Supporting Information

Guanidine – Guanidinium Cooperation in Bifunctional Artificial Phosphodiesterases Based on Diphenylmethane Spacers. The *gem*-Dialkyl Effect on Catalytic Efficiency

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Potentiometric titrations with $(CH_3)_4NOH$ in 80% DMSO (25 °C), 10 mM Me_4NClO_4, and distribution diagrams of the given compounds.

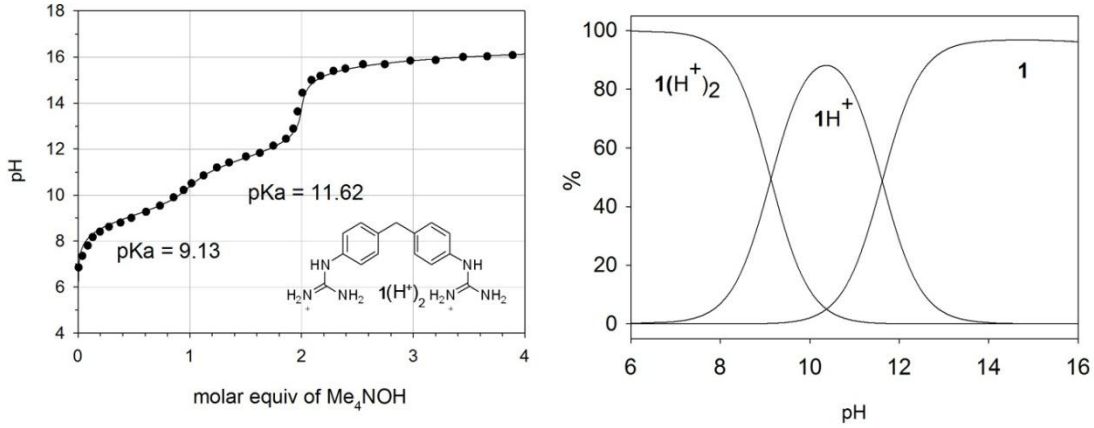


Figure 1S

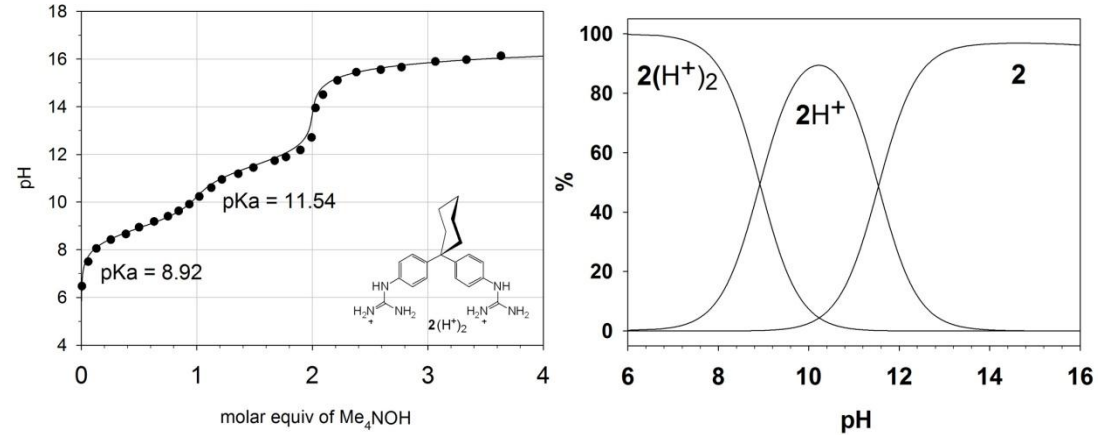


Figure 2S

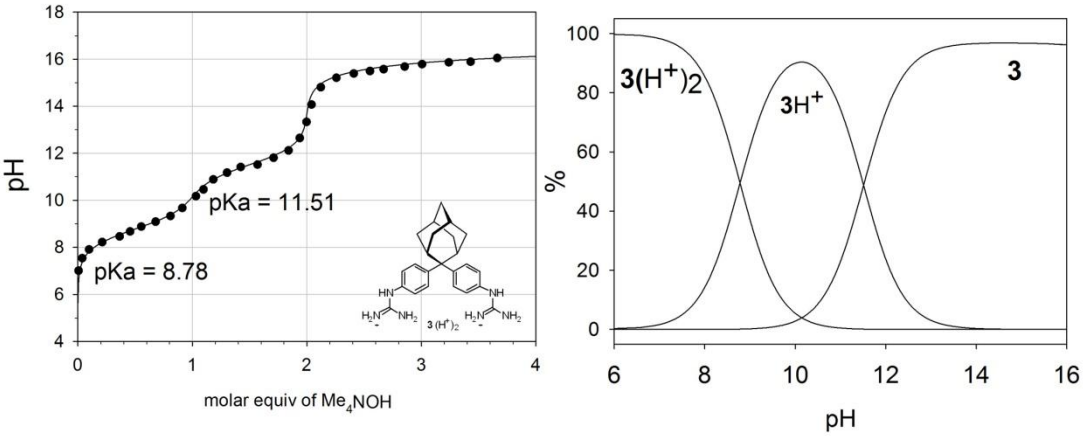
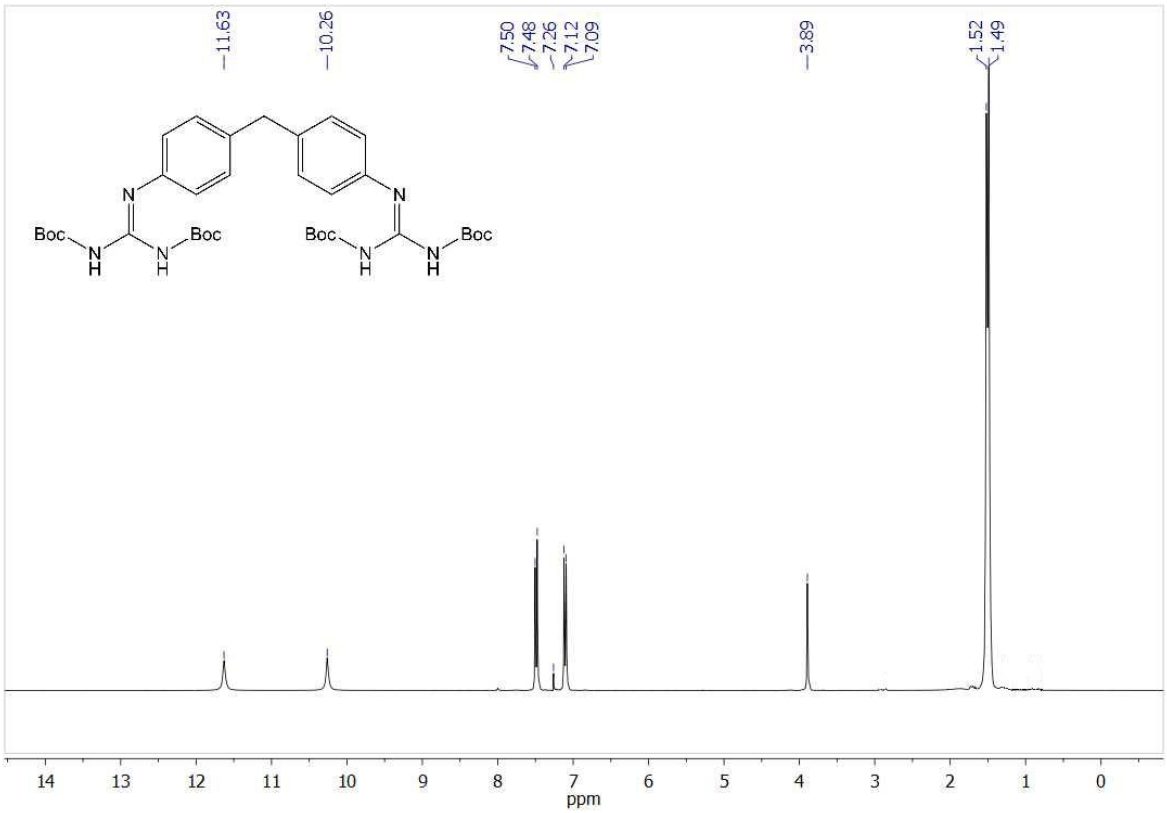
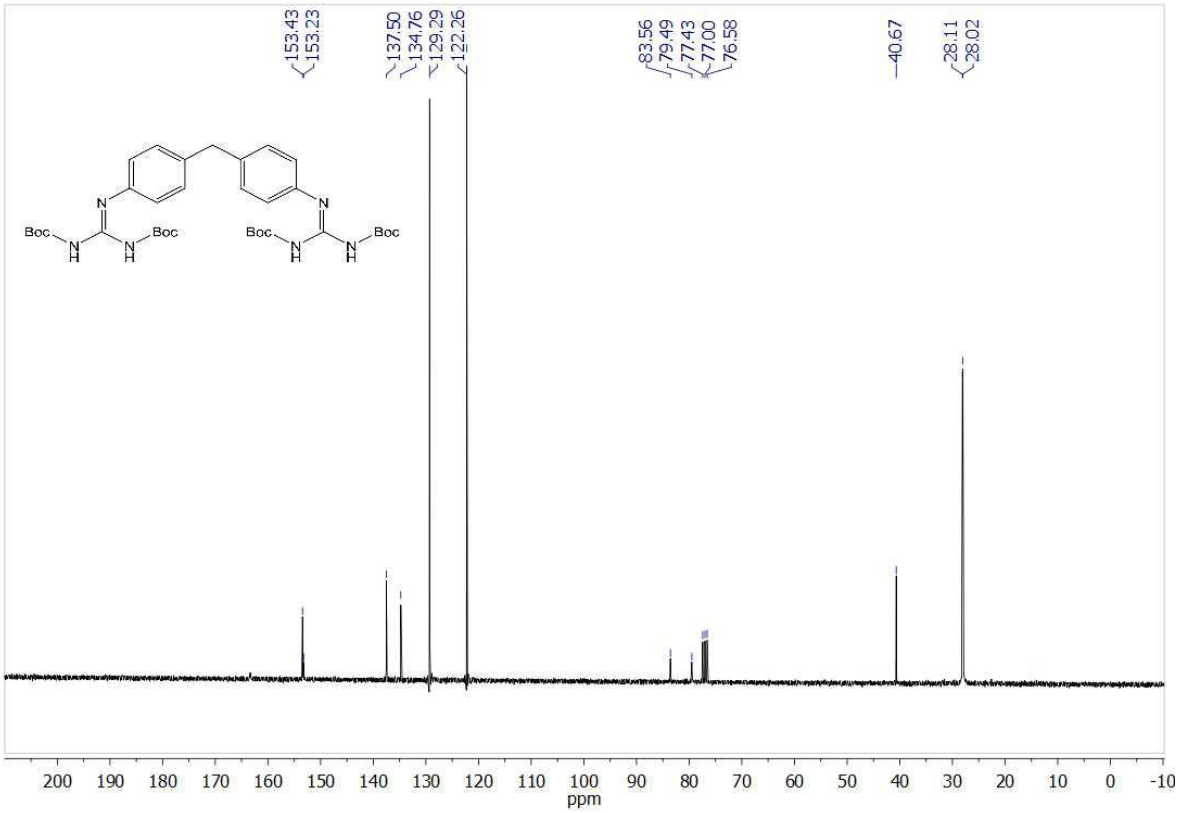


Figure 3S

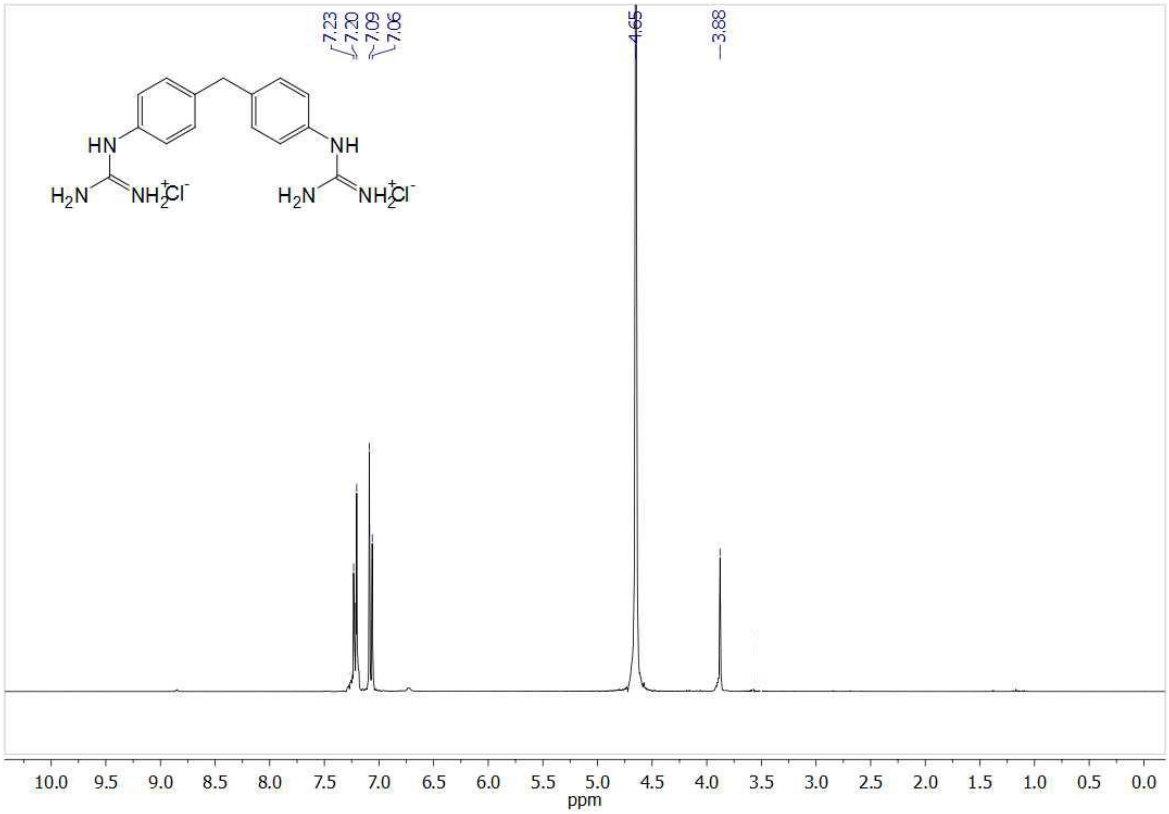
^{1}H NMR of **5a** ($CDCl_3$, 300 MHz)



^{13}C NMR of **5a** ($CDCl_3$, 75 MHz)



^{1}H NMR of **1** (D_2O, 300 MHz)



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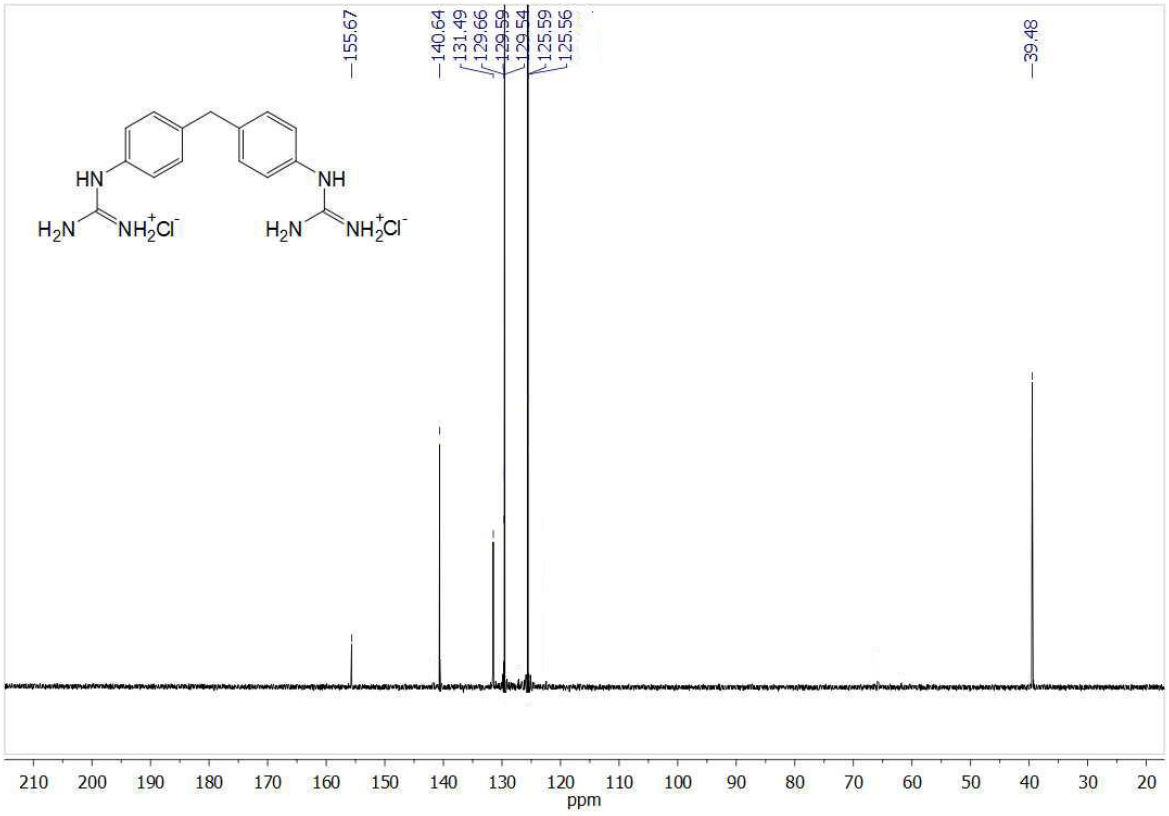
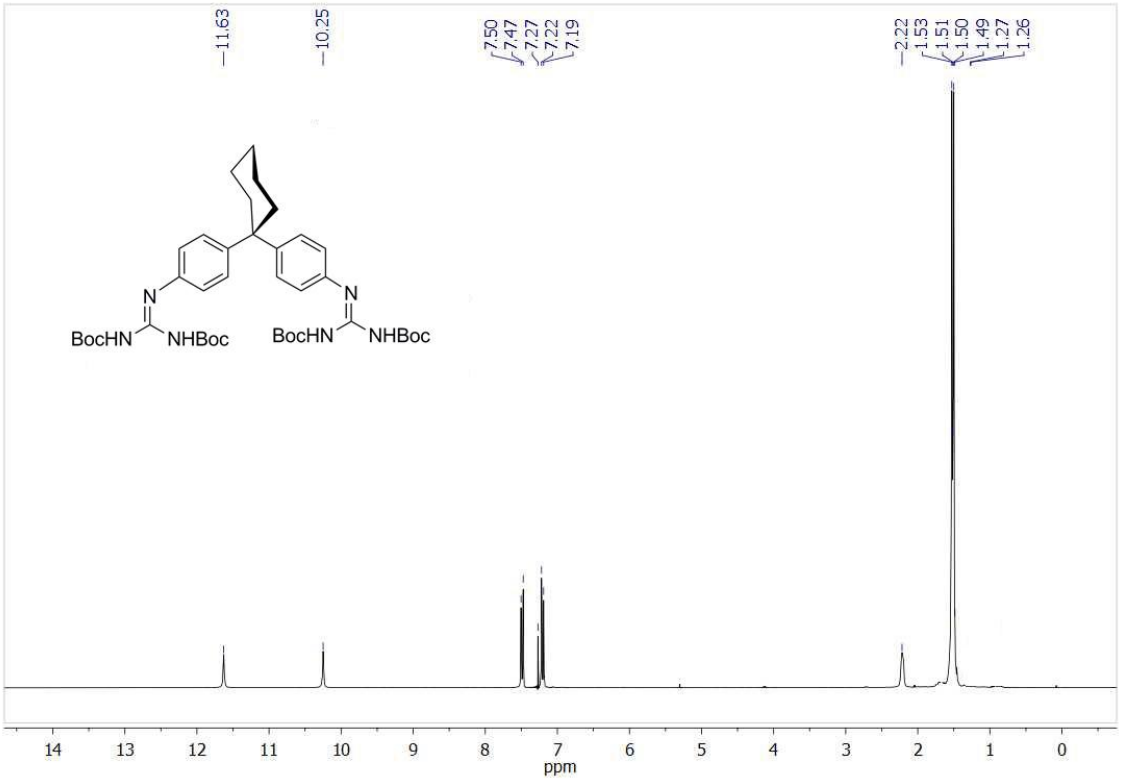
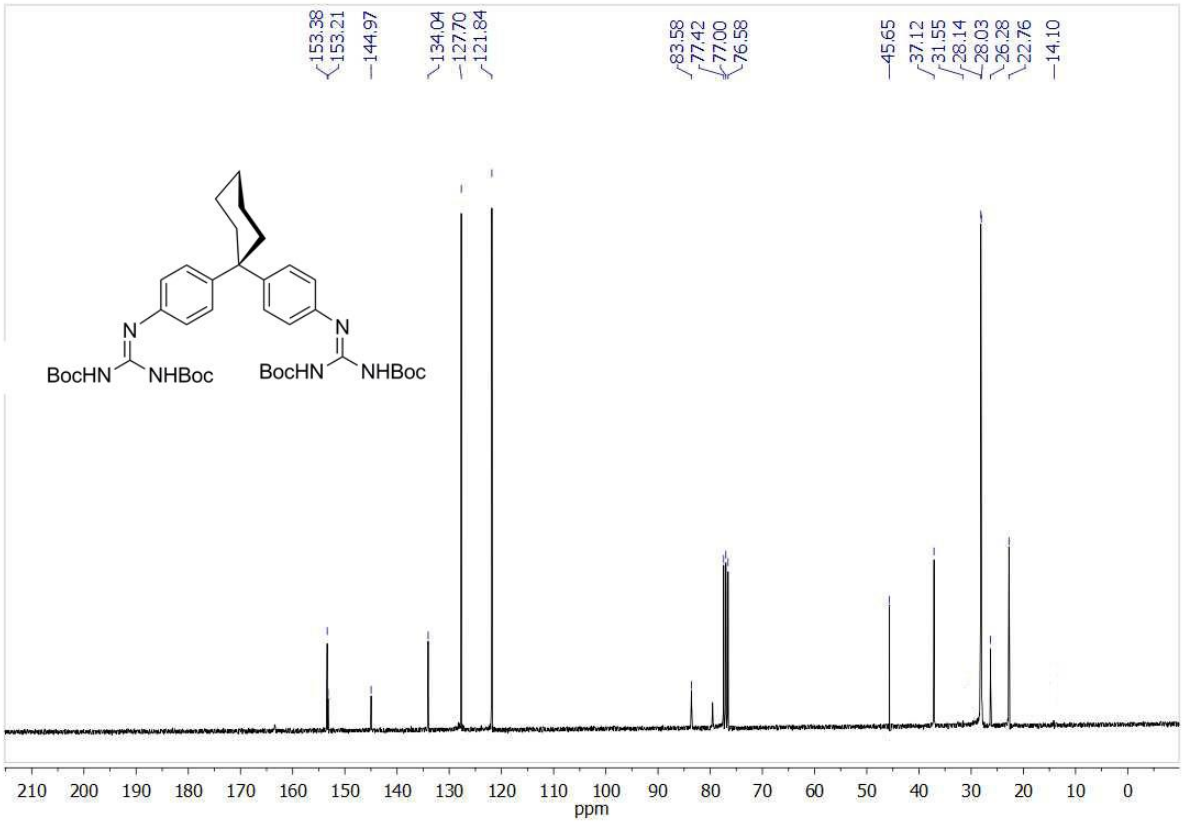


^{1}H NMR of **5b** ($CDCl_3$, 300 MHz)



^{13}C NMR of **5b** ($CDCl_3$, 75 MHz)



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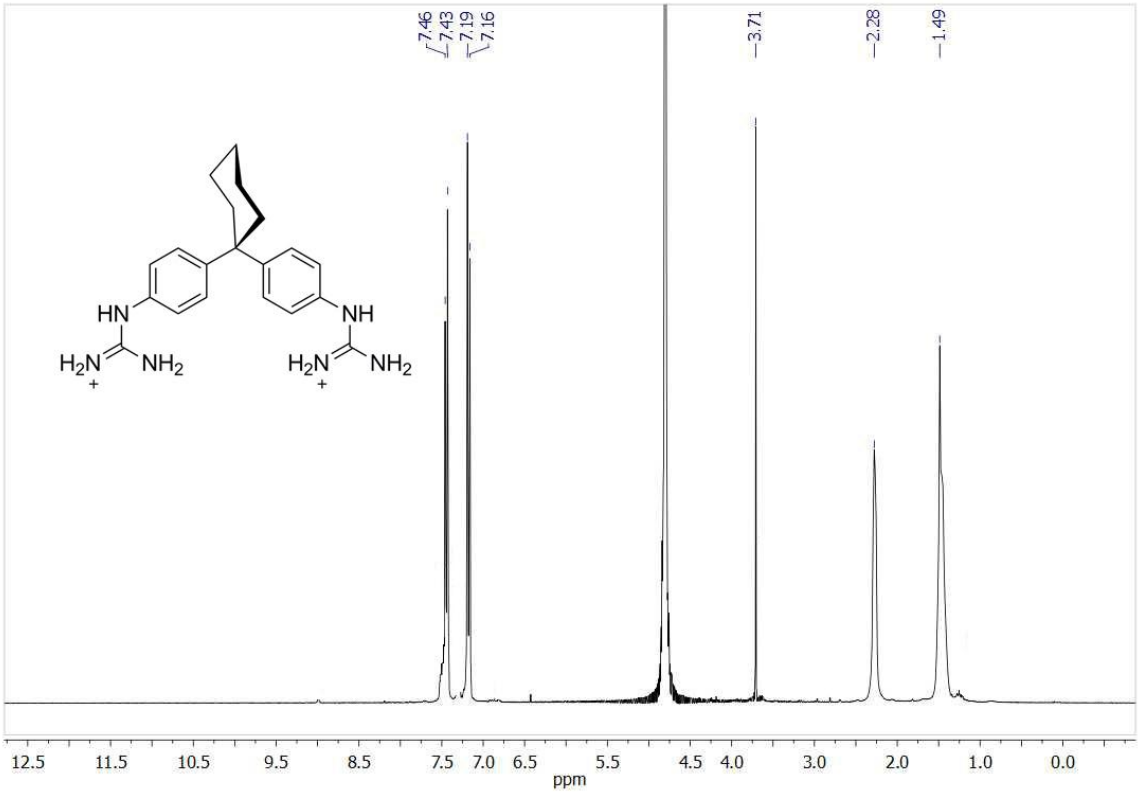

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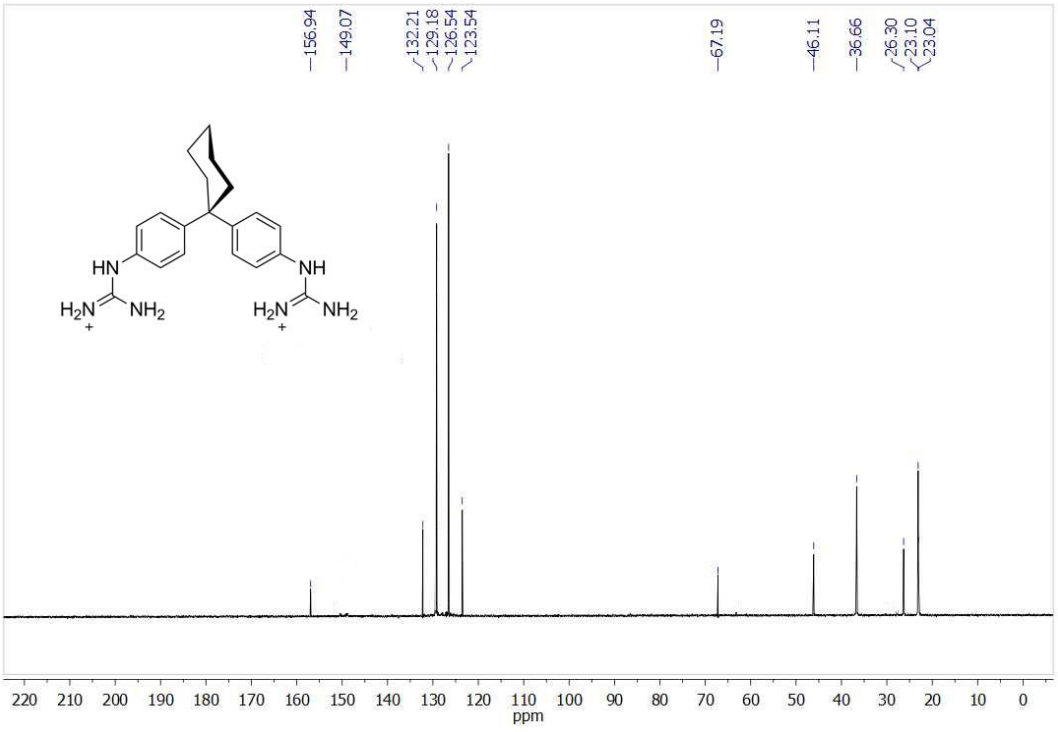

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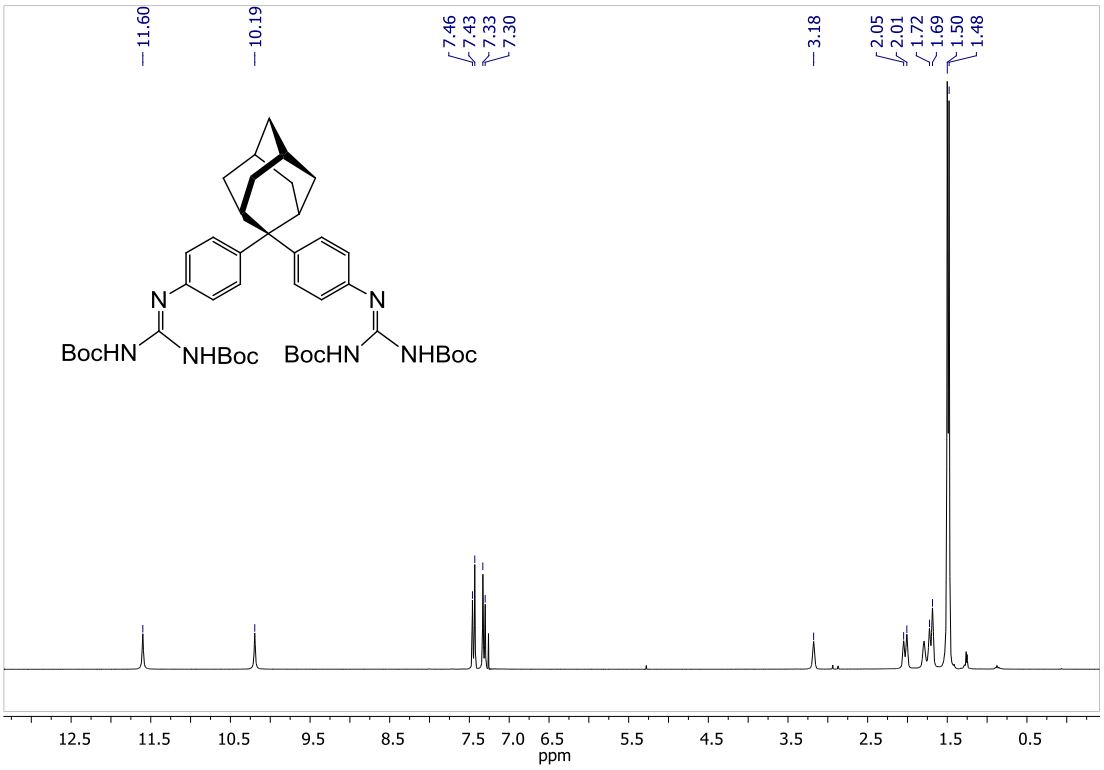
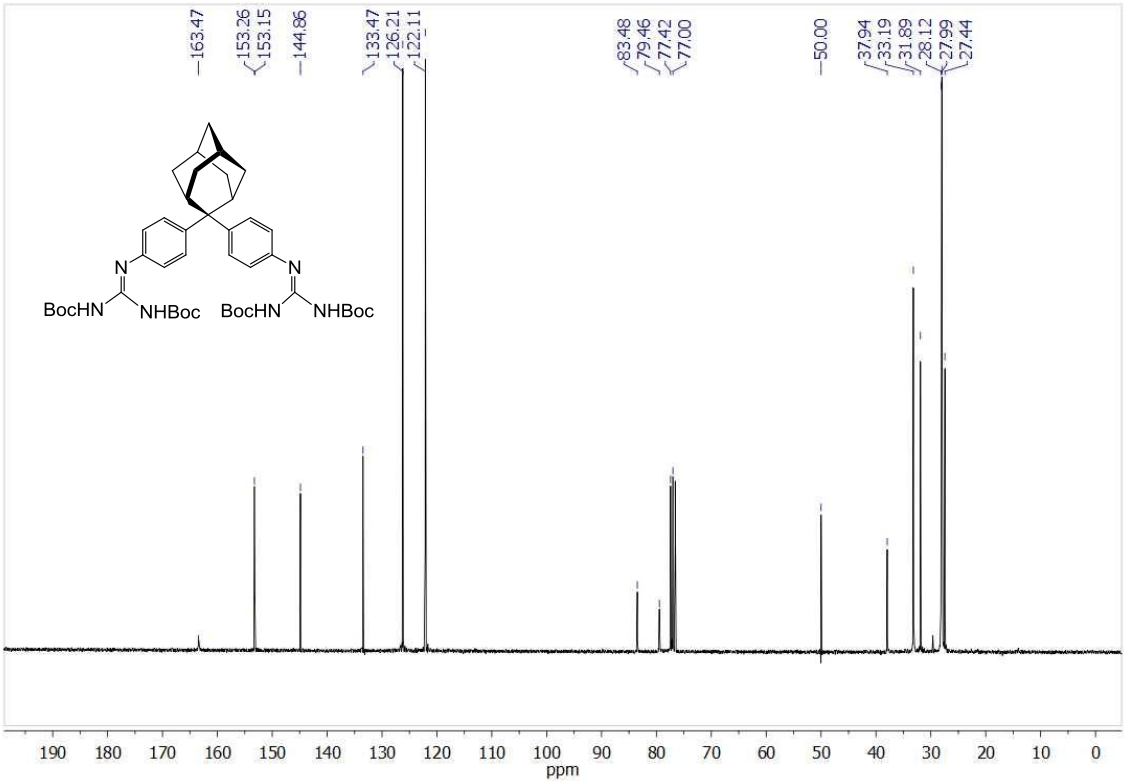
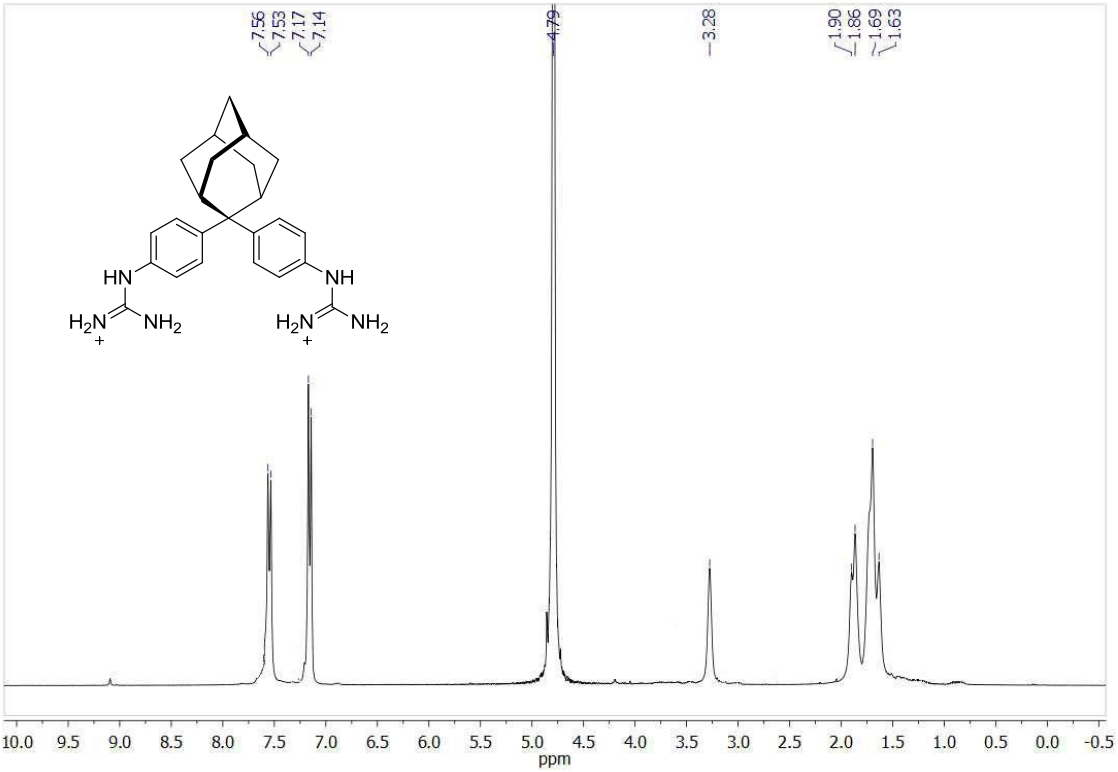


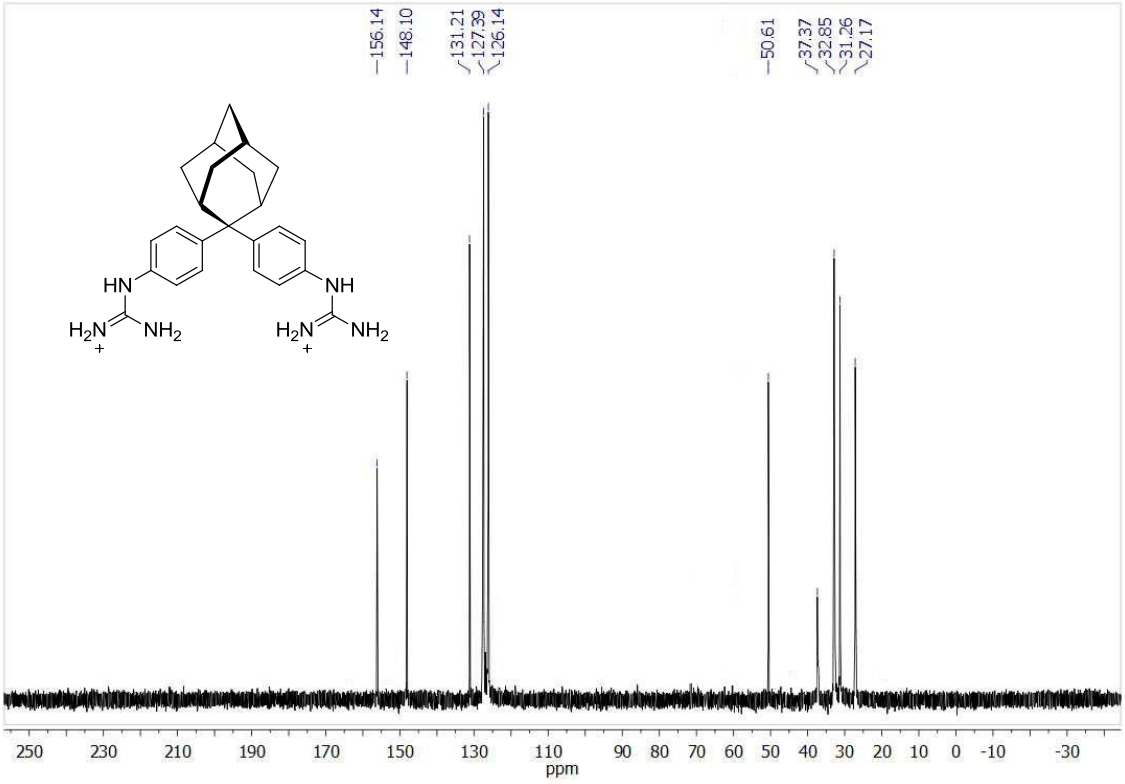
^{13}C NMR of **5c** ($CDCl_3$, 75 MHz)



^{1}H NMR of **3** (D_2O, 300 MHz)



^{13}C NMR of **3** (D_2O, 75 MHz)



Kinetics

The reaction progress was monitored spectrophotometrically at 400 nm. Data collected in the first 5-8% reaction gave initial rates (v_o) which were converted into pseudo-first-order rate constant (k_{obs}). The following plot is typical.

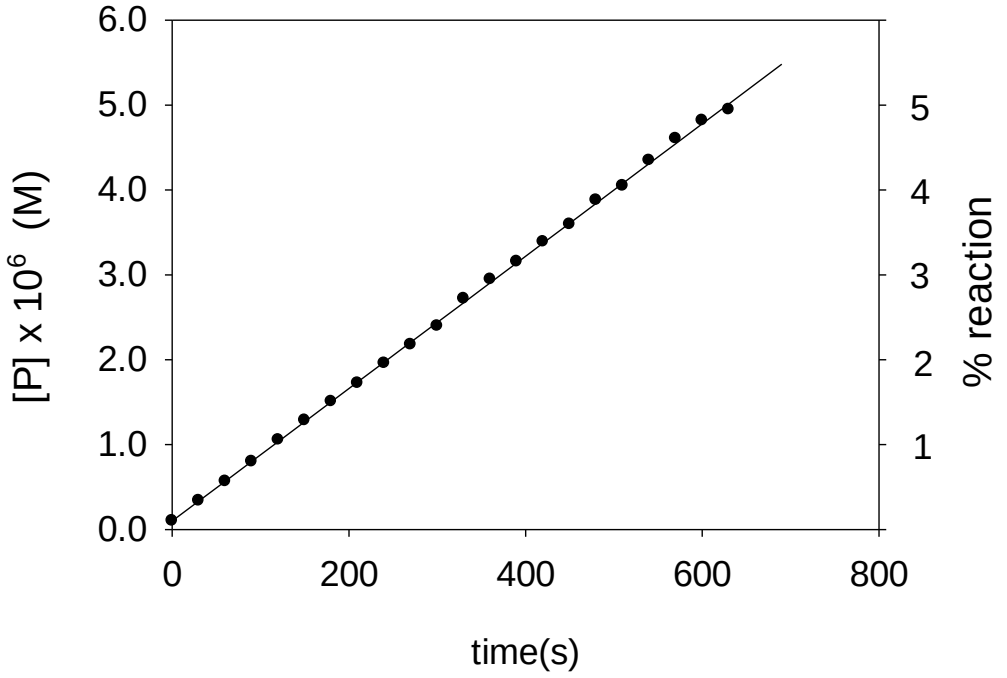


Figure S1 Liberation of *p*-nitrophenol [P] in the transesterification of 0.10 mM HPNP catalyzed by **3** at pH 10.16, from the slope of the straight line $v_o = 7.8 \times 10^{-9}$ M s^{-1}, $k_{obs}=7.8 \times 10^{-5}$ s^{-1}.

DFT Calculations and Evaluation of Entropy of Internal Rotations

Table S1 Ground state and transition state energy,[a] and height of the potential barrier (V_o) [b] for hindered internal rotation around the C-Ar bonds obtained from B3LYP 6-31g(d) calculations.

Compound	$E+E_o$ (au)[c]	$E^{\#} + E_o^{\#}$ (au)[c]	V_o (kcal/mol)[b]
Diphenylmethane	-502.405011	-502.404165	0.53
1,1-Diphenylcyclohexane ax	-697.633990	-697.624985	5.65
1,1-Diphenylcyclohexane eq	-697.633990	-697.631726	1.42
2,2-Diphenyladamantane	-852.399683	-852.383934	9.88

[a] corrected for the zero-point vibrational energies; [b] height of the potential barrier for internal rotation: $V_o=(E^{\neq}+E_o^{\neq}) - (E+E_o)$; [c] au= atomic units.

The contribution of a restricted internal rotation to the entropy (S_{conf}) was calculated according to Pitzer treatment[1S] (eq. 1S and 2S), where Q_{free} is the partition function which would apply if the rotation were

$$S_{conf} = S_{free} - S \quad (1S)$$

$$S_{free} = R(^1/_2 + lnQ_{free}) \quad (2S)$$

free and S, the entropy decrease from free rotation, was obtained from Table 27-13 (p. 446 in ref. 2S), where differences between the entropy for restricted rotation and for free rotation are reported in tabular form. For the rotation of a phenyl group Q_{free}=29.1 and S_{free} 7.7 cal K^{-1} mol^{-1}.

References

(1S) (a) Pitzer, K. S.; Gwinn, W. D. *J. Chem. Phys.* **1942**, *10*, 428. (b) Pitzer, K. S. *J. Chem. Phys.* **1946**, *14*, 239. (c) Kilpatrick, J. E.; Pitzer, K. S. *J. Chem. Phys.* **1949**, *17*, 1064.

(2S) Pitzer, K. S., Brewer, L *Thermodynamics*, McGraw-Hill Book Company, New York, 1961.

Determination of activation parameters

Rate constants were measured in 80% DMSO at three temperatures: 25.0, 40.0 and 55.0 ^{o}C. All measurements were in duplicate (see Tables S2-S4). $\Delta H^{\neq}$ and $\Delta S^{\neq}$ values were obtained from a least-squares fitting procedure of $\ln(k_2/T)$ *vs* 1/T (Fiure S2). Conditions: [cat] = 2.0 mM, 10.0 mM NMe_4ClO_4, 0.10 mM HPNP.

Table S2 Compound 1H^+ (pH 10.16)

T (^{o}C)	k_2 (M^{-1} s^{-1})
25.0	4.25×10^{-3}
	4.59×10^{-3}
40.0	1.94×10^{-2}
	2.09×10^{-2}
55.0	1.00×10^{-1}
	9.25×10^{-2}

Table S3 Compound 2H^+ (pH 10.24)

T (^{o}C)	k_2 (M^{-1} s^{-1})
25.0	1.90×10^{-2}
	1.80×10^{-2}
40.0	9.85×10^{-2}
	1.05×10^{-1}
55.0	4.08×10^{-1}
	4.33×10^{-1}

Table S4 Compound 3H^+ (pH 10.39)

T (^{o}C)	k_2 (M^{-1} s^{-1})
25.0	3.90×10^{-2}
	4.06×10^{-2}
40.0	1.96×10^{-1}
	1.85×10^{-1}
55.0	1.09
	1.06

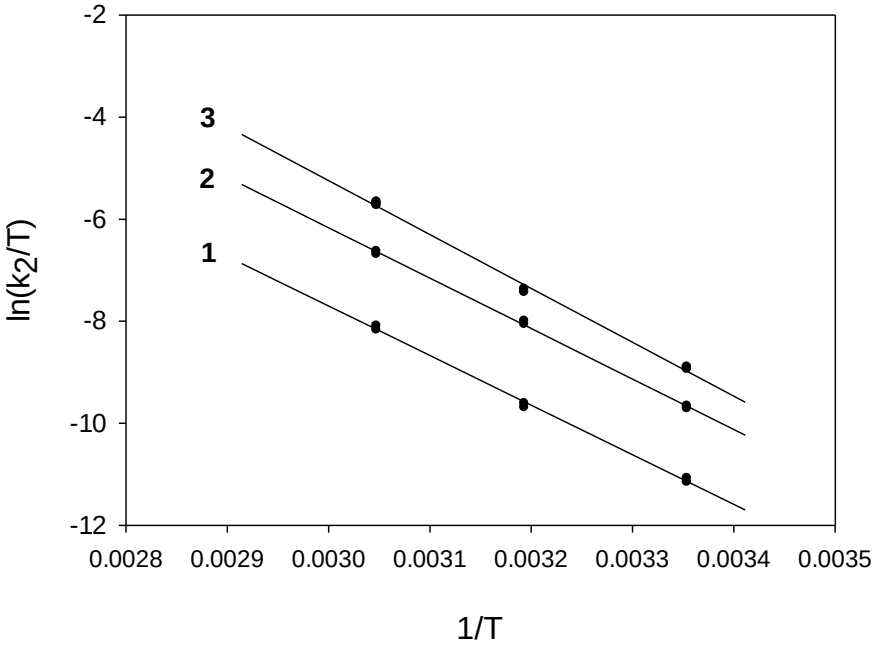


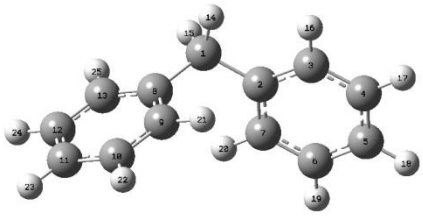
Figure S2 Eyring plot of the data reported in the Tables S2-4

Appendix 1

Coordinates, imaginary frequencies, energies and ZPVE from DFT calculations

Diphenylmethane

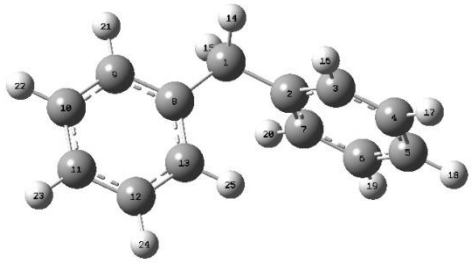
Ground State



C	0.00086200	-0.22689100	1.42754600
C	1.27939900	-0.04318600	0.62474500
C	2.29246900	-1.00811100	0.65555700
C	3.47661600	-0.83063300	-0.06477200
C	3.66359600	0.32050600	-0.82895000
C	2.65824300	1.29061800	-0.86975000
C	1.47785900	1.10817900	-0.15158800
C	-1.27876100	-0.15357900	0.60912100
C	-1.48624600	-1.01974200	-0.47445200
C	-2.66710500	-0.96963900	-1.21289200
C	-3.66440700	-0.04758900	-0.88305200
C	-3.46879400	0.82148500	0.18957900
C	-2.28375000	0.76648200	0.92809000
H	0.04759400	-1.19450800	1.94455700
H	-0.04538700	0.53392900	2.21792100
H	2.15508200	-1.90740400	1.25246700
H	4.25026400	-1.59339400	-0.02734400
H	4.58321500	0.46190200	-1.39062400
H	2.79414500	2.19037200	-1.46452300
H	0.69544900	1.86209100	-0.19645800
H	-0.71049100	-1.73322300	-0.74239300
H	-2.81001900	-1.65020600	-2.04846800
H	-4.58457300	-0.00732700	-1.45999300
H	-4.23622300	1.54456600	0.45406200
H	-2.13893800	1.44580600	1.76570100

No imaginary frequency found, E=-502.6153773 au E+ZPVE= -502.405011 au

Transition state of rotation of phenyl group:

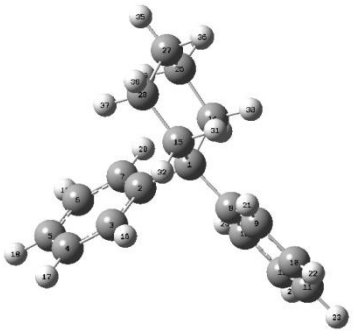


C	-0.05389500	-1.40081800	0.00009100
C	1.27362100	-0.67245800	0.00006600
C	1.90192700	-0.32470600	-1.20327200
C	3.12385400	0.34956200	-1.20621000
C	3.73940800	0.68870200	0.00002100
C	3.12381400	0.34971500	1.20627500
C	1.90188700	-0.32455300	1.20338000
C	-1.30802800	-0.52697700	0.00001000
C	-2.56406400	-1.15310700	0.00001700
C	-3.74026000	-0.40649100	-0.00005000
C	-3.68344700	0.98989200	-0.00012800
C	-2.44192200	1.62312500	-0.00013700
C	-1.26355000	0.87069900	-0.00006800
H	-0.09736700	-2.06425200	-0.87441200
H	-0.09739800	-2.06413400	0.87468100
H	1.42917700	-0.58863700	-2.14689500
H	3.59682500	0.60587100	-2.15074900
H	4.69287700	1.21019800	0.00000400
H	3.59675300	0.60614400	2.15079700
H	1.42910500	-0.58836400	2.14702200
H	-2.61764900	-2.24041600	0.00007800
H	-4.70187200	-0.91366400	-0.00004300
H	-4.59897100	1.57550500	-0.00018100
H	-2.38393300	2.70874100	-0.00019700
H	-0.30361800	1.37749100	-0.00007700

One imaginary frequency, E= -502.6143642 au, E+ZPVE = -502.404165 au

1,1-Diphenylcyclohexane

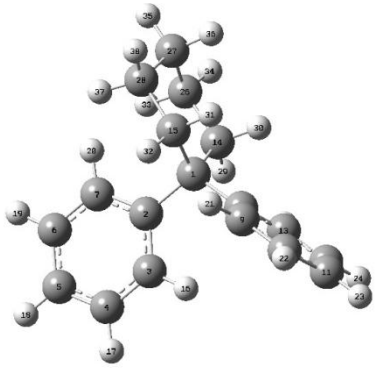
ground state



C	0.04194000	-0.63831500	0.00406100
C	0.89296900	0.65349900	0.06128600
C	0.88268500	1.43467400	1.23026000
C	1.60356700	2.62321300	1.32113300
C	2.35484000	3.07617900	0.23449600
C	2.36298700	2.32769400	-0.93981300
C	1.64005400	1.13377100	-1.02357600
C	-1.44535200	-0.20944500	-0.01939800
C	-2.38864900	-0.65016300	0.91834100
C	-3.72754500	-0.25346600	0.84085700
C	-4.15538600	0.59274900	-0.17892900
C	-3.22719600	1.04644100	-1.11928000
C	-1.89399900	0.65310200	-1.03482400
C	0.30598600	-1.50186600	-1.26973900
C	0.36406700	-1.54671500	1.22541300
H	0.28402400	1.12071800	2.08039800
H	1.57214600	3.20047900	2.24178600
H	2.91861300	4.00272500	0.30218700
H	2.93326000	2.66759900	-1.80075000
H	1.66524000	0.58259800	-1.95694100
H	-2.09302100	-1.30811400	1.72767600
H	-4.43387700	-0.61131800	1.58591400
H	-5.19583000	0.90080000	-0.23948800
H	-3.54070200	1.71454000	-1.91757700
H	-1.18349500	1.03644600	-1.76188300
C	1.69354600	-2.16776800	-1.32901900
C	1.99576400	-2.98222300	-0.06480400
C	1.78450700	-2.12825500	1.19140600
H	0.12997400	-0.91117600	-2.17586800
H	-0.46053400	-2.28839700	-1.27952900
H	-0.34373100	-2.38641700	1.22467500
H	0.20141000	-1.00753600	2.16487000
H	2.47413600	-1.40782200	-1.45282000
H	1.74134000	-2.81065000	-2.21776000
H	3.02129700	-3.37116100	-0.10011000
H	1.32939300	-3.85683100	-0.02246200
H	2.52145200	-1.31442200	1.21677900
H	1.95019100	-2.73069300	2.09368700

No imaginary frequencies, Energy = -697,9676623 au Energy+ZPVE = -697.63399 au

Transition state of the rotation of the axial phenyl group



C	-0.09889400	-0.55753400	0.00000000
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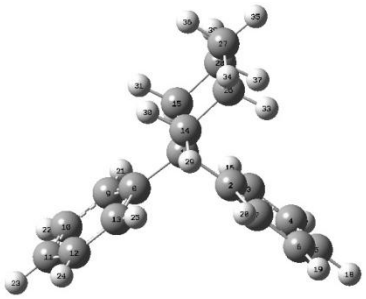
C	-0.95190400	3.22824900	-0.00000100
C	-2.34475700	3.23089800	-0.00000100
C	-3.01528500	2.00892100	0.00000000
C	-2.30241400	0.80935800	0.00000000
C	1.42166100	-0.24844100	0.00000000
C	2.13691800	-0.08248800	-1.19760200
C	3.50082100	0.21462100	-1.20094000
C	4.19397900	0.36151300	0.00000000
C	3.50082000	0.21462700	1.20093900
C	2.13691700	-0.08248300	1.19760100
C	-0.42295000	-1.41569500	1.27507800
C	-0.42295200	-1.41569200	-1.27507800
H	0.83884400	2.06790500	0.00000000
H	-0.40324500	4.16690500	-0.00000100
H	-2.89805300	4.16629700	-0.00000100
H	-4.10220500	1.98093500	0.00000000
H	-2.86951300	-0.11028700	0.00000200
H	1.62970400	-0.17900000	-2.15124000
H	4.01969000	0.33123800	-2.14915300
H	5.25634300	0.59035000	0.00000000
H	4.01968800	0.33124900	2.14915200
H	1.62970200	-0.17899000	2.15124000
C	-1.72463700	-2.23450600	1.26184500
C	-1.84427000	-3.09626200	0.00000000
C	-1.72464000	-2.23450300	-1.26184300
H	-0.41800600	-0.76955400	2.15982500
H	0.40523100	-2.12558400	1.40143900
H	0.40522800	-2.12558100	-1.40144300
H	-0.41801100	-0.76954900	-2.15982400
H	-2.59967600	-1.58101500	1.35421800
H	-1.73392700	-2.87184500	2.15578500
H	-2.79189700	-3.64974600	0.00000000
H	-1.04112800	-3.84831800	-0.00000200
H	-2.59967800	-1.58101200	-1.35421200
H	-1.73393200	-2.87184000	-2.15578500

One imaginary frequency; Energy = -697.9588976 au, Energy+ZPVE = -697.624985 au

Transition state of the rotation of the equatorial phenyl group

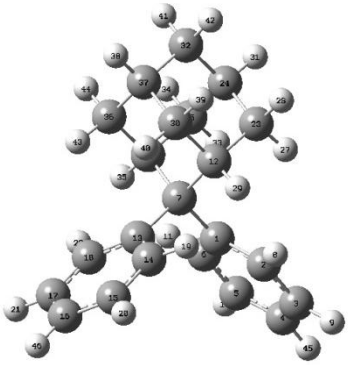


C	0.07515200	-0.66180800	0.00003300
C	0.84967300	0.68381500	-0.00006900
C	1.17989000	1.33954100	1.19700400
C	1.81982400	2.57971000	1.20044500
C	2.14709300	3.20821300	-0.00022900
C	1.82019200	2.57936800	-1.20082300
C	1.18025800	1.33919700	-1.19722800
C	-1.43621000	-0.30611300	-0.00000200
C	-2.14371500	-0.11324800	1.19750400
C	-3.49341600	0.24101500	1.20062300
C	-4.17948900	0.41834400	-0.00005300
C	-3.49360400	0.24014400	-1.20070200
C	-2.14389900	-0.11412000	-1.19753400
C	0.42581400	-1.53637900	-1.24188200
C	0.42574600	-1.53619700	1.24210200
H	0.93475700	0.88723000	2.15206100
H	2.06119700	3.05343000	2.14873100
H	2.64660200	4.17326000	-0.00028900
H	2.06184900	3.05282000	-2.14917100
H	0.93535200	0.88666800	-2.15224000
H	-1.64484000	-0.23602400	2.15253100
H	-4.00723900	0.37795500	2.14890600
H	-5.23086300	0.69319000	-0.00007000
H	-4.00757100	0.37639600	-2.14900600
H	-1.64517500	-0.23759600	-2.15254800
C	1.87485100	-2.04814200	-1.25774700
C	2.20126300	-2.86006600	0.00028700
C	1.87480000	-2.04788700	1.25814200
H	0.22839700	-1.00558200	-2.17678100
H	-0.25905100	-2.39544900	-1.23865600
H	-0.25908400	-2.39529700	1.23891600
H	0.22821400	-1.00530400	2.17692000
H	2.56477000	-1.19733600	-1.33274200
H	2.02999900	-2.65747300	-2.15751500
H	3.25593900	-3.16329800	0.00033300
H	1.60678700	-3.78588700	0.00037100
H	2.56466800	-1.19702000	1.33297900
H	2.02995300	-2.65701500	2.15804500

One imaginary frequency; Energy = -697.9652926 au, Energy+ZPVE = -697.631726 au

2,2-Diphenyladamantane

ground state

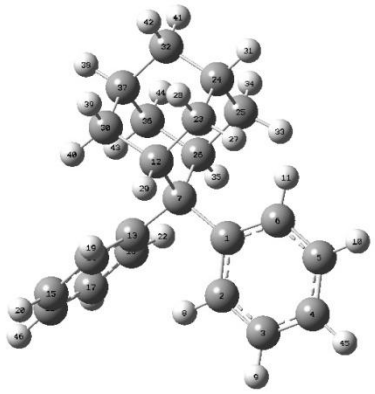


C	-0.84653200	1.22491200	-0.00995100
C	-1.38679700	1.71311300	-1.21088200
C	-2.30881200	2.75991400	-1.22727900
C	-2.72761100	3.35027400	-0.03526500
C	-2.21295700	2.87351000	1.16933400
C	-1.28967200	1.82669800	1.17861300
C	0.11122100	-0.00000100	0.00000100
H	-1.09501100	1.27113700	-2.15789100
H	-2.70131400	3.11108600	-2.17837200
H	-2.52857000	3.31508300	2.11133700
H	-0.91721100	1.48035100	2.13688100
C	1.06951000	-0.00313200	-1.24781600
C	-0.84653300	-1.22491200	0.00995400
C	-1.28970600	-1.82667200	-1.17860900
C	-2.21299000	-2.87348500	-1.16932600
C	-2.72760900	-3.35027500	0.03527800
C	-2.30877800	-2.75993800	1.22729300
C	-1.38676300	-1.71313700	1.21089200
H	-0.91727200	-1.48030400	-2.13688000
H	-2.52862900	-3.31504000	-2.11132800
H	-2.70125200	-3.11113000	2.17839000
H	-1.09495000	-1.27118100	2.15790100
C	1.97235100	1.25217600	-1.25035200
C	2.87449800	1.25785200	-0.00221700
C	1.97684900	1.25551100	1.24859100
C	1.06951800	0.00312600	1.24781300
H	1.36625100	2.16457600	-1.28229300
H	2.58720700	1.24521000	-2.16110700
H	0.48443100	-0.00237700	-2.17261700
C	1.97684600	-1.25551300	-1.24859800
H	3.50272200	2.15858700	-0.00451100
C	3.76540700	0.00000500	-0.00001100
H	1.37706100	2.17149000	1.28226200
H	2.59472400	1.24496700	2.15737000
H	0.48444500	0.00236600	2.17261800
C	1.97236400	-1.25217800	1.25034100
C	2.87450500	-1.25784800	0.00220100

H	3.50273300	-2.15857900	0.00449000
H	2.59471300	-1.24497100	-2.15738300
H	1.37706100	-2.17149500	-1.28226200
H	4.42035700	0.00216700	0.88279400
H	4.42035100	-0.00215200	-0.88282000
H	1.36626900	-2.16458100	1.28228500
H	2.58722800	-1.24521100	2.16109100
H	-3.44561000	4.16585300	-0.04513800
H	-3.44560600	-4.16585500	0.04515500

no imaginary frequency; Energy= -852.8063072 au, Energy+ZPVE = -852.399683 au

transition state of rotation of the phenyl group



C	-0.88632500	1.31217100	0.00000600
C	-2.28745200	1.14407500	-0.00005100
C	-3.17578900	2.22077000	-0.00006100
C	-2.70586200	3.53061100	-0.00001300
C	-1.32881700	3.73460400	0.00004200
C	-0.44549000	2.65337900	0.00005000
C	0.07114700	0.06426500	0.00000500
H	-2.71532400	0.15200300	-0.00009000
H	-4.24457300	2.02122300	-0.00010600
H	-0.92410200	4.74373200	0.00007900
H	0.60419800	2.89496900	0.00009100
C	1.04110000	0.01842800	-1.25338600
C	-0.84654000	-1.19237400	0.00000800
C	-1.32308900	-1.75329500	-1.19593000
C	-2.20733800	-2.83339700	-1.20057500
C	-2.65310700	-3.38518900	0.00001900
C	-2.20736400	-2.83336400	1.20060800
C	-1.32311600	-1.75326200	1.19595200
H	-1.01239300	-1.34006500	-2.14967200
H	-2.54887700	-3.23999100	-2.14920600
H	-2.54892300	-3.23993200	2.14924200
H	-1.01244000	-1.34000600	2.14968900
C	2.08862700	1.15723000	-1.26731800
C	2.96730200	1.10038700	0.00000100
C	2.08865000	1.15720100	1.26733700
C	1.04111300	0.01840800	1.25338800
H	1.62016900	2.13487000	-1.39325100
H	2.72441600	1.01894700	-2.15308600

H	0.44699900	0.09489800	-2.17118800
C	1.84675100	-1.30798800	-1.25801000
H	3.67143900	1.94331900	0.00000400
C	3.74499400	-0.23017200	-0.00001700
H	1.62020700	2.13484200	1.39331200
H	2.72445300	1.01888300	2.15308900
H	0.44702200	0.09486100	2.17119700
C	1.84675900	-1.30801200	1.25797700
C	2.73564400	-1.39440500	-0.00002100
H	3.27434800	-2.35146300	-0.00003100
H	2.47482300	-1.33382500	-2.15946000
H	1.18741900	-2.17864400	-1.30883900
H	4.39600800	-0.29026000	0.88346600
H	4.39599500	-0.29024500	-0.88351200
H	1.18742400	-2.17866600	1.30879100
H	2.47483700	-1.33387100	2.15942100
H	-3.39428600	4.37150700	-0.00001900
H	-3.33962800	-4.22752200	0.00002300

one imaginary frequency; Energy = -852.7913137 au, Energy+ZPVE = -852.383934 au