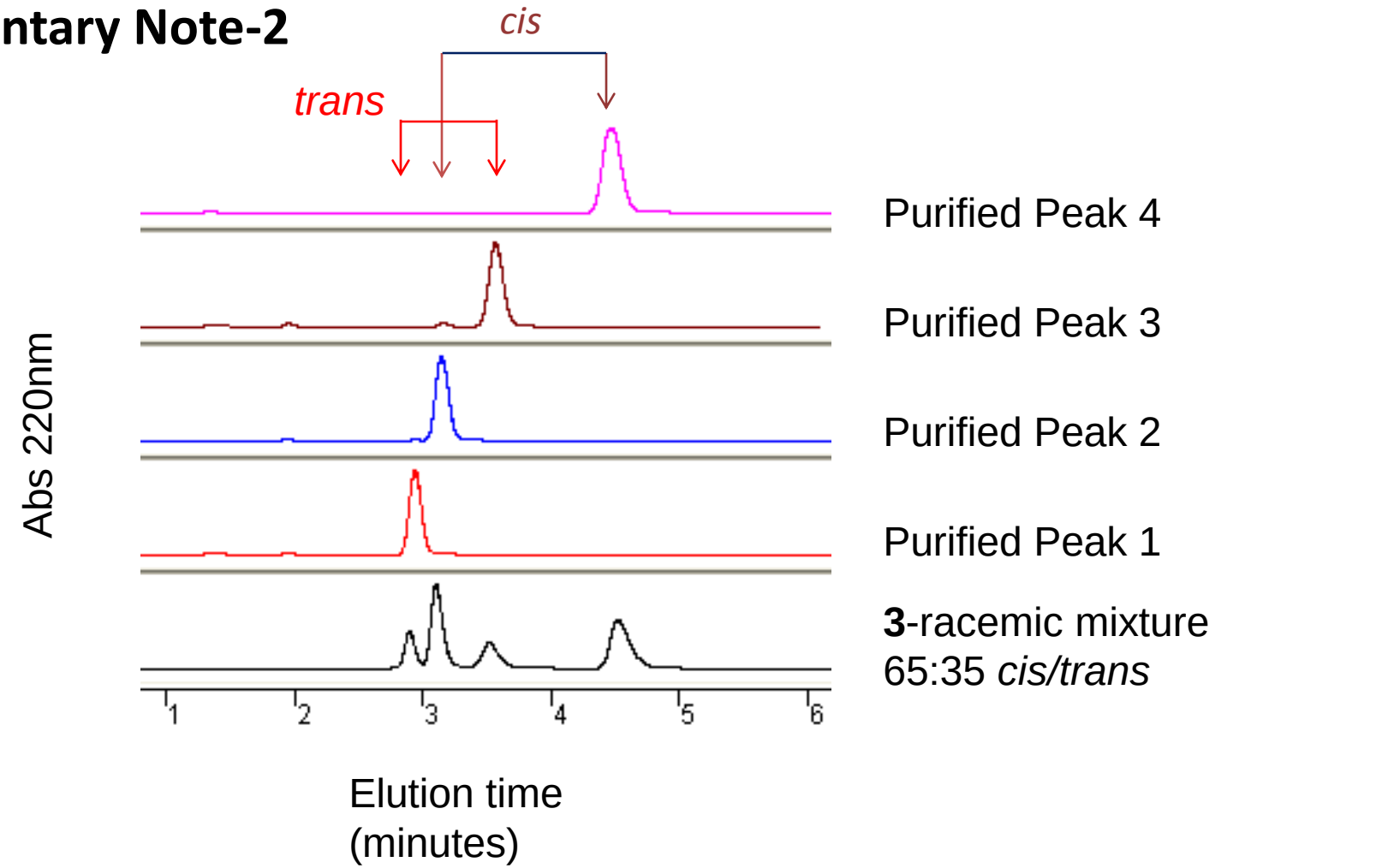
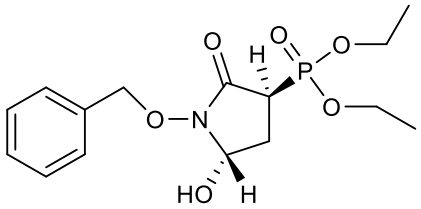
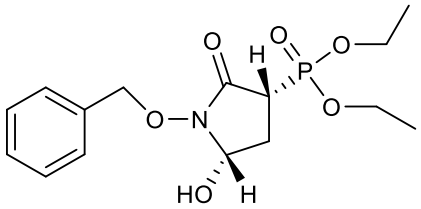
Supplementary Note-2
Figure A

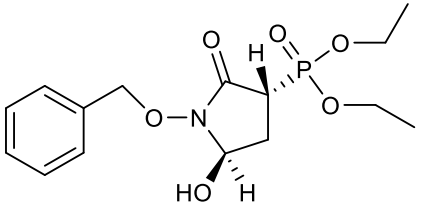




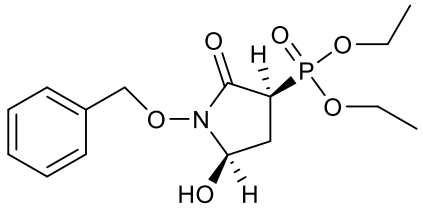
S,S - *trans*



R,S - *cis*



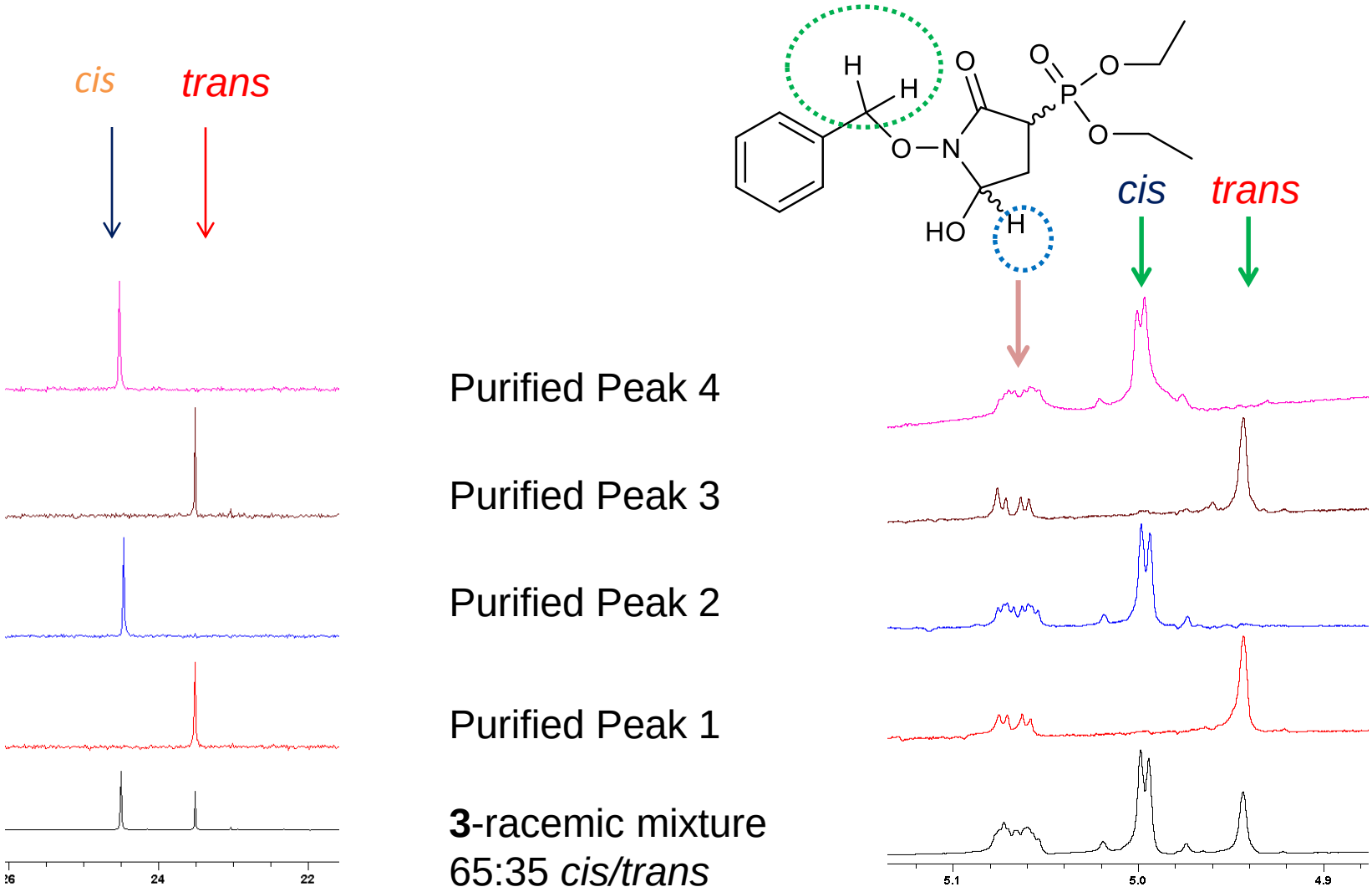
R,R - *trans*



S,R - *cis*

Supplementary Note-2 Figure A: *Chiral chromatographic separation of intermediate **3***
Intermediate **3**, consisting of a mixture of *cis*/*trans* isomers in a 65:35 ratio, was analyzed by chiral HPLC. The chromatogram showed 4 peaks, two majors and two minors, in a ratio of 65:35. Based on relative abundance, these were assigned to the *cis* and *trans* isomers; this was confirmed by NMR (see Figure S2). The four isomers were separated and each one was re-analyzed on the same chiral HPLC to confirm chiral purity. HPLC conditions were as follow: Mobile phase, Isocratic 76% Hexane, 18% Ethanol, 4% Isopropanol, 2% acetonitrile, 0.1% TFA; flow rate: 20 mL/minute. Column: Normal phase Lux Cell-1 21.2 x 150 mm (Phenomenex, Torrence, CA). The experiment was reproduced once independently.

Supplementary Note-2
Figure B

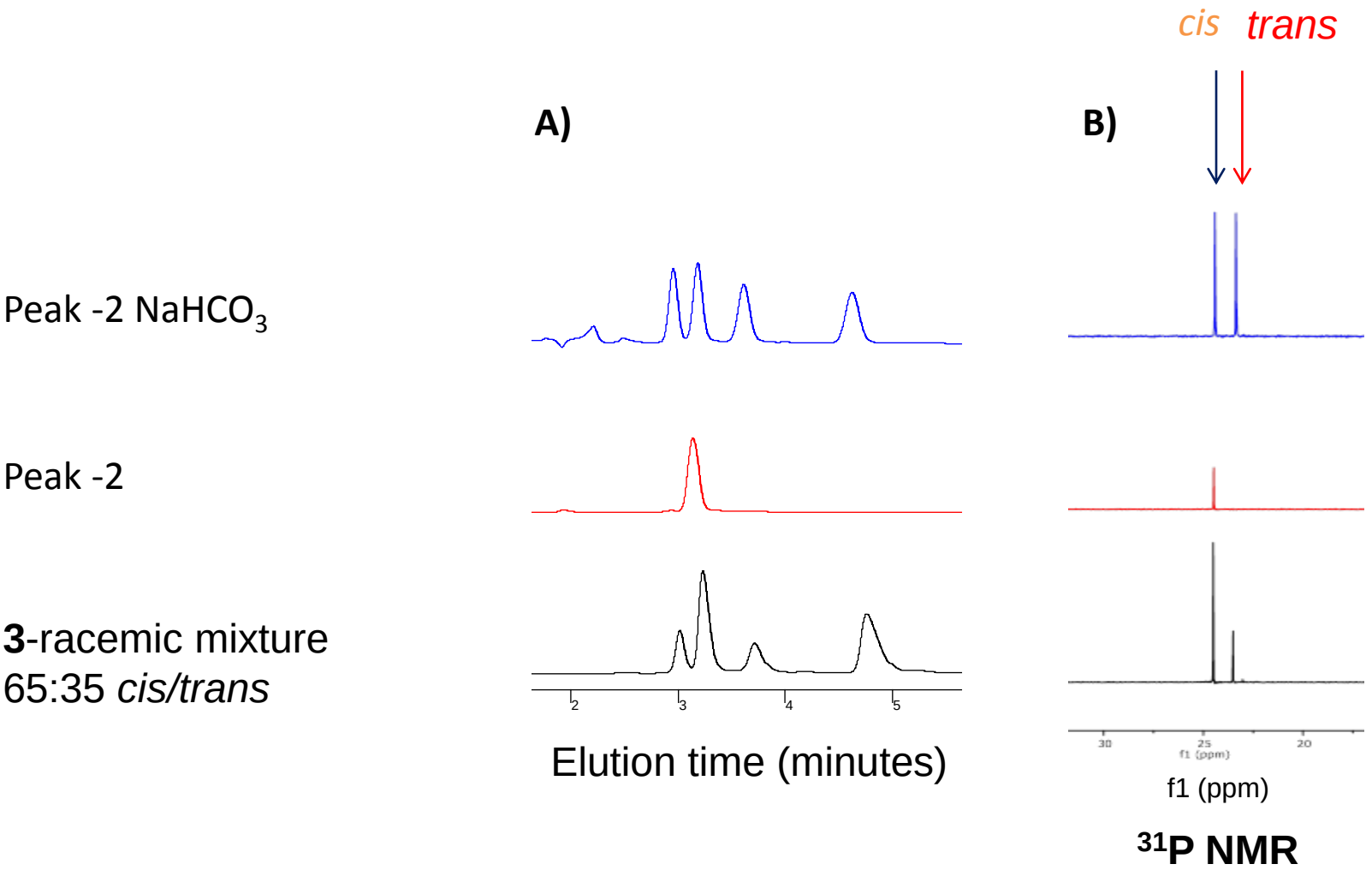


^{31}P NMR

^{1}H NMR

Supplementary Note-2 Figure B : *NMR characterization of chiral chromatography purified entities.* We performed NMR on the chiral chromatography purified enantiomers as they came off the column. In order to minimize time between purification and NMR recording (to avoid racemization), mobile phase solvents were not evaporate but one equivalent volume of deuterated Acetonitrile was added for signal-lock. Because of the presence of solvents from the mobile phase (hexane, ethanol, isopropanol, acetonitrile, TFA), the ^{1}H spectrum upfield of 4 ppm is obfuscated. However, the hemiaminal (blue arrow and dashed circle) and benzyl protons (green arrows and dashed circle) are readily identifiable. The initial intermediate **3**, is characterized by two sets of hemiaminal protons (multiplet, 5.08-5.06 ppm) and benzyl methylene (*cis*: ab-system 4.99 ppm; *trans*: 4.94) protons in 65:35 ratio, in complete agreement with ref (13). In the ^{31}P NMR spectrum, two peaks are evident, previously identified as the *cis* and *trans* isomers (downfield at 24.5 ppm and upfield at 23.5 ppm, respectively; ref (13)), present in 65:35 ratio. Each purified enantiomer showed a single peak on ^{31}P NMR (*trans*: 24.5 ppm; *cis*: 23.5 ppm) as well as one set of hemiaminal and benzyl methylene protons (13). The NMR measurements were performed once.

Supplementary Note-2
Figure C



Supplementary Note-2 Figure C: *Loss of enantiopurity upon mild alkaline aqueous treatment.* Immediately after chiral chromatography, each enantiomer was washed with saturated $NaHCO_3$ (to neutralize TFA) and extracted with ethyl acetate; the organic phase was dried over $MgSO_4$ and evaporated. Chiral HPLC analysis showed the presence of the initial four distinct peaks, proving chiral instability of this intermediate (blue trace in Panel A; the red trace shows the purified enantiomer peak 2 before racemization, while the black trace shows the initial racemic mixture of intermediate **3**). Racemization was confirmed by ^{31}P NMR (Panel B): only one *cis*-diastereomer is detected in isolated peak 2 (red trace) while both *cis* and *trans* diastereomers are evident after aqueous treatment (blue trace). The experiment was repeated with purified peaks 1, 3 and 4, with identical results.