Convenient Parallel Synthesis Of Alkyl- and Aryl-S-tert-Butyl Thiothers.

Rebecca Norcross, Jessica Stanfield and Richard W. Fitch, Department of Chemistry and Physics, Indiana State University, 600 Chestnut Street, Terre Haute, IN 47809

While preparing novel cysteine derivatives as oxidation catalysts, we needed S-tert-butylcysteine. We also examined acid-promoted tert-butylation of thiols using tert-butanol as reagent and solvent. While cysteine and aminoethanethiol work well using tBuOH in 4M HCl, other thiols fail in the aqueous environment and aerobic conditions. We examined a variety of aliphatic and aromatic thiols in tBuOH with H2SO4 catalysis and found that argon sparging and the use of 1 eq of acid led to good yields in a parallel format.

R—SH
$$\frac{\text{tBuOH/H}_2\text{SO}_4}{\text{80}^{\circ}\text{C/sealed vial}}$$
 R—S $\frac{0 - 95\%}{\text{Structure-dependent}}$