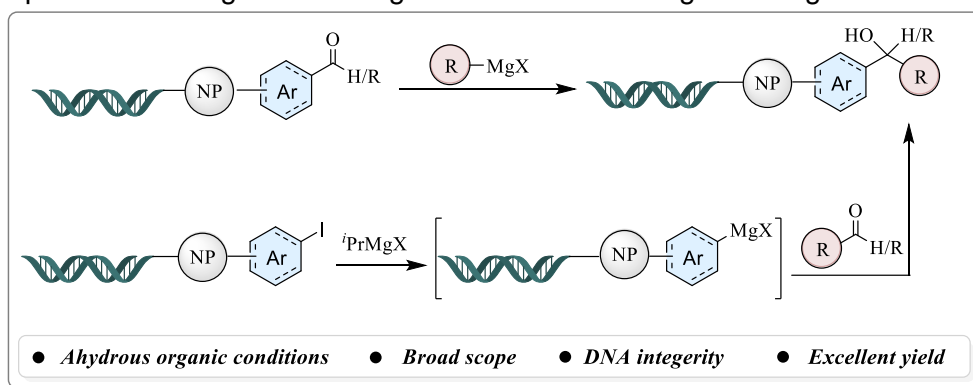


## Nanoparticle-enabled on-DNA Grignard reactions for DNA-encoded library synthesis

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Recently, there has been a growing attention towards the utilization of DNA encoded libraries (DEL) as a tool for target-based small molecule screening in drug discovery owing to the time effectiveness, reduced cost, and storage space for the identification of target compounds. However, the peculiarity of DNA-compatible reactions has limited the application of many C–C and C–X bond formation protocols into the DNA encoded chemical libraries. Grignard reaction has remained one of the most powerful tools for C–C bond formation in organic synthesis. However, due to its stringent reaction conditions (moisture and air-sensitivity), its application in DELs has remained elusive. Herein, we report the first on-DNA Grignard reaction using nanoparticle-support which is readily dispersible anhydrous organic. Broad substrate scope was obtained in good to excellent yield and various sensitive functional groups were remarkably tolerated. Also, the on-DNA magnesium-halogen exchange reaction was found to be compatible with the system and was used in expansion of the scope which proceeds through an *in-situ* generation of DNA-Grignard reagent.



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