





Table 1. Effect of microwave irradiation at low temperature

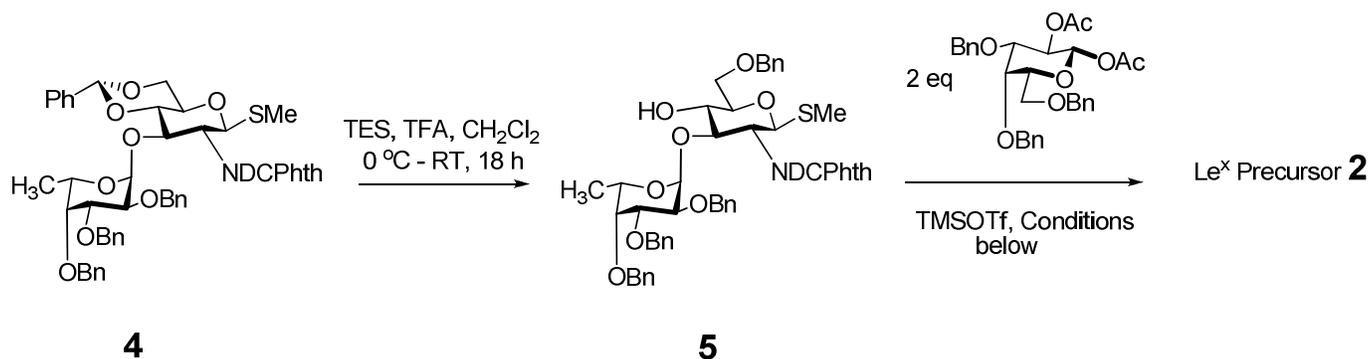
Solvent	Microwave Power (W)	Temperature (°C)	Time (h)	Yield (%)
Ether	none	-10	1	27
Ether/THF (5/1)	none	-45	6	71
Ether	300 W	-10	1	90
Ether	100 W	-18	2.5	83
CH <sub>3</sub> CN	300 W	-20	1	21
CH <sub>2</sub> Cl <sub>2</sub>	300 W	-20	2.5	9



Figure 2. CEM Discover with CoolMate attachment

For the trisaccharide synthesis (Scheme 2), selective reduction of the benzylidene group with triethylsilane and trifluoroacetic acid afforded **5** in 88 % yield. Glycosylation of the glucosamine unit in the presence of TMSOTf gave the desired product **2**. Many attempts under conventional methods to obtain product failed. The results of the trisaccharide synthesis are summarized in Table 2. Di- and trisaccharide byproducts were the only materials recovered from entry 4 and 5. It was unclear why the solvent affects the yield of desired product; however, ether consistently gave higher yields. Maintaining a temperature below 0 °C during the course of the reaction was crucial to generate the desired product: entry 2 reached -5 °C, while entry 3 reached 30 °C and the isolated yield was decreased by half. The reduction in yield was attributed to the formation of di- and trisaccharide byproducts which were isolated and characterized. Microwave irradiation at low temperatures was an effective method to control the reaction pathway and reduce byproducts in the synthesis of LeX derivatives. In the words of the authors “microwave irradiation turned the ‘impossible’ into a ‘possible’.”

**Scheme 2.** Synthesis of thiomethyl Le<sup>X</sup> derivative



**Table 2.** Results of trisaccharide synthesis using CoolMate

Entry	Solvent	Microwave Power (W)	Temperature (°C)	Time (h)	Yield of <b>2</b> (%)
1	ether	none	-20 to RT	24	0
2	ether	300	-20 to -5	5	82
3	ether	300	-20 to 30	6	43
4	CH <sub>2</sub> Cl <sub>2</sub>	300	-20 to 5	2	0
5	CH <sub>3</sub> CN	300	-20 to 5	6	0

**References and Remarks**

- Shimizu, H.; Yoshimura, Y.; Hinou, H.; Nishimura, S. *Tetrahedron* **2008**, *64*, 10091 – 10096. DOI: [doi:10.1016/j.tet.2008.08.011](https://doi.org/10.1016/j.tet.2008.08.011)
- For information on the CoolMate including applications and theory, see <http://cem.com/coolmate.html>