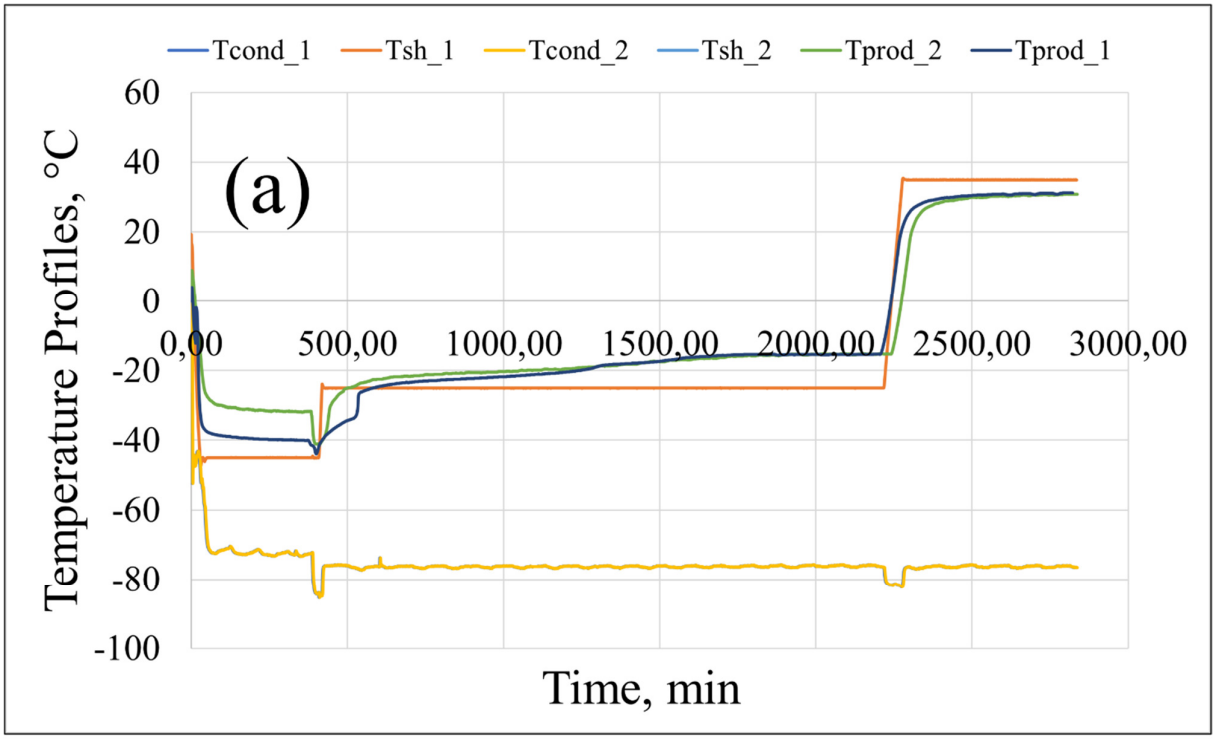

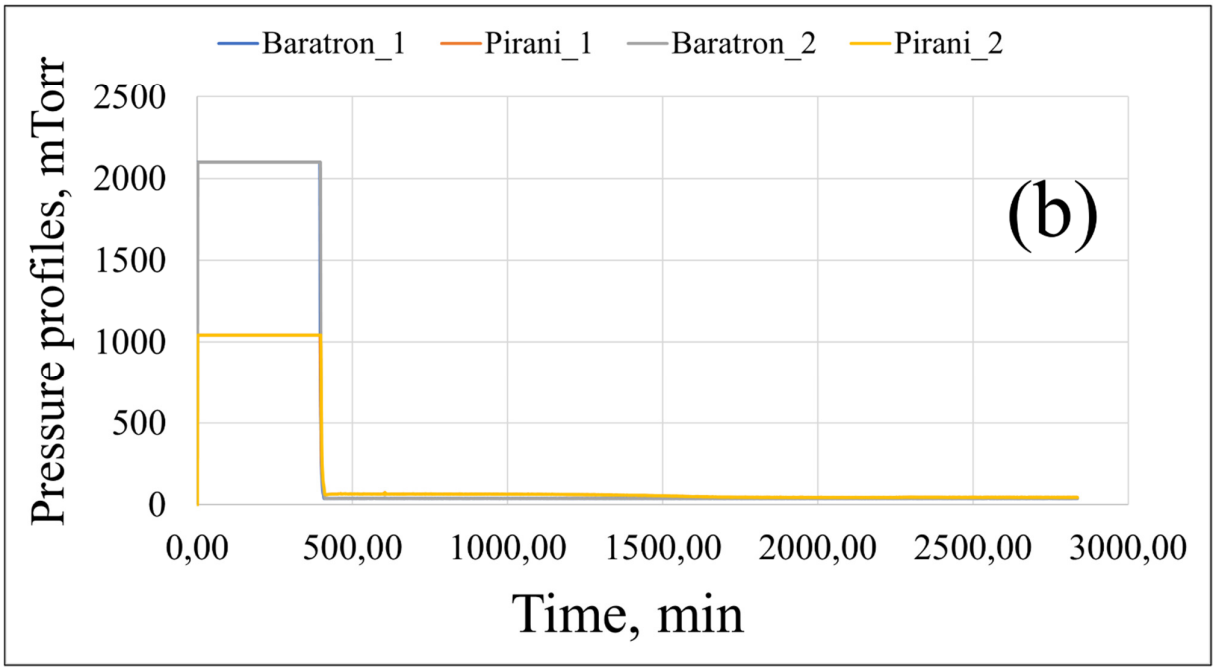

Figure S1: Process variables for the reference cycles; graph (a): Temperature profiles and (b) Pressure profiles.

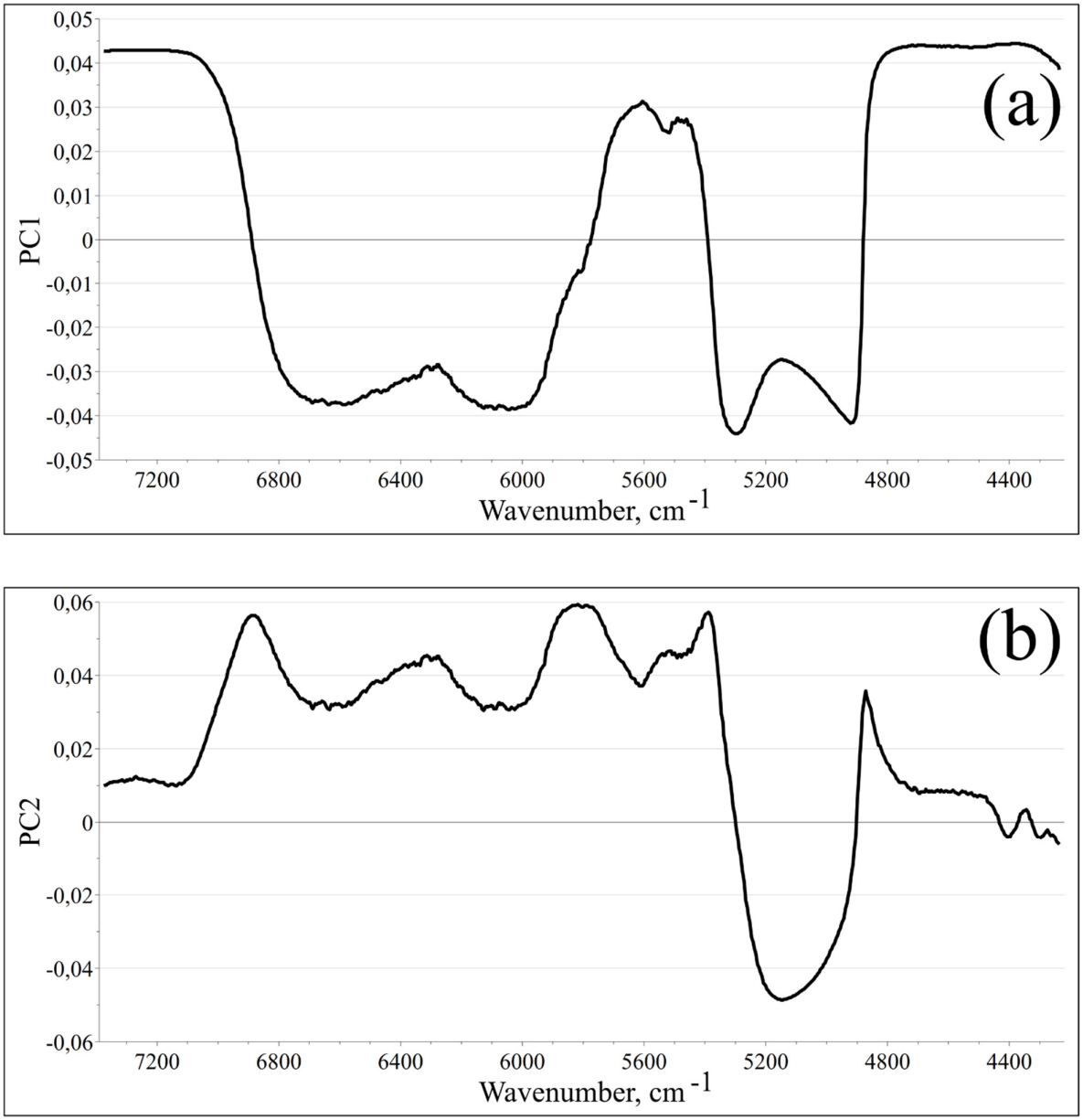

Figure S2: Loadings plot relating the first principal component (a) and the second one (b) as a function of the wavenumber. Data were processed by PCA in the range 7400 -4230 cm^{-1}.

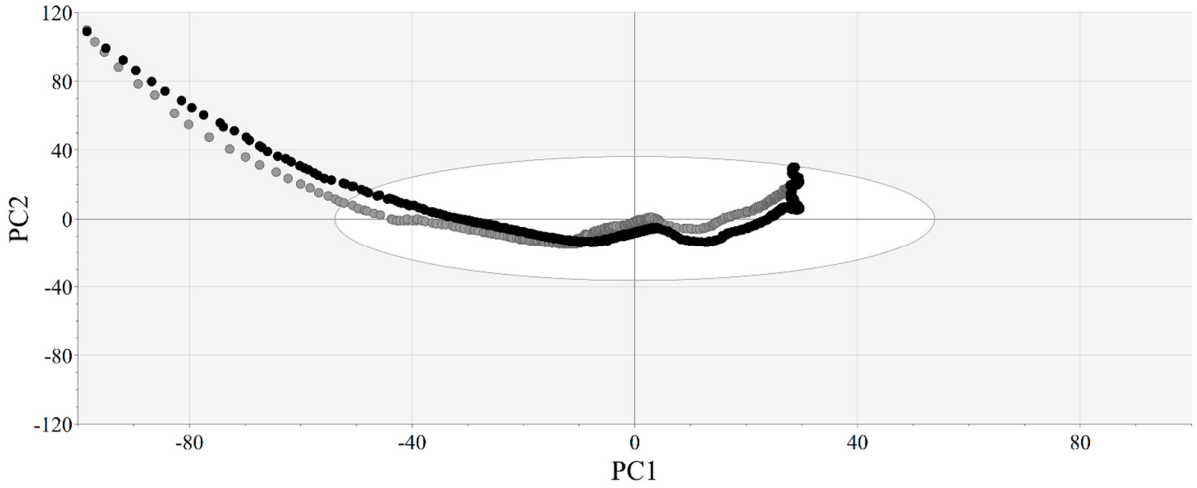

Figure S3: Scores plot relating the first two principal components of the NIR spectra acquired in-line during the freeze-drying process by considering only the drying stages. Data were processed by PCA in the range 7400 – 4230 cm^{-1}. The data are colored respectively in black or grey for reference cycle 1 and 2

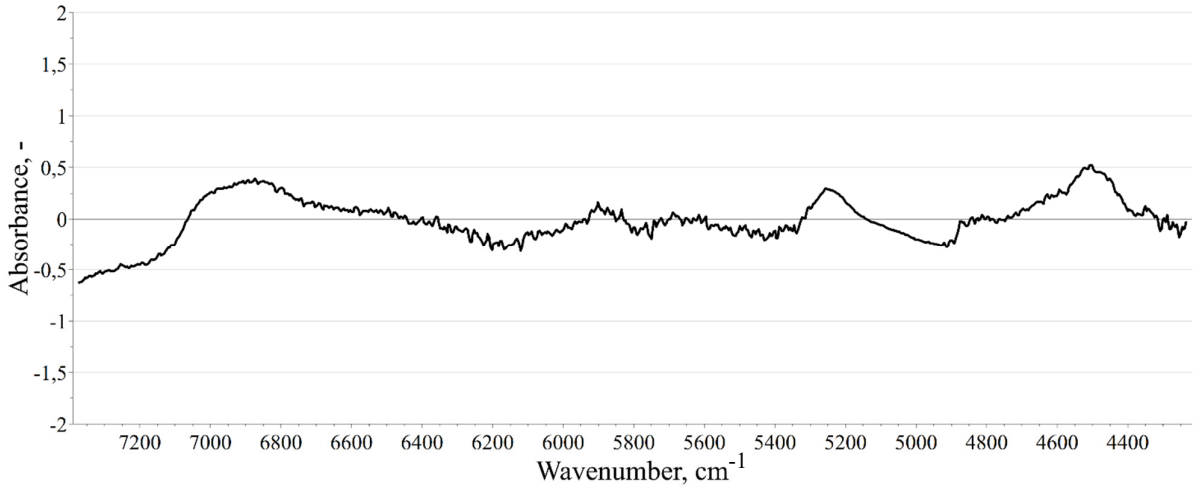

Figure S4: NIR spectra investigation of the anomalous sample noticed in the Hotelling's T2 plot for the reference cycle 1.