

Supporting Information

Cavitand templated catalysis of acetylcholine

Felix H. Zelder and Julius Rebek Jr.*

*The Skaggs Institute for Chemical Biology and The Department of Chemistry, The
Scripps Research Institute,
North Torrey Pines Road, La Jolla, California 92037.*

jrebek@scripps.edu

I Preparation of the chloride salt of TCh

Triethylcholine iodide (TCI America) was dissolved in water, filtrated over a short column of Amberlyst[®] A-26(OH). It was neutralized with HCl_{aq} (pH 7) and the solution was lyophilized to dryness. TCh⁺Cl⁻ was obtained as a white solid and used without further purification.

II Kinetic study of the esterfication reactions

II-1 General Information

All reagents were obtained from commercial suppliers and used without further purification. TCh was prepared as described above. The synthesis of the salen-cavitand (**1**), the Zn-salen-cavitand (**Zn-1**), Zn-salen-wall (**Zn-2**) has been described elsewhere.¹ Dms_o-d₆ used for the kinetic experiments was obtained from Cambridge Isotope Laboratories, Inc.

Kinetic experiments were performed in a NMR tube (V=600ul) on a Varian/Mercury+300MHz spectrometer.

The T1 value was determined for all participating molecules. The longest T1 was found for acetic acid. Therefore the parameters for data acquisition of the kinetic experiments were set as follows: d1=15sec (>5 times T1), nt=8, ss=4.

II-2. Kinetic experiments

The substrate (**Ch**, **TCh**) (50mM) and the catalyst (1mM) were added to d_6 -dmsO. The solution was mixed and the reaction was initiated after 20min by adding acetic anhydride (**4**) (50mM). The reaction volume was 600 μ l. At definite times, $^1\text{H-NMR}$ spectra were acquired. The reaction was performed at $T=25\pm 2^\circ\text{C}$. The esterification reactions were also performed at lower concentrations with the anhydrides **4-6**: Substrate (**Ch**, **TCh**) (5mM), catalyst (0.1mM), anhydride (**4-6**) (5mM) (see II-3).

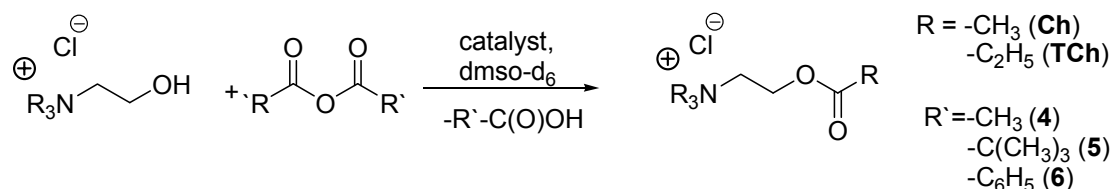
The relative conversion of the esterification was calculated from the integrals at 4.4ppm of the product (**ACh** or **ATCh**) and 3.7ppm of the educt **Ch** and **TCh** (see II-4: representative $^1\text{H-NMR}$ spectra): $rel.conv. = \int 3b / (\int 3 + \int 3b)$. An example is given below.

The k_{ob} was estimated by the initial rate method. The error limit calculated from different experiments was 20%.

Example (entry 6; table 1)

time/min	III_20_2 (zn-sal-wall+choline)		
	choline (3)	acetcholin (3b)	rel. conv.
27	1,56	0,06	0,03703704
102	0,98	0,55	0,35947712
490	0,29	0,75	0,72115385
1590	0,23	1	0,81300813

II-3. Esterification at lower concentrations with the anhydrides 4-6

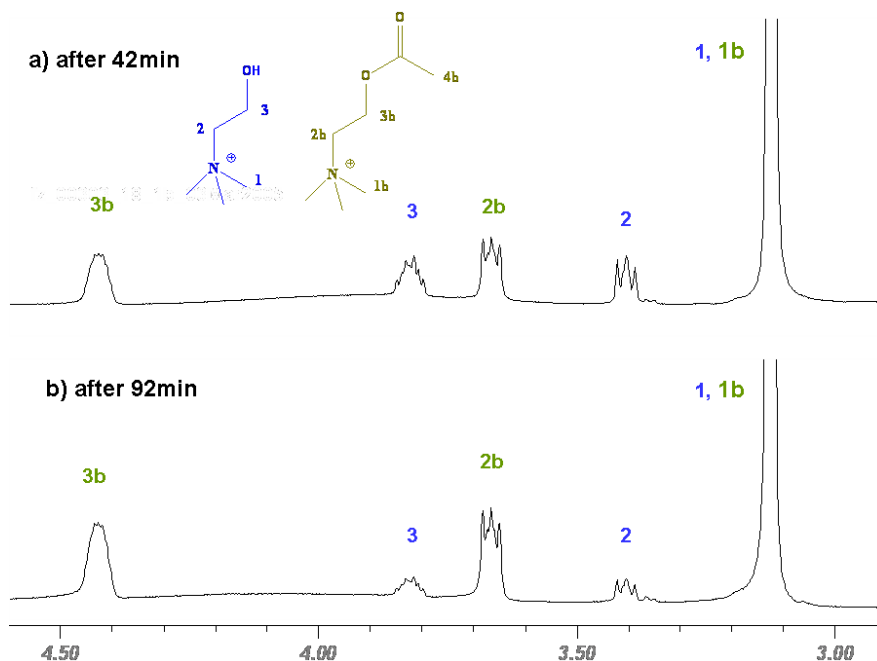


entry	cat	anhydride	substrate	k_{ob} (10^{-4} min $^{-1}$)	k_{ob}/k_{uncat}
16	Zn-1	4	Ch	9	90
17	Zn-2	4	Ch	1	10
18	Zn-1	5	Ch	0.6	n.d.
19	Zn-2	5	Ch	0.08	n.d.
20	Zn-1	6	Ch	1	n.d.
21	Zn-2	6	Ch	0.5	n.d.

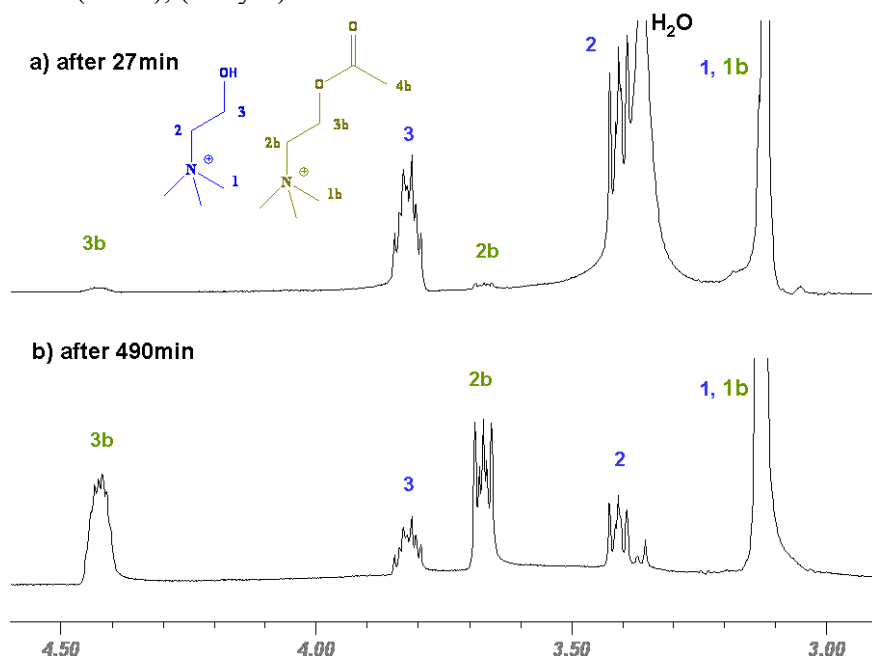
Conditions: **Ch** (5mM), anhydride **4-6** (5mM), cat (2mol%); $dmsO-d_6$, $25\pm 2^\circ\text{C}$. Detection method: $^1\text{H-NMR}$; n.d. not determined.

II-4. Representative $^1\text{H-NMR}$ of the reaction solutions

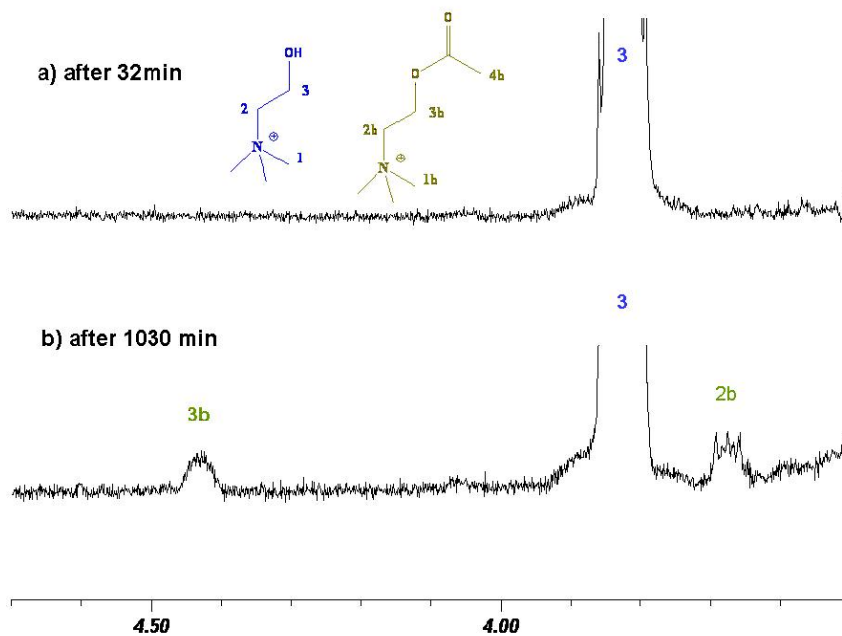
Representative $^1\text{H-NMR}$ spectra of reaction solutions at definite times are shown.



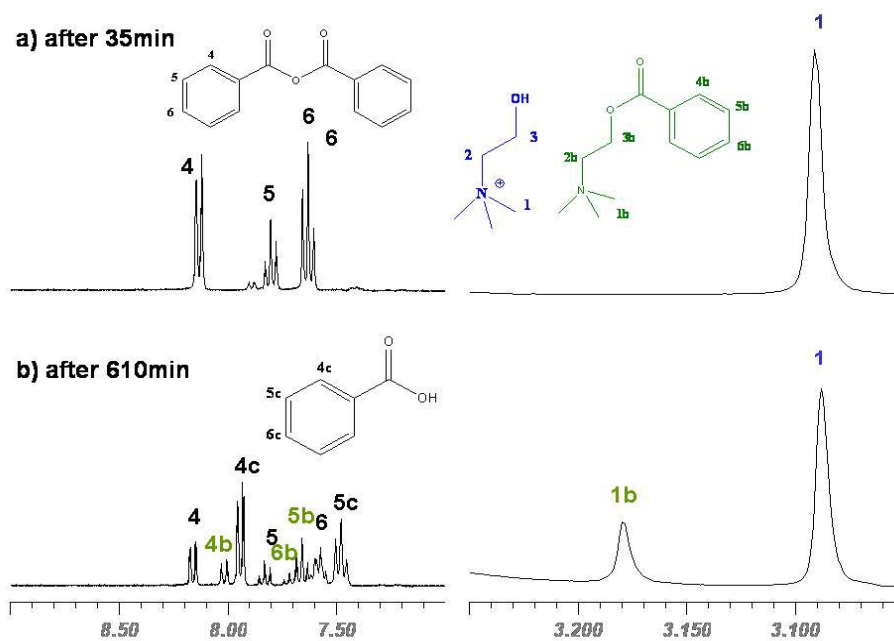
$^1\text{H-NMR}$ spectra in $\text{dms-}d_6$, 300 MHz, 25±2°C; Choline **Ch** (50mM), acetic anhydride **4** (50mM), **Zn-1** (1mM), (entry 5).



$^1\text{H-NMR}$ spectra in $\text{dms-}d_6$, 300 MHz, 25±2°C; Choline **Ch** (50mM), acetic anhydride **4** (50mM), Zn-salen-wall **Zn-2** (1mM), (entry 6).

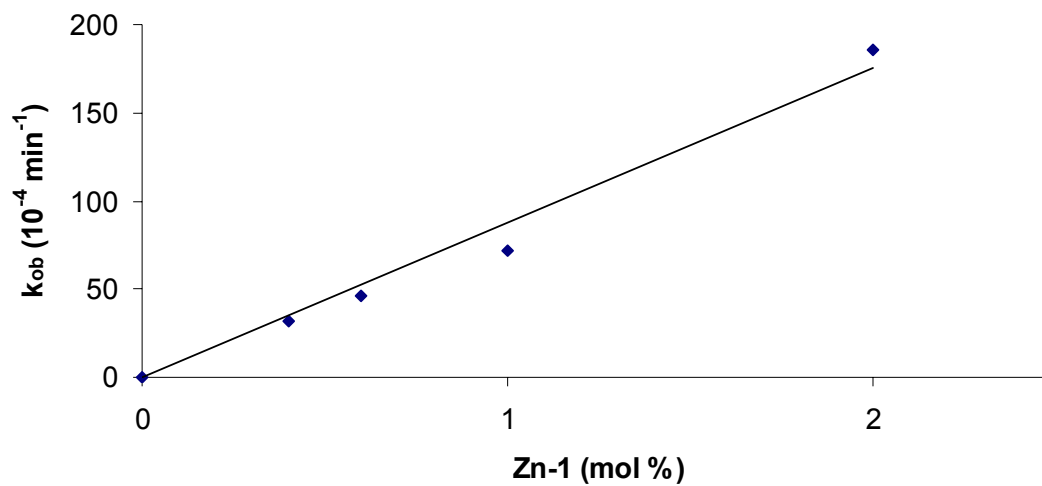


$^1\text{H-NMR}$ spectra in $\text{dms}\text{-d}_6$, 300 MHz, $25\pm 2^\circ\text{C}$; Choline **Ch** (50mM), acetic anhydride **4** (50mM), no catalyst, (entry 1).



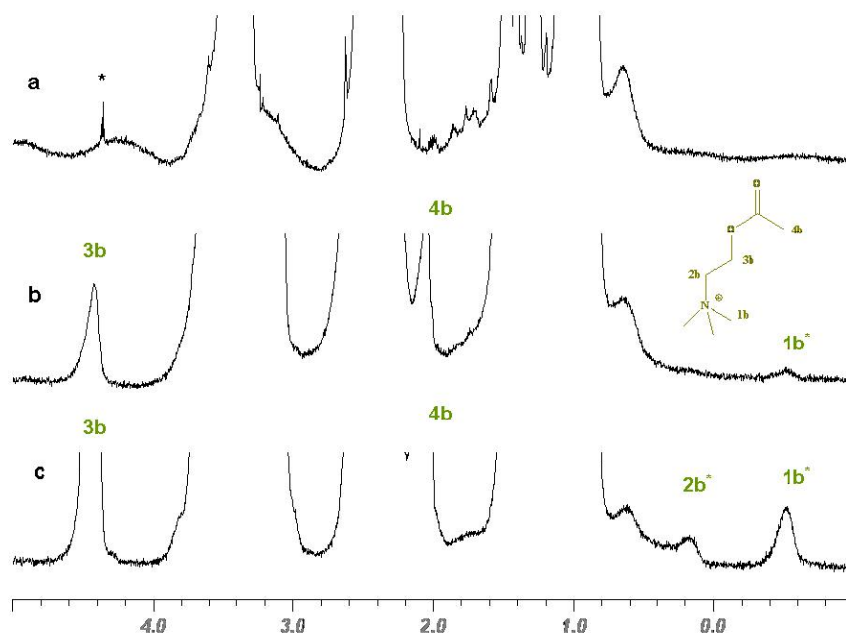
$^1\text{H-NMR}$ spectra in $\text{dms}\text{-d}_6$, 300 MHz, $25\pm 2^\circ\text{C}$; Choline **Ch** (5mM), Benzoic acid anhydride **6** (5mM), **Zn-1** (0.1mM), (II-3; entry 20)

II-5. Correlation of k_{ob} versus Zn-1

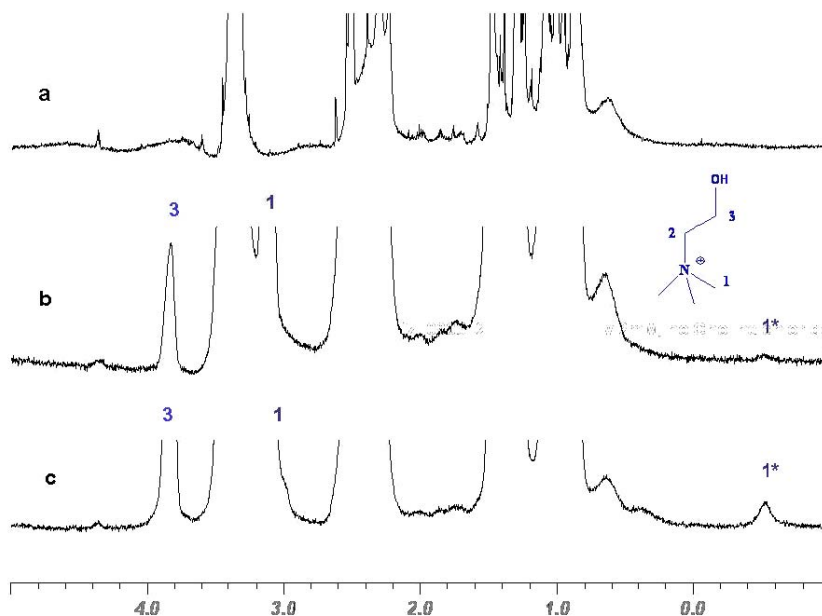


A linear correlation of the relative reaction constant k_{ob} from the catalyst concentration **Zn-1** was observed (adapted from entries 1-5).

III $^1\text{H-NMR}$ study of the ACh@Zn-1 and Ch@Zn-1 inclusion complex



$^1\text{H-NMR}$ study of the inclusion complex of ACh@Zn-1 (600MHz, $\text{d}_6\text{-dmsO}$, 300K)
a) guest free cavitand Zn-1 (2mM); b) inclusion complex ACh@Zn-1 with 1.2 eq. of ACh ; c) same as b) with 8 eq. of ACh ; * = impurity.



$^1\text{H-NMR}$ study of the inclusion complex of Ch@Zn-1 (600MHz, $\text{d}_6\text{-dmsO}$, 300K)
a) guest free cavitand Zn-1 (2mM); b) inclusion complex Ch@Zn-1 with 1.2 eq. of Ch ; c) same as b) with 8 eq. of Ch .

¹ Richeter, S.; Rebek, J., Jr. *J. Am. Chem. Soc.* **2004**, *126*, 16280-16281.