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# Electronic Supplementary Information

# Amide rotation trajectories probed by symmetry

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Т, К	compo	und 2a	compo	und 3a	compound <b>4a</b>		
	MeO <sub>2</sub> C	CO <sub>2</sub> Me	MeO <sub>2</sub> C''''	CO <sub>2</sub> Me	Ń		
	H <sub>3</sub> C	6	H <sub>3</sub> C		H <sub>3</sub> C		
	k, s <sup>-1</sup>	E <sup>≠</sup> , kJ mol <sup>-1</sup>	k, s <sup>-1</sup>	E <sup>≠</sup> , kJ mol <sup>-1</sup>	k, s <sup>-1</sup>	E <sup>≠</sup> , kJ mol <sup>-1</sup>	
297.9	0.017 ±	83.06 ±	-	-	-	-	
	0.002	0.29					
303.3	0.032 ±	83.0 ± 0.24	-	-	-	-	
	0.003						
309.7	-	-	0.0015 ±	92.68 ±	0.010 ±	87.79 ±	
			0.0008	1.53	0.002	0.52	
313.9	0.109 ±	82.80 ±	0.0025 ±	92.66 ±	0.018 ±	87.50 ±	
	0.003	0.07	0.0010	1.11	0.002	0.29	
319.3	0.190 ±	82.78 ±	0.0055 ±	92.18 ±	0.032 ±	87.51 ±	
	0.007	0.10	0.0013	0.64	0.001	0.08	
324.6	-	-	0.011 ±	91.89 ±	0.057 ±	87.46 ±	
			0.002	0.50	0.002	0.09	
329.9	0.569 ±	82.63 ±	0.019 ±	91.95 ±	0.098 ±	87.45 ±	
	0.010	0.05	0.002	0.29	0.002	0.06	
335.3	0.949 ±	82.58 ±	0.032 ±	92.03 ±	0.165 ±	87.46 ±	
	0.026	0.08	0.002	0.17	0.003	0.05	

**Table S1.** Activation energies for *N*-acetylated compounds as function of temperature (in deuterium oxide solution)

**Table S2.** Activation energies for *N*-aceturylated compounds as function of temperature (in buffered deuterium oxide solution)

Т, К	compor	und <b>2c</b>	compo	und <b>3c</b>	compound <b>4c</b>		
		CO <sub>2</sub> Me		CO <sub>2</sub> Me			
	k, s <sup>-1</sup>	E <sup>≠</sup> , kJ mol <sup>-1</sup>	k, s <sup>-1</sup>	E <sup>≠</sup> , kJ mol <sup>-1</sup>	k, s <sup>-1</sup>	E <sup>≠</sup> , kJ mol <sup>-1</sup>	
297.9	0.083 ±	79.13 ±	-	-	-	-	
	0.006	0.18					
303.3	0.145 ±	79.18 ±	-	-	0.013 ±	85.26 ±	
	0.009	0.16			0.002	0.39	
309.7	0.294 ±	79.09 ±	0.012 ±	87.32 ±	0.028 ±	85.14 ±	
	0.015	0.13	0.002	0.43	0.004	0.37	
313.9	0.452 ±	79.09 ±	0.022 ±	86.98 ±	0.044 ±	85.17 ±	
	0.019	0.11	0.004	0.48	0.005	0.30	
319.3	0.781 ±	79.03 ±	0.036 ±	87.19 ±	0.077 ±	85.18 ±	
	0.076	0.26	0.004	0.30	0.005	0.17	
324.6	1.278 ±	79.06 ±	0.063 ±	87.18 ±	0.131 ±	85.21 ±	
	0.058	0.12	0.005	0.21	0.010	0.21	
329.9	2.127 ±	79.01 ±	0.111 ±	87.11 ±	0.219 ±	85.24 ±	
	0.135	0.17	0.007	0.17	0.009	0.11	
335.3	3.467 ±	78.97 ±	0.184 ±	87.15 ±	0.352 ±	85.34 ±	
	0.238	0.19	0.007	0.11	0.019	0.15	

compound	ΔH, kJ mol <sup>-1</sup>	$\Delta S$ , J mol <sup>-1</sup> K <sup>-1</sup>
2a	+ 86.5 ± 0.3	+ 11.9 ± 0.9
За	+ 94.5 ± 3.0	+ 7.6 ± 9.0
4a	+ 88.5 ± 0.6	+ 3.2 ± 1.8
2c	+ 80.5 ± 0.3	+ 4.7 ± 0.9
Зc	+ 87.8 ± 1.1	+ 2.0 ± 3.4
4c	+ 83.4 ± 0.7	- 5.7 ± 2.2

Table S3. Energetic terms for the amide rotation in *N*-acyl compounds in aqueous medium

Table S4. Amide rotation kinetics for the examined substances measured in deuterium oxide solution

compound	structure	Τ, Κ	k,	s <sup>-1</sup>	E <sup>≠</sup> , kJ mol <sup>-1</sup>			
		I	N-acetyl compour	nds	•			
2a	MeO <sub>2</sub> C	298	0.019 ±	0.002	82.8	± 0.3		
	н₃с∽о							
3а	MeO <sub>2</sub> C <sup>1</sup> <sup>1</sup> N CO <sub>2</sub> Me	310	0.0015 ±	0.0008	92.8	± 1.9		
	н₃с∽о							
4a		310	0.009 ±	0.001	88.2	± 0.3		
	н <sub>з</sub> с о				-	-		
5a	COoMe	310	trans→cis	cis→trans	trans→cis	cis→trans		
	H <sub>3</sub> C O		0.0070 ± 0.0005	0.033 ± 0.002	88.8 ± 0.2	84.8 ± 0.2		
		N	-pivaloyl compou	unds				
2b		298	20.0	± 0.2	65.6	± 0.1		
	MeO <sub>2</sub> C CO <sub>2</sub> Me							
			0.424					
3b	MeO <sub>2</sub> C <sup>····</sup>	298	0.431 ±	: 0.018	/5.1 ± 0.1			
4b	$\square$	298	14.2 :	± 0.9	66.4	± 0.2		
	~~~~							
5b		298	trans→cis	cis→trans	trans→cis	cis→trans		
	N CO <sub>2</sub> Me		0.622 ± 0.043	36.5 ± 2.0	74.2 ± 0.1	64.1 ± 0.1		
		1	1		I			
2c	MeO <sub>2</sub> C	310	0.292 ±	0.029	79.2	± 0.3		
3c	MeO <sub>2</sub> C <sup>1</sup> <sup>1</sup> , CO <sub>2</sub> Me	310	0.012 ±	0.002	87.4	± 0.5		
	0, _NH							
	l ì							
4c	$\Box$	310	0.029 ±	0.005	85.1	± 0.5		
	Ň							
	ON NH							
5c		310	trans→cis	cis→trans	trans→cis	cis→trans		
	N∕ <sup>CO</sup> ₂Me ↓		0.020 ± 0.001	0.123 ±	86.1 ± 0.1	81.4 ± 0.2		
				0.006				

*Note:* for the *N*-aceturyl compounds **2c**-**5c** the measurements were conducted in buffered deuterium oxide (potassium phosphate buffer, 70 mM, pH 7)

solvent	ET,	compound 2a				compound	3a	compound 4a			
	kJ mol <sup>-1</sup>	$\square$						$\square$			
		Me	PO2C	CO <sub>2</sub> Me	Me	02C''''	CO <sub>2</sub> Me	N			
			н₃с∽о			н₃с∕∽о		н₃с∕о			
		Т, К	k, s <sup>-1</sup>	E <sup>≠</sup> ,	Т, К	k, s <sup>-1</sup>	E <sup>≠</sup> ,	Т, К	k, s <sup>-1</sup>	E <sup>≠</sup> ,	
				kJ mol <sup>-1</sup>			kJ mol <sup>-1</sup>			kJ mol <sup>-1</sup>	
toluene-d <sub>8</sub>	141.8	298	2.81 ±	70.4 ±	298	0.024	82.2 ±	298	0.090	79.0 ±	
			0.25	0.3		±	0.6		±	0.1	
						0.005			0.005		
benzene-d <sub>6</sub>	143.5	298	2.42 ±	70.8 ±	298	0.024	82.2 ±	298	0.073	79.5 ±	
			0.05	0.1		±	0.2		±	0.2	
						0.002			0.005		
THF-d <sub>8</sub>	156.5	298	2.55 ±	70.7 ±	298	0.019	82.8 ±	298	0.103	78.6 ±	
			0.03	0.1		±	0.3		±	0.1	
						0.002			0.005		
CD <sub>2</sub> Cl <sub>2</sub>	171.9	298	0.742	73.7 ±	298	0.0067	85.4 ±	298	0.028	81.8 ±	
			±	0.1		±	0.4		±	1.8	
			0.010			0.0010			0.014		
$acetone-d_6$	176.5	298	1.07 ±	72.8 ±	310	0.037	84.5 ±	310	0.197	80.2 ±	
			0.03	0.1		±	0.2		±	0.1	
						0.002			0.005		
CD <sub>3</sub> CN	190.8	298	0.469	74.9 ±	310	0.019	86.2 ±	298	0.029	81.8 ±	
			±	0.1		±	0.2		±	0.1	
			0.011			0.001			0.001		
$ethanol-d_6$	217.1	310	0.787	76.6 ±	310	0.011	87.6 ±	310	0.027	85.3	
			±	0.1		±	0.6		±	±0.2	
			0.022			0.002			0.002		
methanol-	232.2	310	0.575	77.4 ±	310	0.0085	88.3 ±	310	0.025	85.5 ±	
d <sub>4</sub>			±	0.2		±	0.4		±	0.5	
			0.035			0.0011			0.004		
D <sub>2</sub> O	264.0	298	0.019	82.8 ±	310	0.0015	92.8 ±	310	0.009	88.2 ±	
			±	0.3		±	1.9		±	0.3	
			0.002			0.0008			0.001		

**Table S5.** Amide rotation kinetics for the *N*-acetyl compounds measured in different solvents

## **Copies of the NMR spectra for the Pdc derivatives** Compound **2a** in deuterium oxide:



ر 173.93						Current Da NAME EXPNO PROCNO	ata Param vk_Pdo 152	eters 2_2 1				~61.16 ~60.15	- 53.12 - 52.83		- 29.35 - 27.69	-21.19	
\$x\*\ <b>\$</b> x\1; <b>\$</b> x\2; <b>\$</b> \$ <b>\$</b> \$ <b>\$</b> \$ <b>\$</b> \$ <b>\$</b> \$ <b>\$</b> \$\$ <b>\$</b> \$ <b>\$</b> \$ <b>\$</b> \$ <b></b>		Many American M	ng paga ang			F2 - Acquis Date_ Time PROBHD PPUEROG TD SOLVENT NS SWH FIDRES AQ RG AQ DW DE TE D1 2011 TD0	sition Para 201705C 201705C 201705C 201705C 5 mm PA 3 2768 8 40760.8 1.2435 0.401954 2050 12.267 10.00 u 299.0 K 2.000000 0.030000C 32	ameters 33 ect ATXI 1H/ 330 20 71 Hz 223 Hz 1 sec 1 sec 1 sec .0 sec 00 sec					Y				
175	174 1	73	ppm		= ;; ; ; ; ; ; ; ; ; ; ; ; ; ; ; ; ; ;	SF01 NUC1 P1 PLW1 SF02 NUC2 CPDPRG[ PCPD2 PCPD2 PCP2 PLW2 PLW12	CHANNE 176.0763 13C 11.50 u 250.00000 CHANNE 700.1728 1H 2 wali 65.00 15.00000 0.37300	EL f1 ==== 711 MHz sec 0000 W EL f2 ===== 007 MHz tz16 00 usec 000 W 000 W									
nskinger Ballannan (n fashi farjer barreska 19 Tanay yarran sa'd galar (ngalar) jarang	10 - 10 - 10 - 10 - 10 - 10 - 10 - 10 -	sag ad di fi dadi. Lip	n i an la tha fa ga gan Mira ng ha ta cag ri	a je bil je bil bil som den narr það fregt friga stör	, bin , bin , p	F2 - Proces SI SF 1' WDW SSB 0 LB 0 PC 0 PC	ssing para 32768 76.057887 EM 1.00 Hz 2.00	ameters 70 MHz z	4 data (h) data, m, et k, n 197 Matematika (h) 19	ille condense ( 4, jei	in dia Jama, dia pao Ji	aste odus object (fig	l de brance and an	fachar an le raf a facha é di Mirigar de le galet de la facha de la fachar d	ands generally a chain	وال المراجع ال	sad al la constantina di Santa Nel a sua constanti a parte
190 180	 170	 160	 150	 140	130	 120	 110	 100	 90			60	 50	40			 10 ppm





⊂ 174.23 - 173.96 - 173.74	Current Data Parameters NAME vk_Pdc_2 EXPNO 172 PROCNO 1	- 59.49 - 59.49 - 53.03	- 29.15 - 26.98 - 21.14
wapely an interest land with land and an interest and an interest	F2 - Acquisition Parameters Date_ 20170504 Time 0.56 INSTRUM spect PROBHD 5 mm PATXI 1H/ PULPROG zgig30 TD 32768 SOLVENT D20 NS 256 DS 8 SWH 40760.871 Hz FIDRES 1.243923 Hz AQ 0.4019541 sec RG 2050 DW 12.267 usec DE 10.00 usec TE 299.0 K D1 2.0000000 sec D11 0.0300000 sec TD0 32	\/ \/	
175 174 173 ppm	====== CHANNEL f1 ======   SF01 176.0763711 MHz   NUC1 13C   P1 11.50 usec   PLW1 250.00000000 W   ====== CHANNEL f2 ======   SF02 700.1728007 MHz   NUC2 1H   CPDPRG[2 waltz16   PCPD2 65.00 usec   PLW12 0.37300000 W		
$\frac{1}{2} \sum_{i=1}^{n} \frac{1}{2} \sum_{i=1}^{n} \frac{1}$	F2 - Processing parameters SI 32768 SF 176.0578870 MHz WDW EM SSB 0 LB 1.00 Hz GB 0 PC 2.00	1/2.2.10.10.2.1.10.10.4.11.4.11.4.14.4.14.	Lade states a fill angle ( 101 , and ) become view filsely also 1 g11 maps 100 7 gg/sp <sup>10</sup> 1 g1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
190 180 170 160 150 140	130 120 110 100 90	80 70 60 50 40	30 20 10 ppm



Compound 2b in deuterium oxide





Compound **3b** in deuterium oxide





Compound **2c** in buffered deuterium oxide





Compound **3c** in buffered deuterium oxide



## **Copies of the NMR spectra for rest of compounds** Bn-(MeO)mPdc-OMe in chloroform-d







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HCl·H-(MeO)mPdc-OMe in methanol-d<sub>4</sub>



HCl·H-(MeO)rPdc-OMe in methanol-d<sub>4</sub>

in deuterium oxide:



### Compound 4a in deuterium oxide:







Compound **4b** in deuterium oxide:





Compound **5b** in deuterium oxide:

### Compound **4c** in buffered deuterium oxide



Compound **5c** in deuterium oxide:

