

modified AON (stable for more than 48h) were found to be more stable than carba-LNA modified AON (stable only for 12h)²⁰ and C7'*R/S*-Me-carba-LNA modified AON (stable for 36h)²¹, respectively, under identical condition. C8'*R*-NH₂-carba-ENA (type **VI**) modified AON showed similar stability as C7'*R*-NH₂-carba-LNA modified AON, and both of them can only sustain in blood serum for only 24h. The better nuclease resistance of carba-ENA analogues modified AONs than carba-LNA analogues modified counterpart can be easily understood in terms of their relative hydrophobic character: Propylene linkage between C2'- and C4' positions in carba-ENA analogues is one carbon longer comparing to ethylene linkage in carba-LNA analogues; Thus the propylene linkage in carba-ENA is more hydrophobic than carba-LNA, and also may render a more pronounced steric hindrance to prevent nuclease binding and attacking on the vicinal phosphate.