Continuous-Flow Pd/C-Catalyzed Reductive Alkylation of Alcohols with Aldehydes

Results:

\[
\begin{align*}
R-OH \quad (15 \text{ mL}) & \quad + \quad O_2 \quad (19.5 \text{ mmol}) \\
\text{internal diameter 4 mm, length 70 mm,} & \quad 5\% \text{ Pd/C (340 mg), H}_2 \text{ (1 bar)} \\
140 \degree C, 0.6 \text{ mL/min} & \quad \text{residence time: 1.5 min} \\
\end{align*}
\]

\[
\begin{align*}
79\% \text{ yield} & \quad 68\% \text{ yield} & \quad 52\% \text{ yield} & \quad 43\% \text{ yield} \\
67\% \text{ yield} & \quad 58\% \text{ yield} & \quad 50\% \text{ yield} & \quad 46\% \text{ yield} \\
88\% \text{ yield} & \quad 59\% \text{ yield} & \quad 71\% \text{ yield} & \quad 57\% \text{ yield} \\
46\% \text{ yield} & \quad 35\% \text{ yield} & \quad 93\% \text{ yield} & \quad 57\% \text{ yield} \\
43\% \text{ yield} & \quad 43\% \text{ yield} & \quad 70\% \text{ yield} & \quad 55\% \text{ yield} \\
\end{align*}
\]

Significance: The authors have developed a continuous-flow system for the reductive alkylation of alcohols with aldehydes catalyzed by Pd/C in the presence of hydrogen, giving the corresponding ethers in 35–93% yield.

Comment: In the long-term flow reaction of butan-1-ol with octanal, butyl octyl ether was obtained in 50% yield after eight hours.