# Solvent Effects on the Energetics of Prolyl Peptide Bond Isomerization

## Supplementary Material

Eric S. Eberhardt, Stewart N. Loh, Andrew P. Hinck, and Ronald T. Raines*

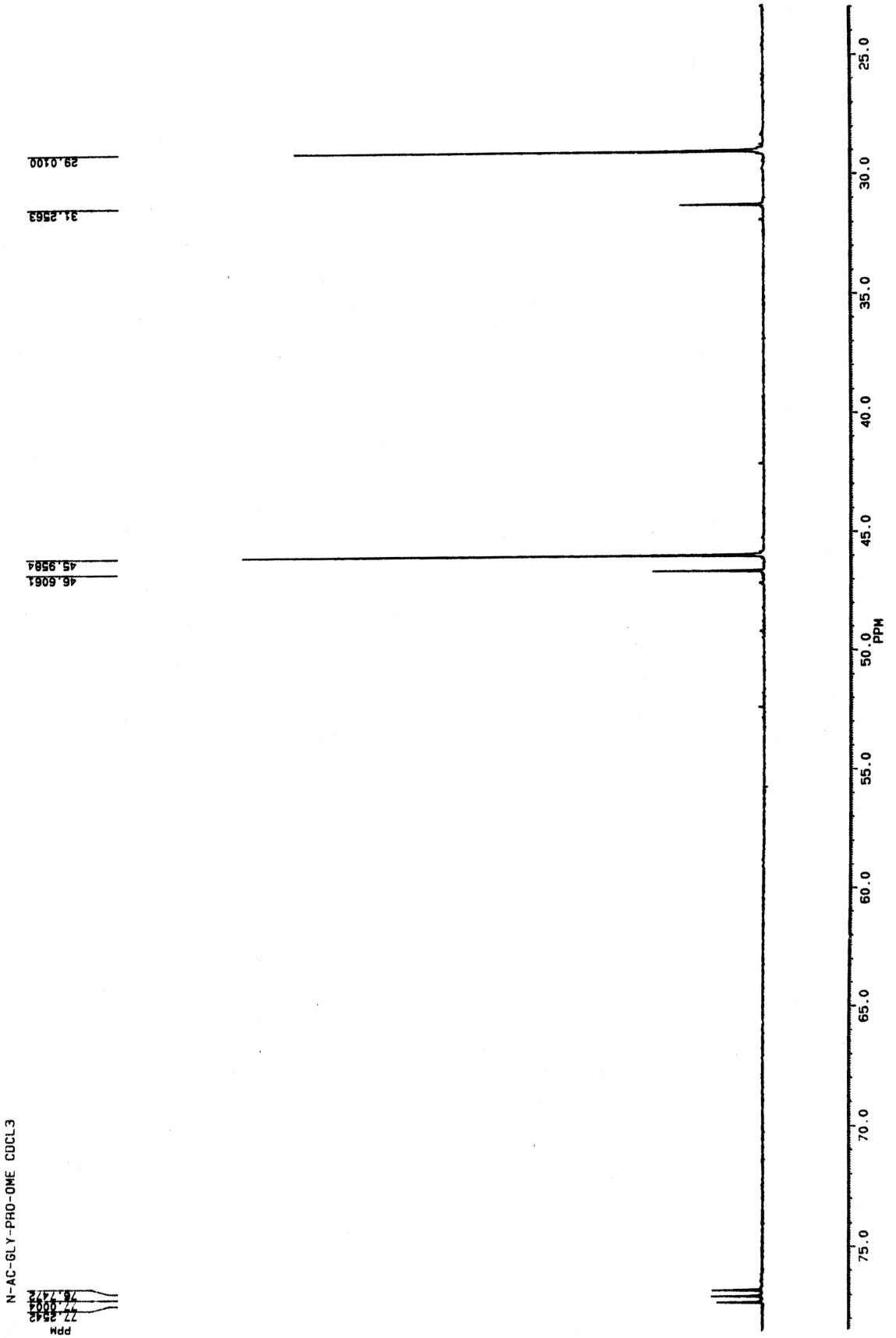
Department of Biochemistry
University of Wisconsin–Madison
Madison, WI 53706

*Author to whom correspondence should be addressed.

## Figure Legends

**Figure 1S**. $^{13}C$ NMR spectrum ($CDCl_3$, 125.77 MHz) of **1**. δ (in ppm): 29.0100 (Pro β, *trans*), 31.2563 (Pro β, *cis*), 45.9584 (Pro δ, *trans*), 46.6061 (Pro δ, *cis*). Pro β was used for inversion transfer experiments. FAB–MS of **1** showed $(M + H)^+$ = 231 u (calculated 231.2 u).

**Figure 2S**. FT-IR spectrum [100 mM sodium phosphate buffer, pH 7.2, containing 20% (v/v) $D_2O$; ZnSe crystal] of Ac-Pro-OMe. υ (in $cm^{-1}$): 1605.95 (amide), 1729.50 (ester).


N-AC-GLY-PRO-OME CDCL3
29.0100
31.2563
45.9584
46.6061
22.2545
24.8021
76.7472
PPM
25.0
30.0
35.0
40.0
45.0
50.0
55.0
60.0
65.0
70.0
75.0
PPM

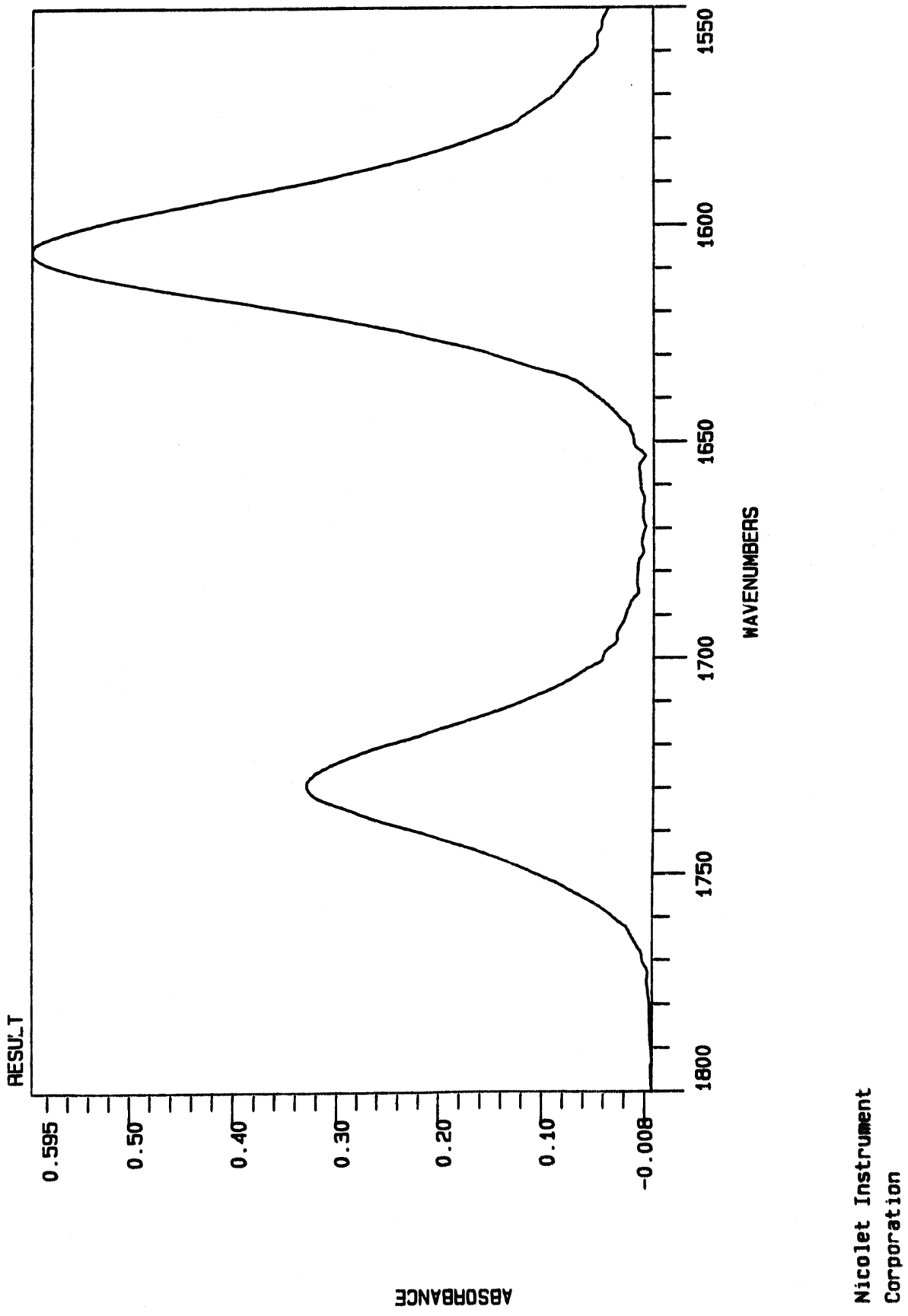

RESULT
0.595
0.50
0.40
0.30
0.20
0.10
-0.008
ABSORBANCE
1800
1750
1700
1650
1600
1550
WAVENUMBERS
Nicolet Instrument
Corporation

**Table IS**. Solvent Effects on Activation Parameters for Isomerization of **1**.

| solvent | rate constant | $\Delta H^{\ddagger}$ [a] [kcal/mol] | $\Delta S^{\ddagger}$ [a] [cal/(mol K)] |
|---|---|---|---|
| acetonitrile | $k_{EZ}$ | 19.25 ± 0.14 | 3.18 ± 0.43 |
| | $k_{ZE}$ | 19.97 ± 0.14 | 2.71 ± 0.43 |
| benzene | $k_{EZ}$ | 20.79 ± 0.29 | 7.74 ± 0.87 |
| | $k_{ZE}$ | 19.46 ± 0.09 | 0.66 ± 0.27 |
| *N*,*N*-dimethylformamide | $k_{EZ}$ | 17.55 ± 0.14 | –2.29 ± 0.41 |
| | $k_{ZE}$ | 18.62 ± 0.05 | –0.73 ± 0.15 |
| dioxane | $k_{EZ}$ | 16.67 ± 0.03 | –3.84 ± 0.08 |
| | $k_{ZE}$ | 18.30 ± 0.09 | –1.85 ± 0.26 |
| ethanol | $k_{EZ}$ | 15.35 ± 0.29 | –9.61 ± 0.88 |
| | $k_{ZE}$ | 14.96 ± 0.10 | –13.59 ± 0.32 |
| isopropanol | $k_{EZ}$ | 17.68 ± 0.29 | –2.01 ± 0.67 |
| | $k_{ZE}$ | 19.42 ± 0.16 | 0.69 ± 1.14 |
| toluene | $k_{EZ}$ | 22.28 ± 0.11 | 12.95 ± 0.34 |
| | $k_{ZE}$ | 23.35 ± 0.06 | 13.86 ± 0.20 |
| trifluoroethanol | $k_{EZ}$ | 20.60 ± 0.29 | 2.97 ± 0.86 |
| | $k_{ZE}$ | 23.08 ± 0.13 | 6.89 ± 0.40 |
| water | $k_{EZ}$ | 18.78 ± 0.13 | –1.42 ± 0.39 |
| | $k_{ZE}$ | 21.21 ± 0.13 | 2.29 ± 0.38 |

[a]Values were calculated from linear regression analysis of plots of ln ($k_{EZ}$/T) vs 1/T and ln ($k_{ZE}$/T) vs 1/T.