Electronic Supplementary Material (ESI) for Polymer Chemistry

Supplementary Information

Pushing the limits of copper mediated azide-alkyne cycloaddition (CuAAC) to conjugate polymeric chains to cyclic peptides

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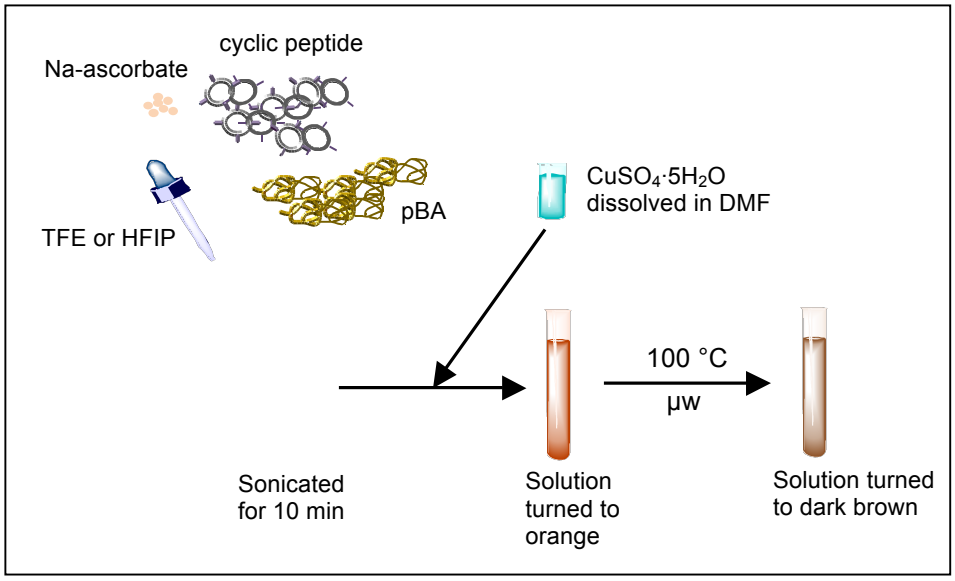
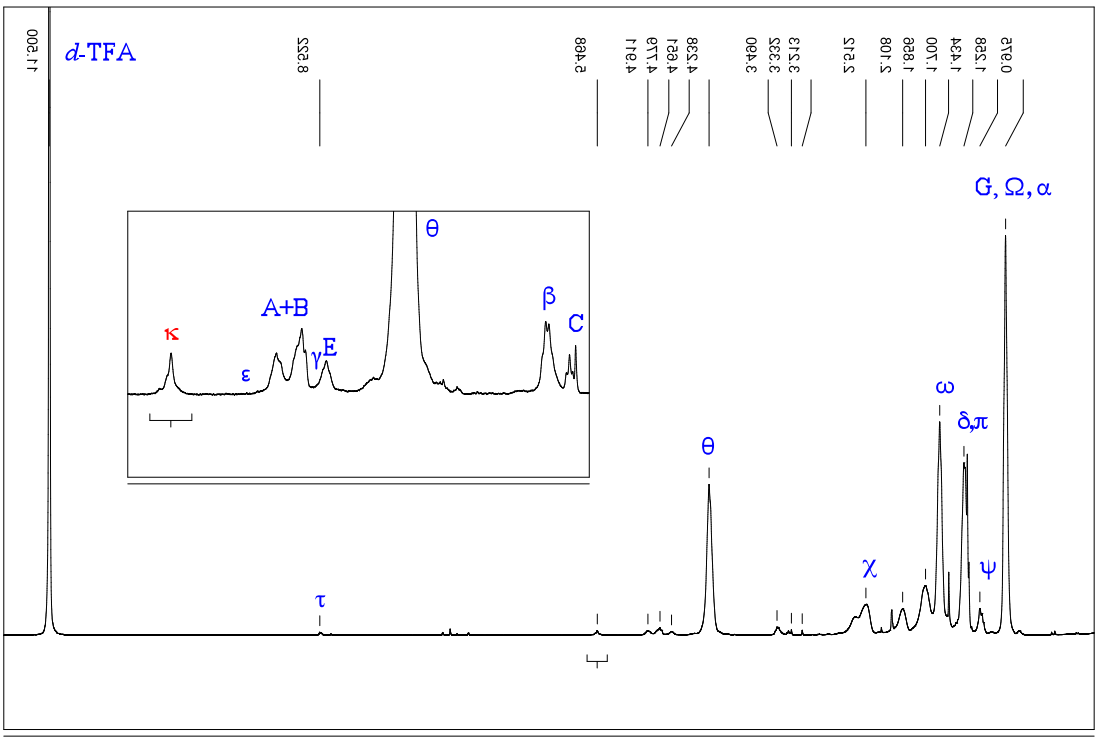
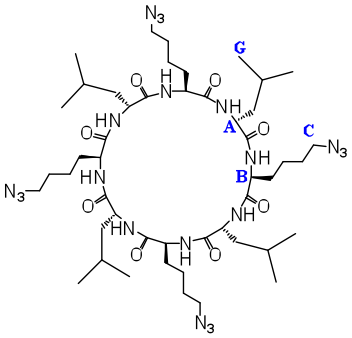
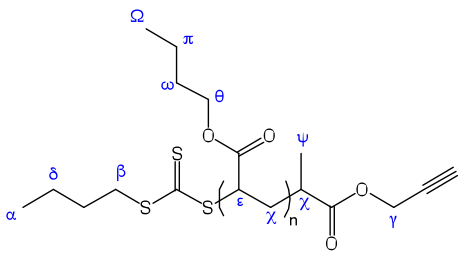


Scheme 1. Preparation of microwave-assisted CuAAC in the synthesis of cyclic peptide-polymer conjugates.

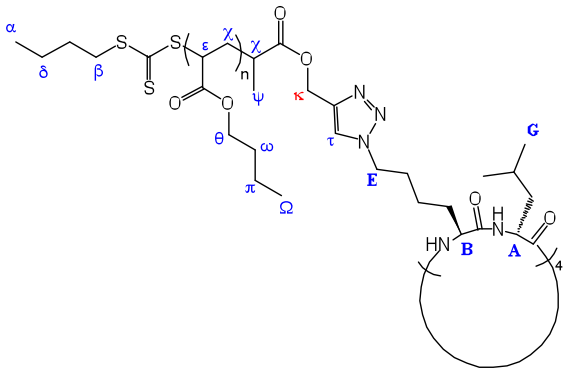




unconjugated *cyclo*-[L-Lys(N_3)-D-Leu]$_4$

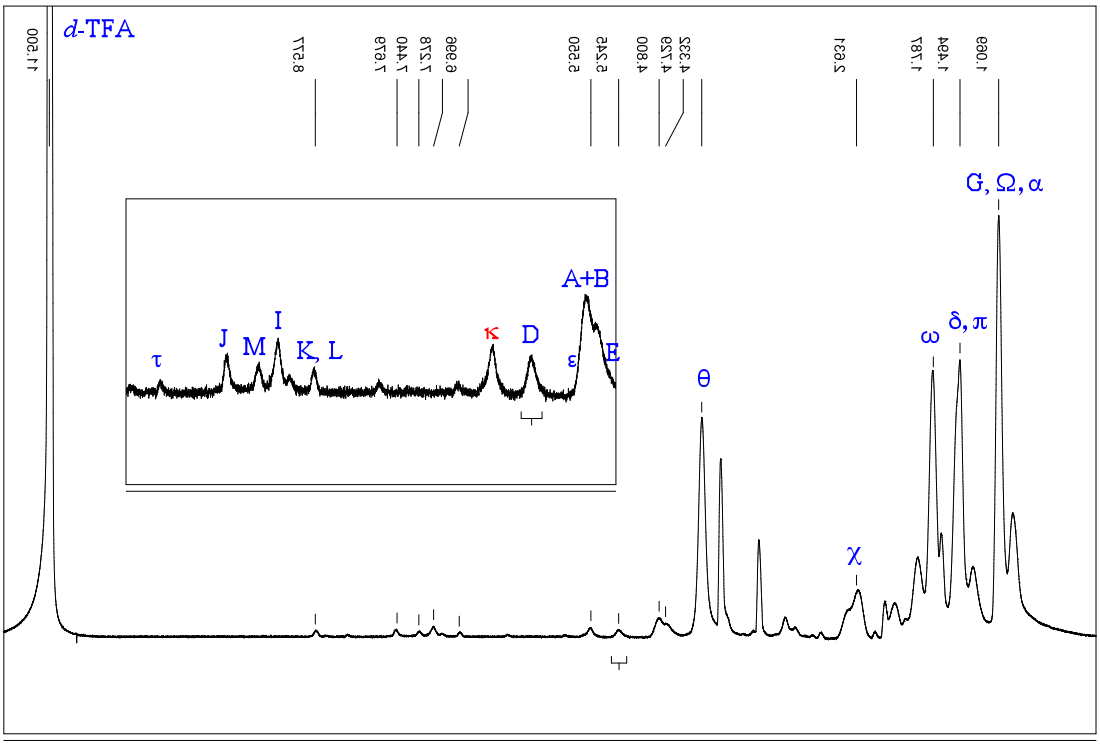


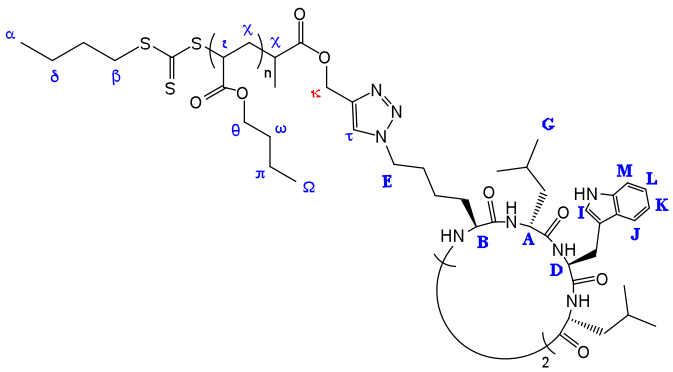
unreacted alkyne-functionalised pBA



cyclo-[L-Lys(N_3)-D-Leu]$_4$-pBA conjugate

Figure S1. Example ^{1}H-NMR (*d*-TFA) spectrum of conjugates prepared from CuAAC between four-arm cyclic peptide and PBA.





cyclo-[L-Lys(N_3)-D-Leu-L-Trp-D-Leu]$_2$-pBA conjugate

Figure S2. Example ^{1}H-NMR (*d*-TFA) spectrum of conjugates prepared from CuAAC between two-arm cyclic peptide and PBA.

Determination of Conjugation Efficiency from ^{1}H-NMR Spectroscopy

The average number of polymers conjugated to every cyclic peptide in the four-arm system (Runs 1-10, Table 1) was determined from integrating the NMR signals corresponding to the protons next to the triazoles according to *Equation S1* as follows:

$$Conjugation\ efficiency = \frac{\int \kappa}{\left(\frac{\int \kappa + \int C}{4}\right)} \times 100\%$$

...Equation S1

The summation between areas of peaks **κ** and **C** represents the total number of azide sites in the precipitates. This calculation was based on the assumption that all the unreacted and / or incomplete reacted cyclic peptides were present in the precipitates; without dispersing to the aqueous supernatant phase from centrifugation and loss between product transfers. The total number of cyclic peptides in the precipitate was calculated by dividing the total number of azide sites by four, in which a single cyclic peptide contains four azide sites.

Table S1. Characterisation of alkyne-functionalised pBA synthesised

pBA DP[#]	**[Monomer]:[RAFT]**	**Conversion (%)**	M_n[##] **(SEC)**	M_n **(NMR)**	***PDI***[###]
16	18:1	80	1900	2400	1.18
36	36:1	100	4900	5000	1.13
108	120:1	84	14150	11400	1.15

[#]DP = degree of polymerisation, [##]M_n = Number average molecular weight, [###]*PDI* = Polydispersity index