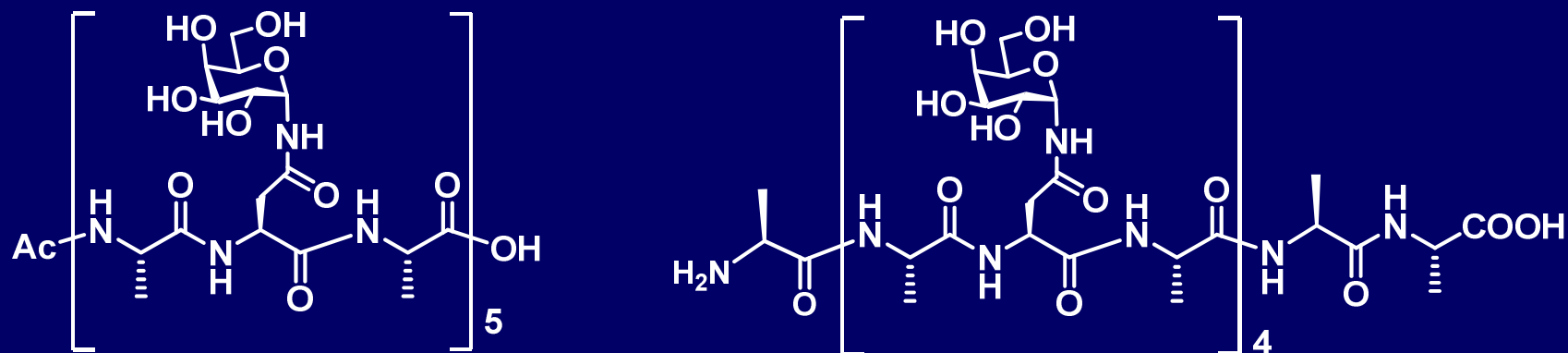


# Synthesis of unnatural $\alpha$ -N-linked glycopeptides with potential antifreeze activity

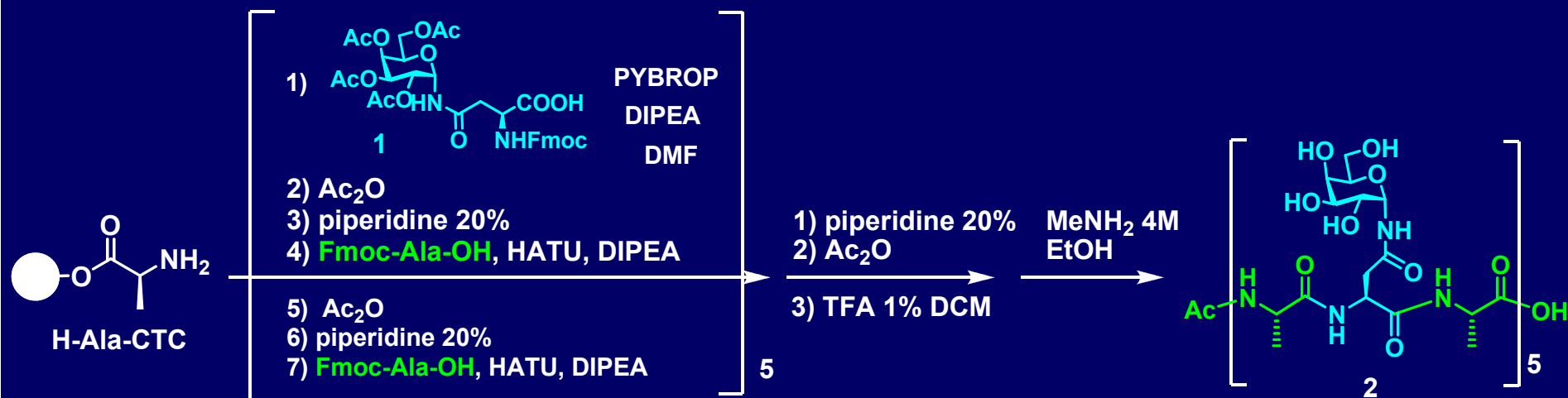
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# Solid Phase Synthesis at Room Temperature



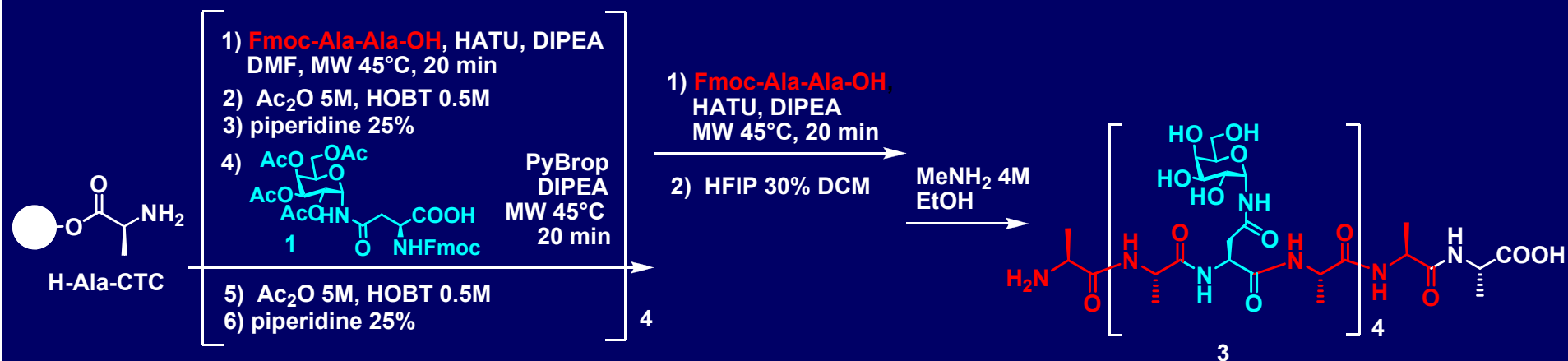
- Coupling reactions with Fmoc-Ala-OH (5 equivalents, 2h, 2 cycles) occurred quantitatively.
- Galactosyl amino acid 1 reacted slowly and in relative low yields (Table 1).

**Table 1**

Repeat (n)	Equivalents	Cycles	[M ] in DMF	Reaction time (h)	Yield(%) <sup>a</sup>
1	1.5	1	0.1	8	~ <sup>b</sup>
2	1.5	2	0.1	8 + 12	80
3	2	2	0.15	8 + 12	83
4	2	3	0.15	8 + 12 + 8	80
5	3	3	0.15	8 + 12 + 8	90

<sup>a</sup> Yield determined by UV spectroscopy after Fmoc-removal. <sup>b</sup> First amino acid loaded on the resin (loading = 0.5 mmol/g).

# Microwave assisted Solid Phase Synthesis

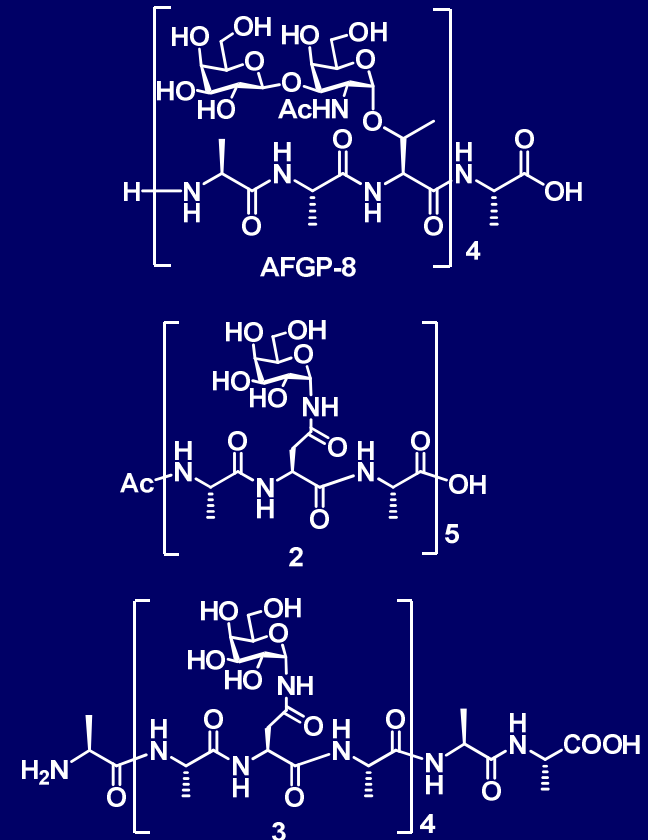
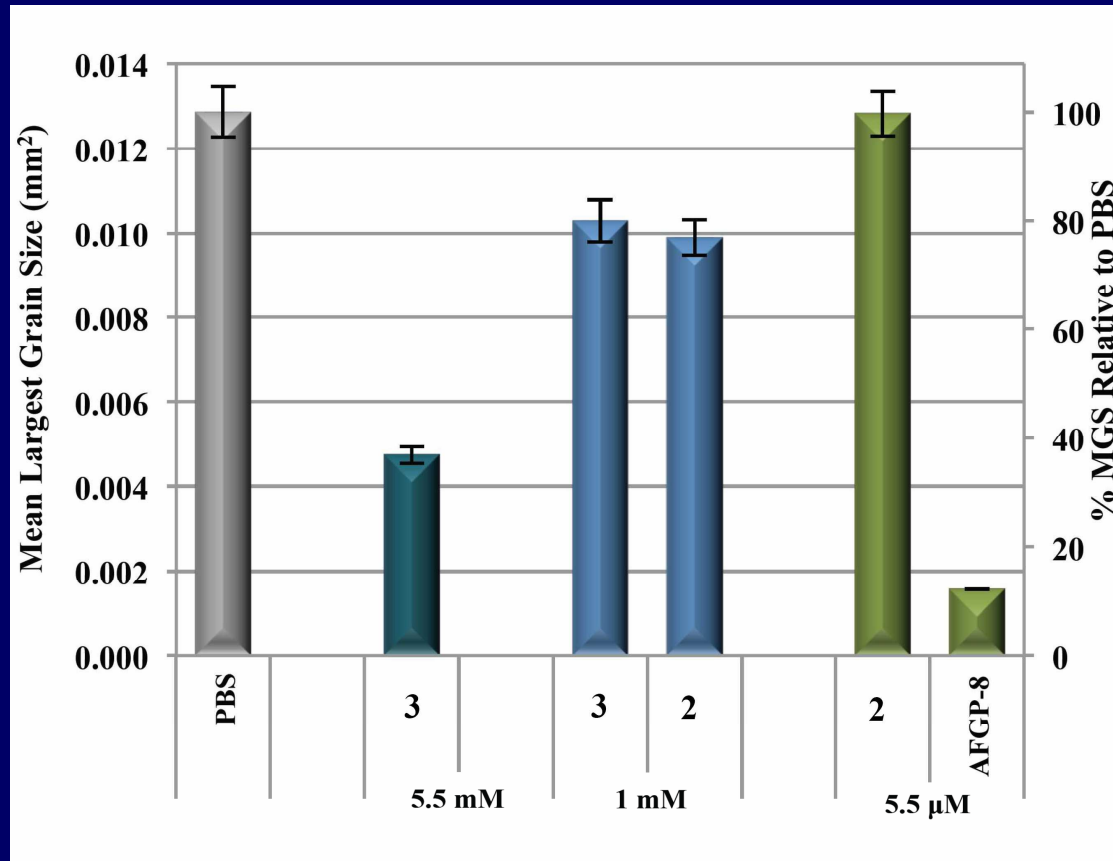


- MW acceleration worked well for coupling of the first unit of 1, bringing the yields up to 95%.
- After the first repeat, the yields of the MW-assisted process were lower than those obtained at room temperature (Table 2).
- A remarkable benefit was observed in terms of reaction time (20 min versus 8-12h).

Table 2	Repeat (n)	Equivalents	Cycles	[M ] in DMF	Reaction time	Yield(%) <sup>a</sup>
	1	3	3	0.37	20min/cycle	95
	2	3	3	0.37	20min/cycle	72
	3	3	3	0.2	20min/cycle	64
	4	3	3	0.2	20min/cycle	51

<sup>a</sup> Yield determined by UV spectroscopy after Fmoc-removal.

# Ice Recrystallization Inhibition (IRI) Assay



IRI activity of  $\alpha$ -N-linked glycopeptides **2** and **3** assayed at the indicated concentrations. The % MGS (mean grain size) of ice crystals relative to PBS control is shown for each glycopeptide. PBS is used as a negative control for IRI activity and AFGP-8 is used as a positive control for IRI activity.

**Unnatural  $\alpha$ -N-linked glycopeptides **2** and **3** have no relevant IRI activity.**