









### 3. Conclusions

In summary, the drug conjugates **7** and **15** were successfully synthesized in water with high Pt loading degrees. The Pt-diaqua drug conjugate containing a six-membered ring **15** was successfully synthesized for the first time. The formation of six-membered ring (**15**) with Pt-diaqua is faster than that of five-membered ring (**7**) formation. This optimized synthetic protocol has the potential to generate cisplatin drug conjugates in kilogram scales to provide high drug loading degrees to meet the demand for these HA-Lys-Pt conjugates for various chemotherapeutics applications. Further studies on these drug conjugates are currently underway in our laboratory.

### 4. Experimental

Detailed synthesis procedures for compounds **2–15**, NMR and MS characterization of these compounds can be found in the Supporting Information.

### Notes

TZ and CG are employees of HylaPharm; LF has ownership interest in HylaPharm, which has licensed portions of this technology from KU. SNS declares no competing financial interest.

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### Appendix A. Supplementary data

Supplementary data related to this chapter can be found at <http://dx.doi.org/10.1016/j.ejmech.2017.05.020>.

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