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# Total Synthesis of Petrosin, Petrosin A, and Petrosin B REVISED

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## Supporting Information

**Isolation of petrosin, petrosin A, petrosin B, and petrosin B'.** The following explains the scheme used to isolate samples of each isomer individually from the isomer mixtures obtained from the synthesis. Note that the isolations were carried out in a manner to obtain pure fractions rather than quantitative results. Initially, several attempts at chromatographic separation of the isomers failed, producing mixtures regardless of the method employed (flash chromatography, chromatotron separation, and HPLC). All petrosin isomers could be conveniently collected together by running a $SiO_2$ column with 5:47.5:47.5 $Et_3N$:hexane:ether. However, if $SiO_2$ chromatography is performed with a methanol/ethyl acetate eluent, the isomers can be separated into three fractions.

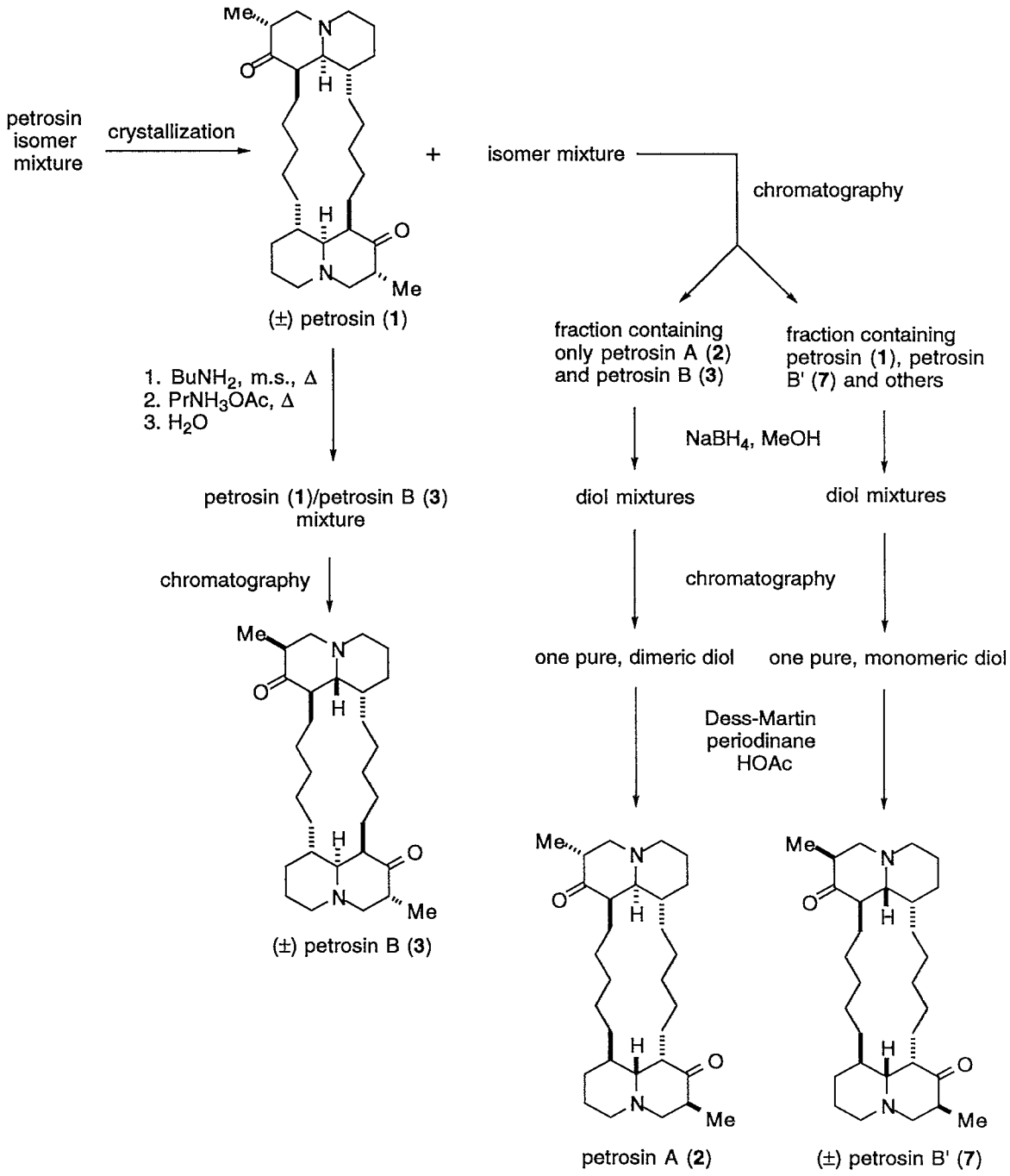
The products of many of the equilibration studies were combined and several silica chromatography separations were performed using a range of 2% MeOH/EtOAc to 10% MeOH/EtOAc solvent systems. The highest $R_f$ spot of the three contained only petrosin A and petrosin B, which were completely inseparable, consistent with the natural product isolation data. The middle fraction contained no known isomers, but represented only a minor fraction of the material. The lowest $R_f$ fraction contained petrosin and what was later determined to be petrosin B' (unnatural). It also contained at least one other compound, which appeared dimeric in structure. Following is the description of the chemistry carried out to isolate fractions of petrosin A, petrosin B, and petrosin B' in a purity amenable to accurate spectral analyses.

The highest $R_f$ material (which contained pet A/pet B) was reduced with $NaBH_4$/MeOH. Separation of the resulting diol led to a higher $R_f$ fraction that appeared dimeric by $^1H$ NMR spectroscopy, a mixture fraction, and a lower $R_f$ fraction that appeared non-dimeric. Oxidation of the dimeric material with Dess-Martin periodinane in the presence of acetic acid led to petrosin A as a single isomer. Oxidation of the lower $R_f$ material produced a product mixture that was enriched in petrosin B relative to the initial mixture before reduction, but disappointingly it still contained a significant amount of petrosin A. Apparently, the reduction with $NaBH_4$ of this material gave a mixture of axial and equatorial alcohols. As a result, one of the reduction isomers of petrosin A was equal in polarity with the reduction isomers of petrosin B, thereby preventing a pure petrosin B sample from being obtained via this route.

As a result of this failure to isolate petrosin B cleanly from petrosin A, we took advantage of a fortuitous situation that arose during the equilibration experiments . Recall Entry 6, Table 3, where pure petrosin was equilibrated to a petrosin/petrosin B mixture free from other isomer contamination. Because the previously described MeOH/EtOAc solvent system effectively separates these isomers, (pet B in highest $R_f$ spot, petrosin in lowest $R_f$ spot), this led to the convenient isolation of a small quantity of reasonably pure petrosin B.

The previously described $NaBH_4$ reduction of the "lower" $R_f$ material (original $SiO_2$ separation) followed by preparative TLC separation led to four fractions of diols. The clean compound from the first

fraction produced petrosin upon oxidation. Oxidation of fraction 2 led to a mixture of petrosin, petrosin B', and some unidentified material. Fraction 3 was discarded on the basis of a complex $^{1}H$ NMR spectrum of the reduced material. However, fraction 4 of the diol mixture provided mainly petrosin B' upon oxidation, though contaminated with a small amount of petrosin. This material was clean enough for accurate $^{1}H$ and $^{13}C$ NMR spectral analysis. The whole separation process is summarized schematically in the accompanying scheme.

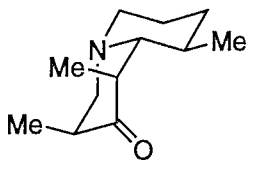
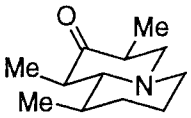
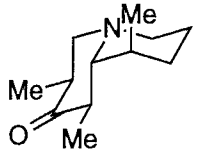
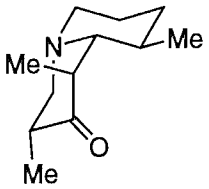
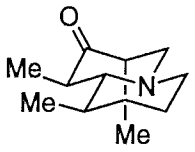
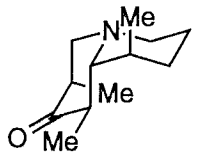
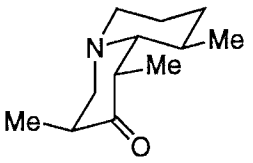
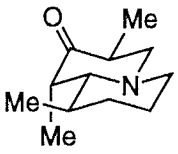
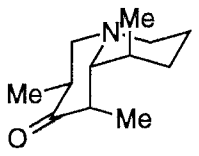
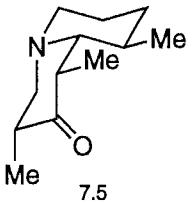
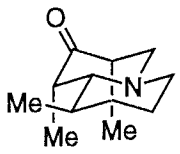
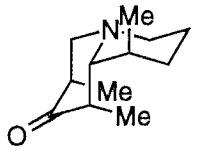
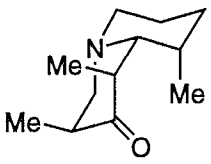
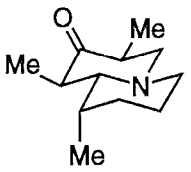
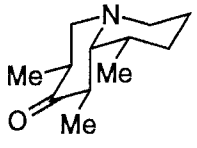
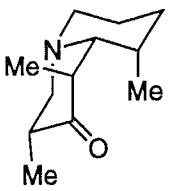
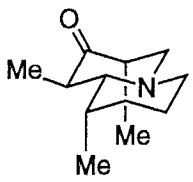
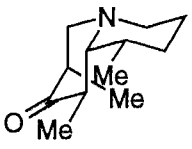
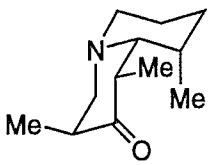
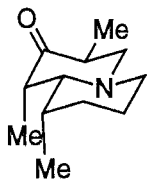
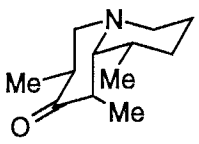
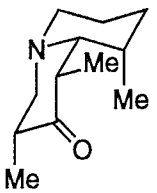
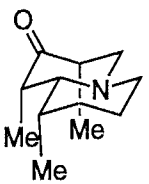
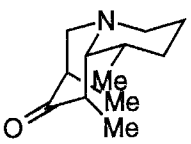


**$^{13}$C NMR Spectra of Petrosin Isomers**

| Carbon atom | Petrosin | Petrosin A | Petrosin B (natural) | Petrosin B' |
|---|---|---|---|---|
| 1 | 51.86 | 51.54 | 51.69 | 51.36 |
| 1' | | | 51.6 | 50.61 |
| 2 | 213.88 | 214.18 | 214.22 | 214.16 |
| 2' | | | 212.43 | 212.27 |
| 3 | 40.47 | 40.25 | 40.25 | 40.5 |
| 3' | | | 44.56 | 44.44 |
| 4 | 64.77 | 64.85 | 64.85 | 64.78 |
| 4' | | | 65.76 | 65.12 |
| 6 | 55.96 | 55.85 | 55.94 | 55.89 |
| 6' | | | 56.61 | 56.7 |
| 7 | 25.08 | 24.99 | 24.99 | 25.03 |
| 7' | | | 19.95 | 20.23 |
| 8 | 29.46 | 30.25 | 29.28 | 29.26 |
| 8' | | | 26.5 | 26.73 |
| 9 | 36.98 | 35.92 | 36.11 | 35.8 |
| 9' | | | 34.67 | 34.7 |
| 10 | 70.39 | 70.71 | 70.52 | 70.87 |
| 10' | | | 71.88 | 71.85 |
| 11-15 | 23.83 | 25.5 | 22.53 | 24.39 |
| | | | 23.03 | 24.77 |
| | 24.04 | 26.03 | 24.24 | 25.72 |
| | | | 24.27 | 26.28 |
| | 24.31 | 26.21 | 24.37 | 27.02 |
| | | | 24.81 | 27.44 |
| | 27.36 | 29.05 | 26.36 | 27.81 |
| | | | 27.57 | 28.45 |
| | 28.66 | 31.97 | 28.08 | 29.76 |
| | | | 29.28 | 30.95 |
| 16 | 11.21 | 11.27 | 11.27 | 11.24 |
| | | | 11.33 | 11.41 |

## Molecular Mechanics Energies of Isomers of Quinolizidone 4

(Macromodel)

| *cis*-Quinolizidones | *trans*-Quinolizidones | *cis*-Quinolizidones |
|---|---|---|
|  11.5 |  6.8 |  7.1 |
|  7.4 |  9.8 |  12.0 |
|  10.8 |  **5.2** |  13.0 |
|  7.5 |  9.0 |  17.7 |
|  16.3 |  **5.0** |  7.7 |
|  12.4 |  8.1 |  11.6 |
|  13.2 |  12.4 |  11.2 |
|  9.8 |  16.4 |  16.0 |