

## Electronic Supplementary Information: Effect of Enantiomeric Ratio and Preparation Method on Proline Polymorphism

Robert T. Berendt<sup>a,b</sup> and Eric J. Munson<sup>\*a</sup>

<sup>a</sup> The University of Kansas, Department of Pharmaceutical Chemistry, Lawrence, KS 66047

<sup>b</sup> Current address: Food and Drug Administration, 10903 New Hampshire Ave, Silver Spring, MD 20910, USA. E-mail: robert.berendt@fda.hhs.gov

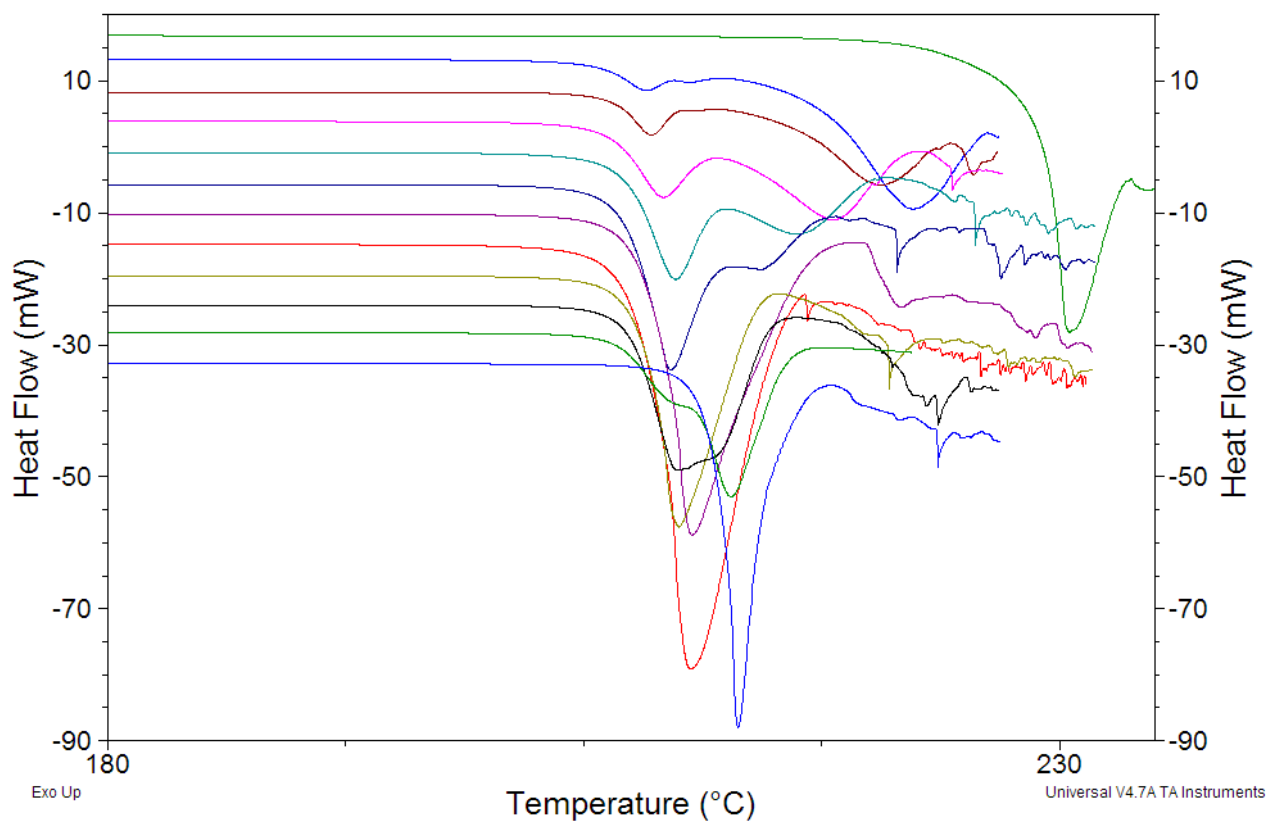
<sup>\*</sup> Corresponding author, current address: The University of Kentucky, Department of Pharmaceutical Sciences, Lexington, KY 40536, USA. Fax: +1 859 257 7564; Tel: +1 859 323 3107; E-mail: eric.munson@uky.edu

### Experimental

#### Sample preparation

*DL*-proline form II (*DL*-II) was obtained in a crystallographically pure state for VTI, SSNMR, and PXRD analyses by cryogrinding an equimolar ratio of D- and L-proline for 60 min, followed by warming to 60°C under anhydrous conditions.

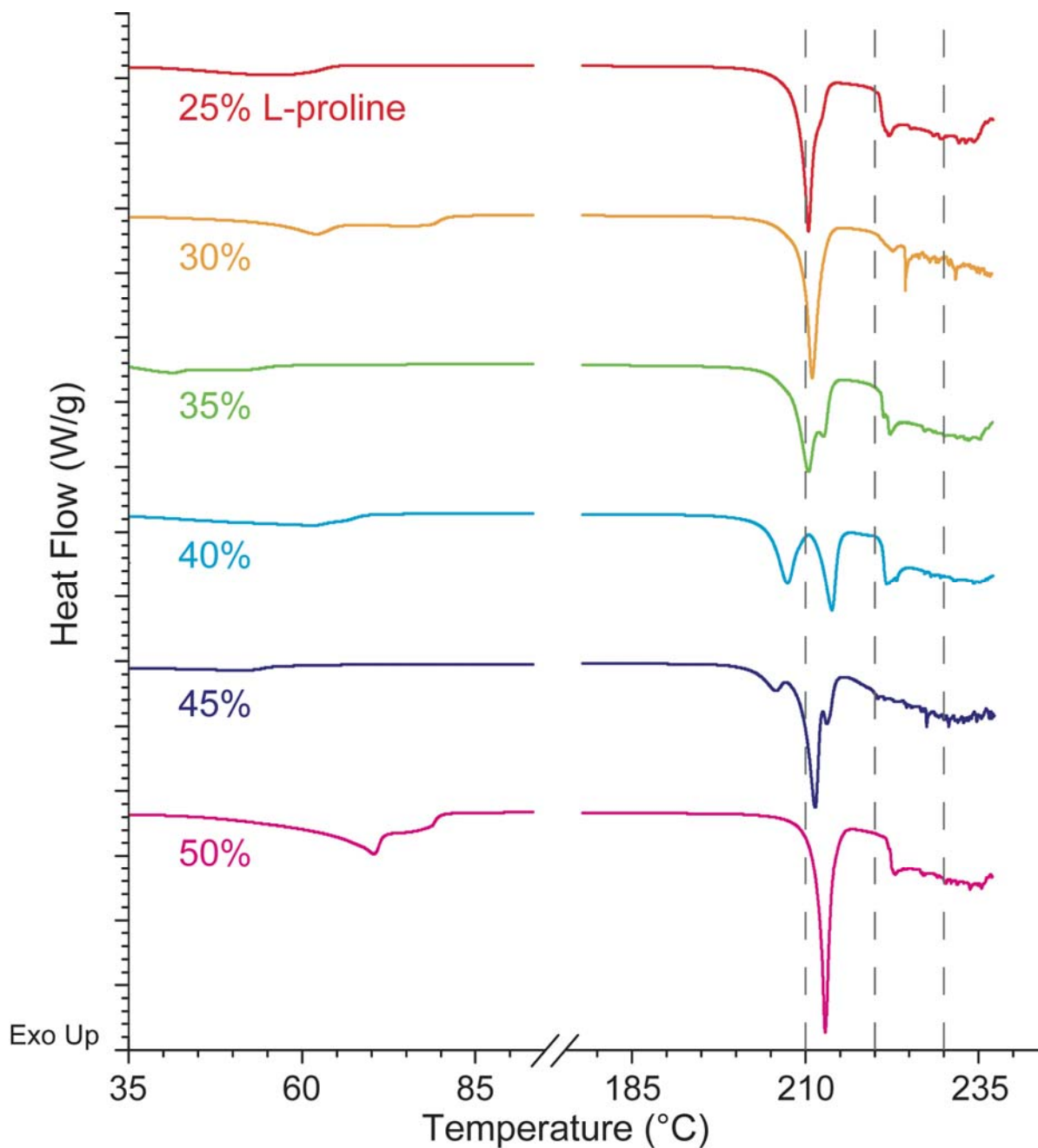
### Results



**ESI Figure 1.** Representative proline DSC thermograms used to construct the binary melting-point phase diagram in Figure 2 of the main text. The thermograms are arranged by increasing level of L-proline in D-proline in the following order: enantiopure D-proline (top), 4, 6, 10, 15, 20, 25, 30, 35, 40, 45, 50% L-proline (bottom).

## Effect of Enantiomeric Ratio and Preparation Method on Proline Polymorphism

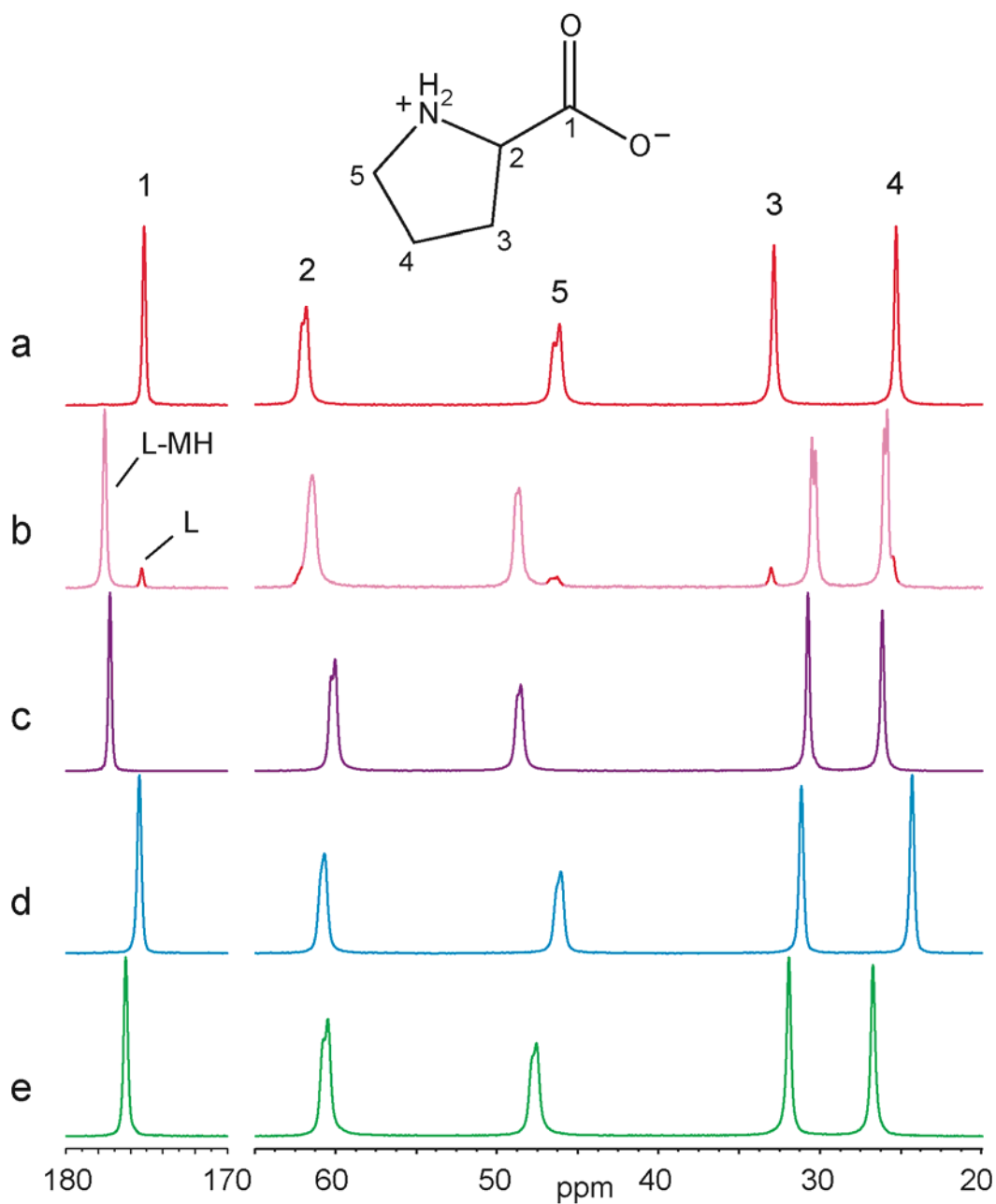
*CrystEngComm*



**ESI Figure 2.** DSC thermograms of 25–50% L-proline samples prepared by lyophilization. The corresponding  $^{13}\text{C}$  CP-MAS NMR spectra are shown in Figure 6 of the main text.

## Effect of Enantiomeric Ratio and Preparation Method on Proline Polymorphism

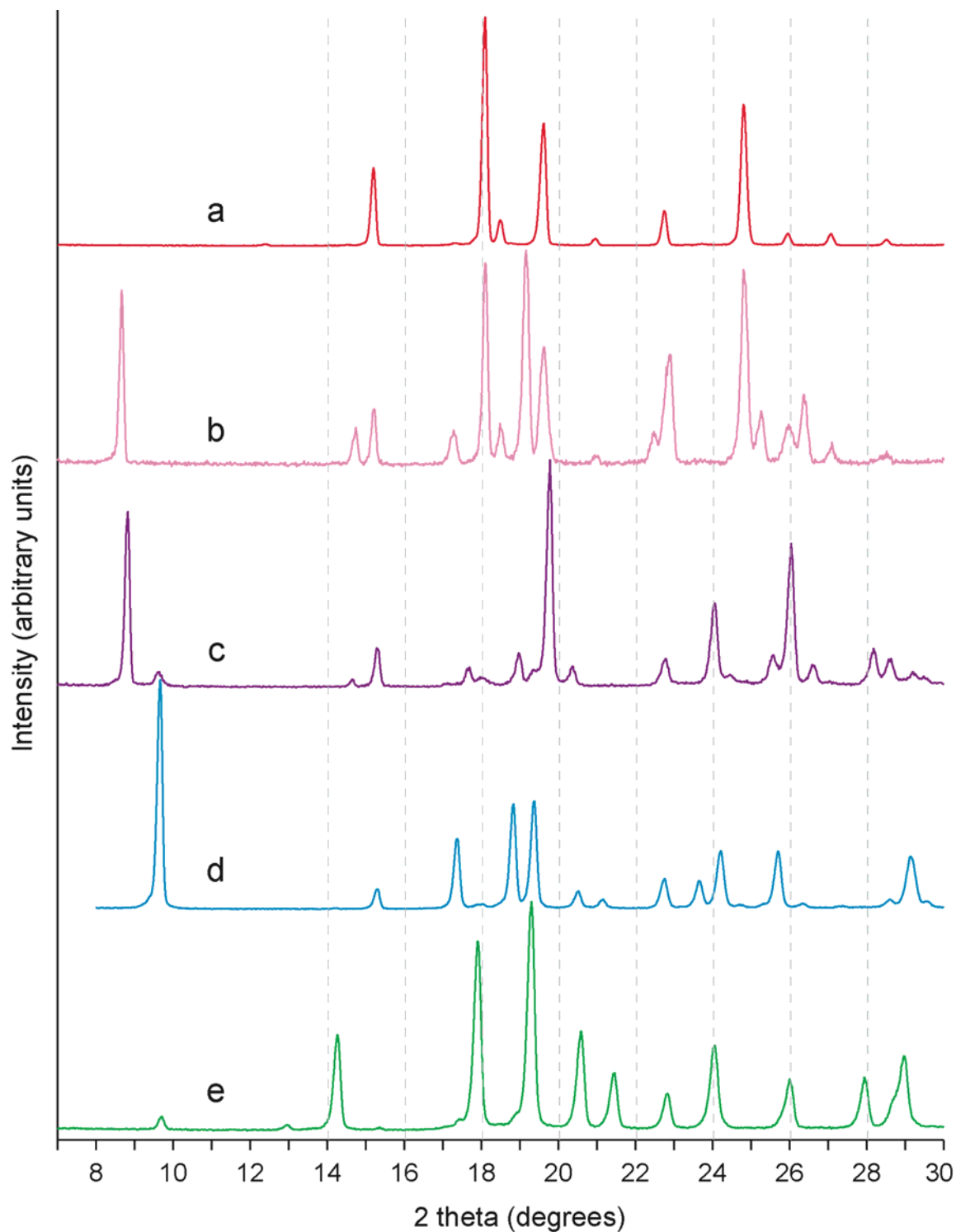
*CrystEngComm*



**ESI Figure 3.** <sup>13</sup>C CP-MAS NMR spectra (top to bottom) of proline crystal forms corresponding to enantiopure a) L and b) L-MH; and racemic cocrystals c) DL-MH, d) DL-I and e) DL-II.

## Effect of Enantiomeric Ratio and Preparation Method on Proline Polymorphism

*CrystEngComm*



**ESI Figure 4.** PXRD patterns of proline crystal forms: a) L, b) L-MH, c) DL-MH, d) DL-I, and e) DL-II.