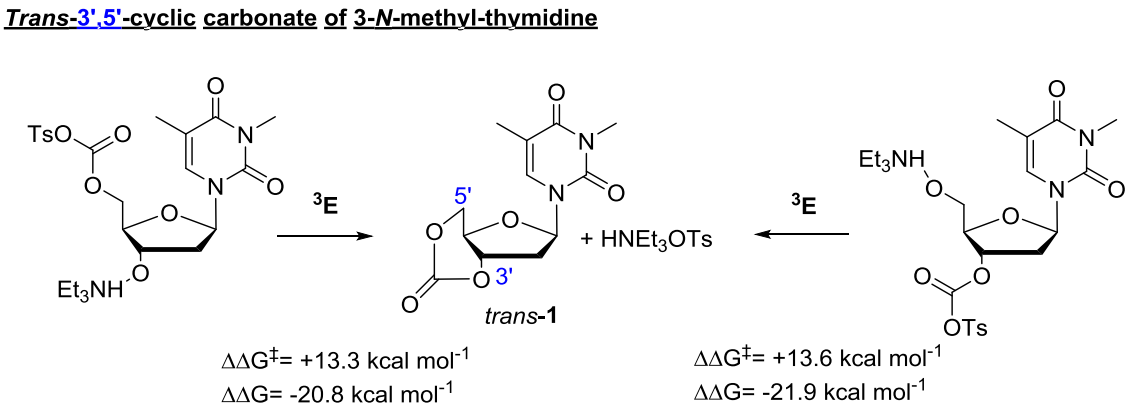
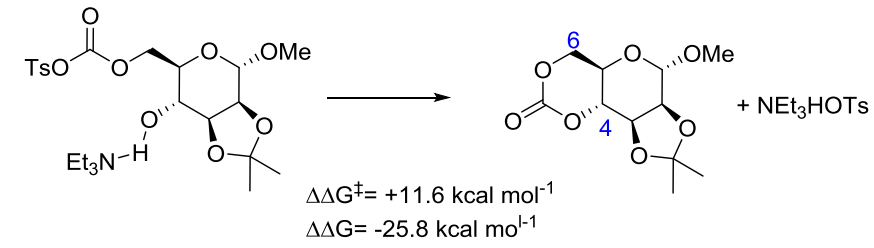
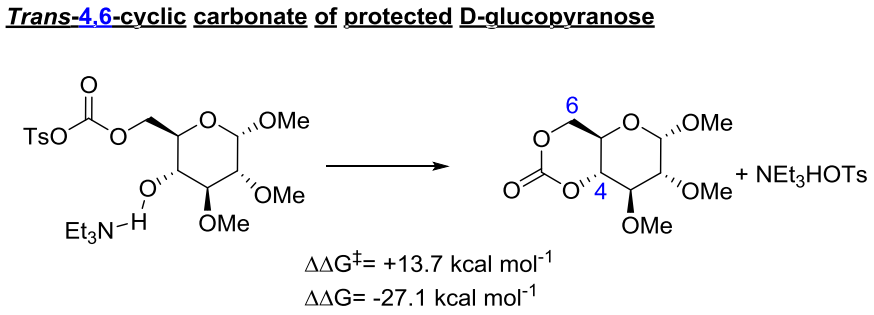
Ring-closing Cyclisation

Nucleophilic Addition-Elimination Pathway

At the rωb97xd/6-31+G(d)/cpcm=acetonitrile/298 K level of theory, both kinetic and thermodynamic barriers to ring-closing by nucleophilic attack of the free hydroxyl group at the tosylated carbonate are reasonable for formation of the *trans*-3',5'-cyclic carbonate of 3-*N*-methyl thymidine. For comparison, the analogous parameters at the same level of theory are calculated for reported *trans*-fused pyranose monomers derived from D-glucose and D-mannose.







Scheme S1. Comparison of the ring-closing kinetic and thermodynamic parameters for the un-isolated trans-3',5'-cyclic carbonate of 3-*N*-methylthymidine and the reported trans-4,6-cyclic carbonates

derived from D-glucose and D-mannose calculated at the rωb97xd/6-31+G(d)/cpcm=acetonitrile/298 K level of theory. 3'-Endo (^{3}E) refers to the envelope conformation of the furanose ring in the lowest energy calculated transition state. The pyranose ring in both mannose and glucose monomers adopt a $^{1}C_{4}$ chair conformation in the transition state.

	Structure	***G /Hartrees***	***ΔG/ kcalmol^{-1}***
	Trans_1	-1026.099913	
	mannoseCC	-954.883603	
	glucoseCC	-916.7632	
	HNEt3OTs	-1187.29434	
Ring-closing by nuc. add. elim. of 3'-OH at 5'-tosylcarbonate	5tosylcarbonate	-2213.361183	0.0
	5tosylcarbonate_TS	-2213.339926	+13.3
	Trans_1 + HNEt3OTs	-2383.018394	-20.8
Ring-closing by nuc. add. elim. of 3'-OH at 5'-tosylcarbonate	3tosylcarbonate	-2213.359407	0.0
	3tosylcarbonate_TS	-2213.337688	+13.6
	Trans_1 + HNEt3OTs	-2213.394253	-21.9
Mannose: Ring-closing by nuc. add. elim. of 4'-OH at 6'-tosylcarbonate	MannCarbonate	-2142.136853	0.0
	MannCarbonate_TS	-2142.118305	+11.6
	MannoseCC+HNEt3OTs	-2104.014351	-25.8
Glucose: Ring-closing by nuc. add. elim. of 4'-OH at 6'-tosylcarbonate	GluCarbonate	-2103.992447	0.0
	GluCarbonate_TS	-1850.210171	+13.7
	GlucoseCC+HNEt3OTs	-2104.05754	-27.1

Table S1. Computed Gibbs Free Energies at the rωB97XD/6-31+g(d)/cpcm=acetonitrile/298K level of theory for cyclic carbonate formation by intramolecular nucleophilic addition-elimination.

Full coordinates for all the stationary points, together with computed free Gibbs energy and vibrational frequency data, are available via the corresponding Gaussian 09 output files, stored in the digital repository: DOI: 10.6084/m9.figshare.4309559 (private link for review purposes: https://figshare.com/s/2587418dd33bfd6c4f68).