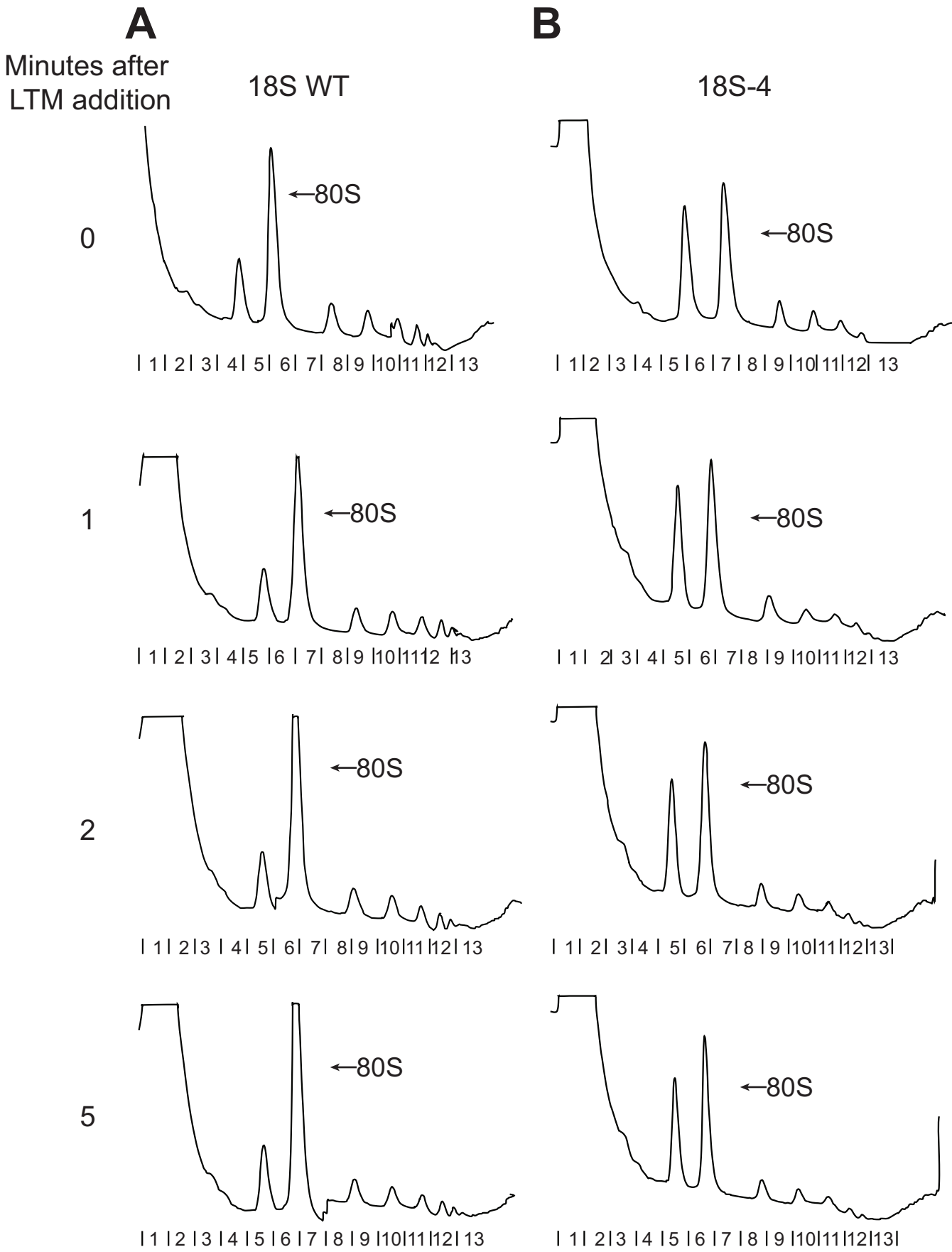Supplemental Figure 4