Supporting Information

Silicon Incorporated Tacrine: Design, Synthesis, and Evaluation of Biological and Pharmacokinetic Parameters

Akshay S. Kulkarni,[a, b] Sreenivasa Rao Ramana,[a] Vijay K. Nuthakki,[b,c] Shipra Bhatt,[b,d] Ashiya Jamwal,[b,d] Laxman D. Nandawadekar,[b,g] Anshika Jotshi,[b,d] Ajay Kumar,[b,d] Utpal Nandi,[b,d,e,*] Sandip B. Bharate,[b,c,f,*] D. Srinivasa Reddy[a,b,c,g,*]

[a]Organic Chemistry Division, CSIR-National Chemical Laboratory, Dr. Homi Bhabha Road, Pune 411008, India.

[b]Academy of Scientific and Innovative Research (AcSIR), Ghaziabad 201002, India.

[c] Natural Products & Medicinal Chemistry Division, CSIR-Indian Institute of Integrative Medicine, Canal Road, Jammu 180001, India.

[d] Pharmacology Division, CSIR-Indian Institute of Integrative Medicine, Canal Road, Jammu 180001, India.

[e] Bose Institute, Unified Academic Campus, Kolkata 700091, India.

[f] Department of Natural products & Medicinal Chemistry, CSIR-Indian Institute of Chemical Technology, Tarnaka, Hyderabad-500007, India.

[g] Department of Organic Chemistry & Process Chemistry, CSIR-Indian Institute of Chemical Technology, Tarnaka, Hyderabad-500007, India

***Corresponding authors**

D. Srinivasa Reddy: CSIR-Indian Institute of Chemical Technology, Tarnaka, Hyderabad-500007, India. Email: ds.reddy@iict.res.in

Sandip B. Bharate: CSIR-Indian Institute of Chemical Technology, Tarnaka, Hyderabad-500007, India. Email: sbharate@iict.res.in

Utpal Nandi: Bose Institute, Unified Academic Campus, Kolkata 700091, India. Email: utpal.nandi@jcbose.ac.in

CONTENTS

S1. X-RAY CRYSTALLOGRAPHIC DATA:

The single crystal X-ray diffraction measurements were performed to determine the crystal structure of compound **3** at 100 K using APEX3 (Bruker, 2016; Bruker D8 VENTURE Kappa Duo PHOTON II CPAD) diffractometer having graphite-monochromatized (MoKα = 0.71073 Å). The X-ray generator was operated at 50 kV and 30 mA. A preliminary set of unit cell parameters and an orientation matrix were calculated from 36 frames, and the cell refinement was performed by SAINT-Plus (Bruker, 2016). An optimized strategy used for data collection consisted of different sets of φ and ω scans with 0.5 ^{o}steps φ/ω. The data were collected with a time frame of 10 sec by setting the sample to detector distance fixed at 40 cm. All the data points were corrected for Lorentzian, polarization, and absorption effects using SAINT-Plus and SADABS programs (Bruker, 2016). SHELXS-97 (Sheldrick, 2008) was used for structure solution, and full-matrix least-squares refinement on F^2.[14] The molecular graphics of ORTEP diagrams were performed by Mercury software. The crystal symmetry of the components was cross-checked by running the cif files through PLATON (Spek, 2020) software and notified that no additional symmetry was observed. The Encifer software was used to correct the cif files. The compound **3**, crystallizes in Trigonal crystal system *R*-3*c* space group, with the presence of one molecule of compound **3** and two molecules of water in the asymmetric unit. Due to the existence of *R*-3*c* symmetry, one of the water molecules reflects its hydrogen atoms as shown in the Figure S1. CCDC number. 2165374.

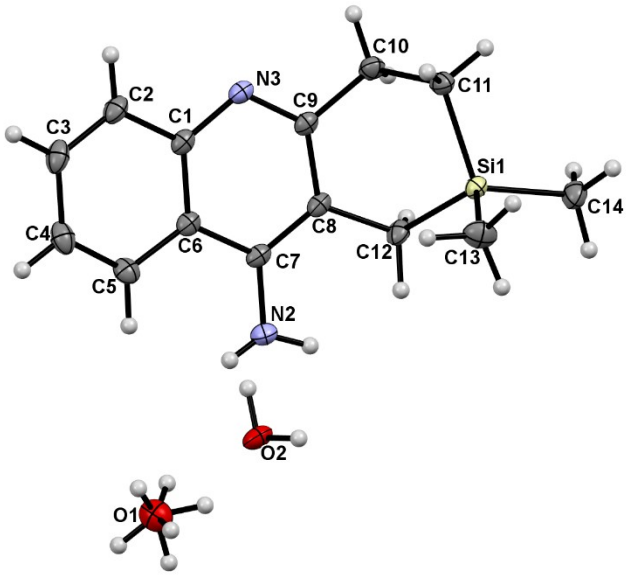


Figure S1. ORTEP diagram of compound **3**, the asymmetric unit, contains a single molecule. Herein, the ellipsoids are drawn with a 50% probability.

Table S1. Crystallographic information details of compound **3**.

Crystal data	Compound **3**
Chemical formula	$3(C_{14}H_{18}N_2Si)\cdot H_6O\cdot 3(H_2O)$
Formula weight (M_r)	803.28
Crystal system	Trigonal
Space group	*R*-3*c*
Temperature T (K)	100(2)
a (Å)	18.8889 (17)
b (Å)	18.8889 (17)
c (Å)	41.373 (4)
α (°)	90
β (°)	90
γ (°)	90
Z	12
Volume (Å^3)	12784 (3)
Source of radiation	MoKα
D_{calc} (g cm^{-3})	1.252
Crystal size (mm)	0.14x 0.1x 0.09
μ (mm^{-1})	0.16
Data collection	
Diffractometer	Bruker D8 VENTURE Kappa Duo PHOTON II CPAD
Absorption correction	Multi-scan (SADABS; Bruker, 2016)
T_{min}, T_{max}	0.706, 0.746
No. of measured, independent and observed [I > 2σ(I)] reflections	229527, 3089, 2957
Theta range (°)	2.61-27.46
R_{int}	0.054

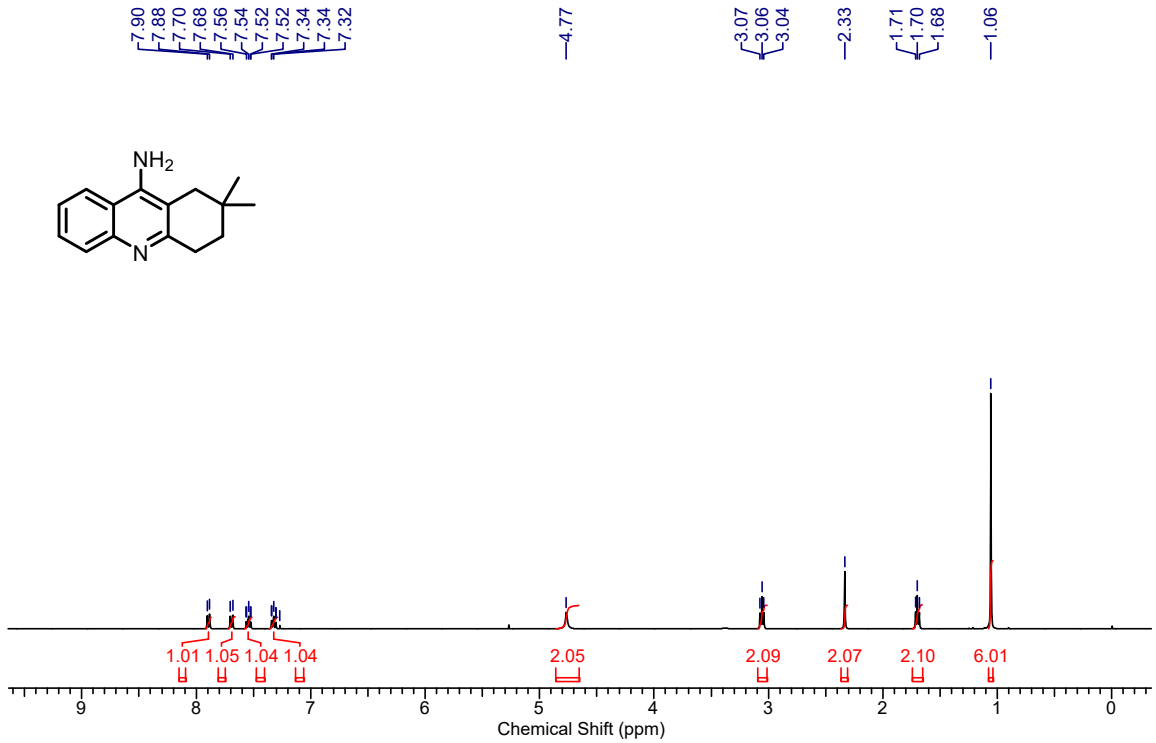
Refinement	
R[F^2 > 2σ(F^2)], wR(F^2)	0.037, 0.106
GOF on F^2	1.07
No. of independent reflections	3089
No. of parameters	393
F_000	179
No. of restraints	0
H-atom treatment	constr
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e A$^{\circ-3}$)	0.40, −0.68
CCDC number	2165374

Table S2. Hydrogen-bond geometry (A˚, °) of compound **3** are given as below.

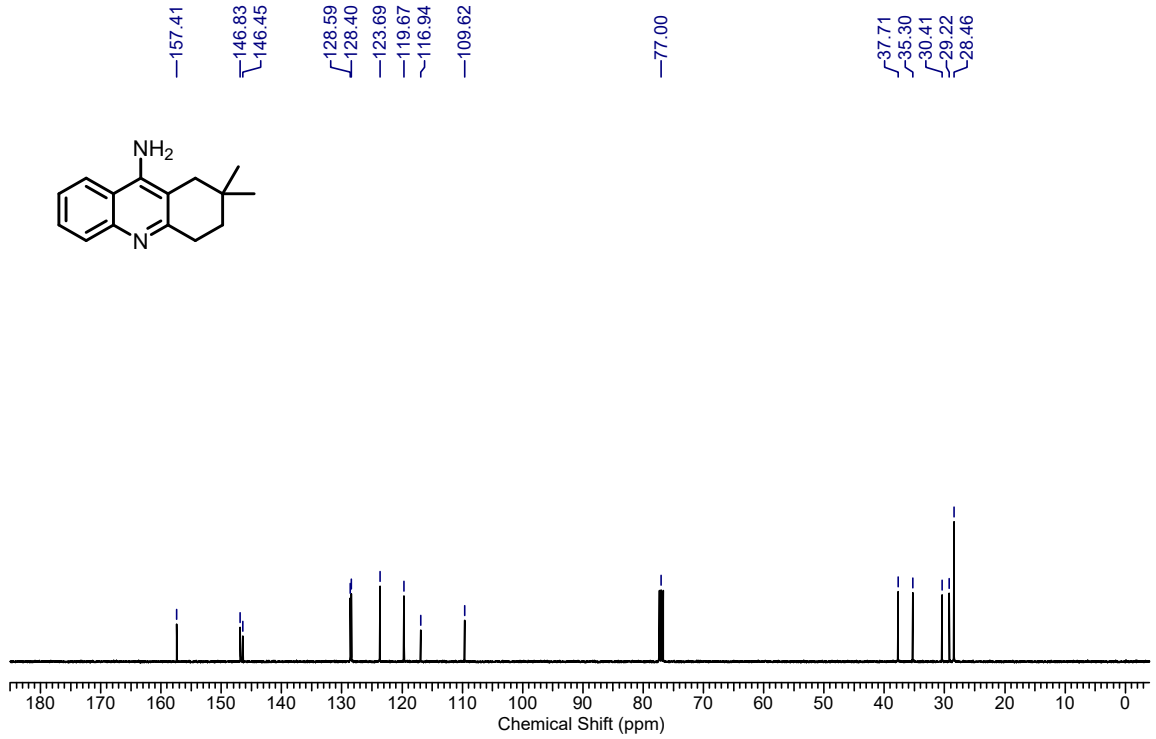
Name of the compound	*D*–H···*A*	*D*–H	H···*A*	*D*···*A*	*D*–H···*A*
Compound **3**	O1−H1A···O2	0.8700	2.0800	2.8251(3)	144
	O1−H1B···O1	0.8700	2.3600	2.8136(3)	113
	O1−H1B···O2	0.8700	2.2100	2.8251(3)	127
	N2−H2A···O2	0.8800	2.4500	3.1256(3)	134
	O2−H2C···N3	0.8700	1.9400	2.8086(3)	178
	O2−H2D···O2	0.8700	2.0200	2.8520(3)	161
	C5−H5···O2	0.9500	2.5300	3.4513(3)	164
	C12−H12B···N2	0.9900	2.5300	2.9524(3)	105

S2. SCANNED COPIES OF SPECTRAL DATA OF COMPOUNDS 2 & 3

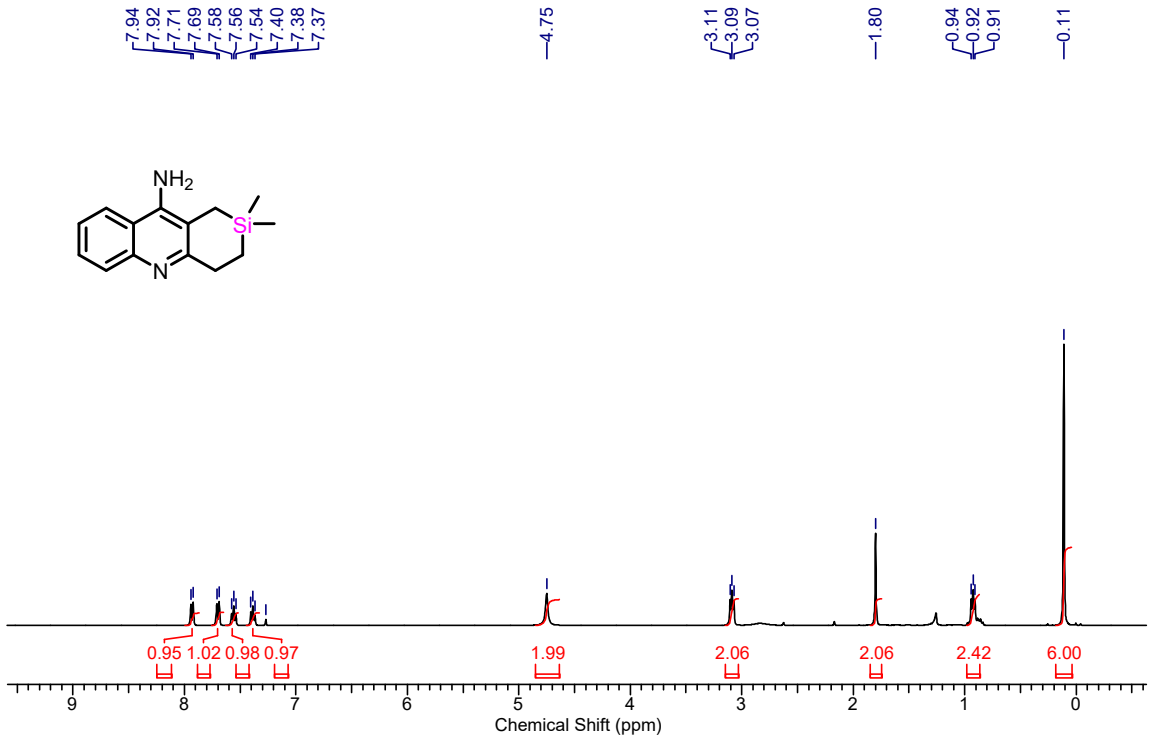
^{1}H NMR of 2 in $CDCl_3$ (400 MHz)



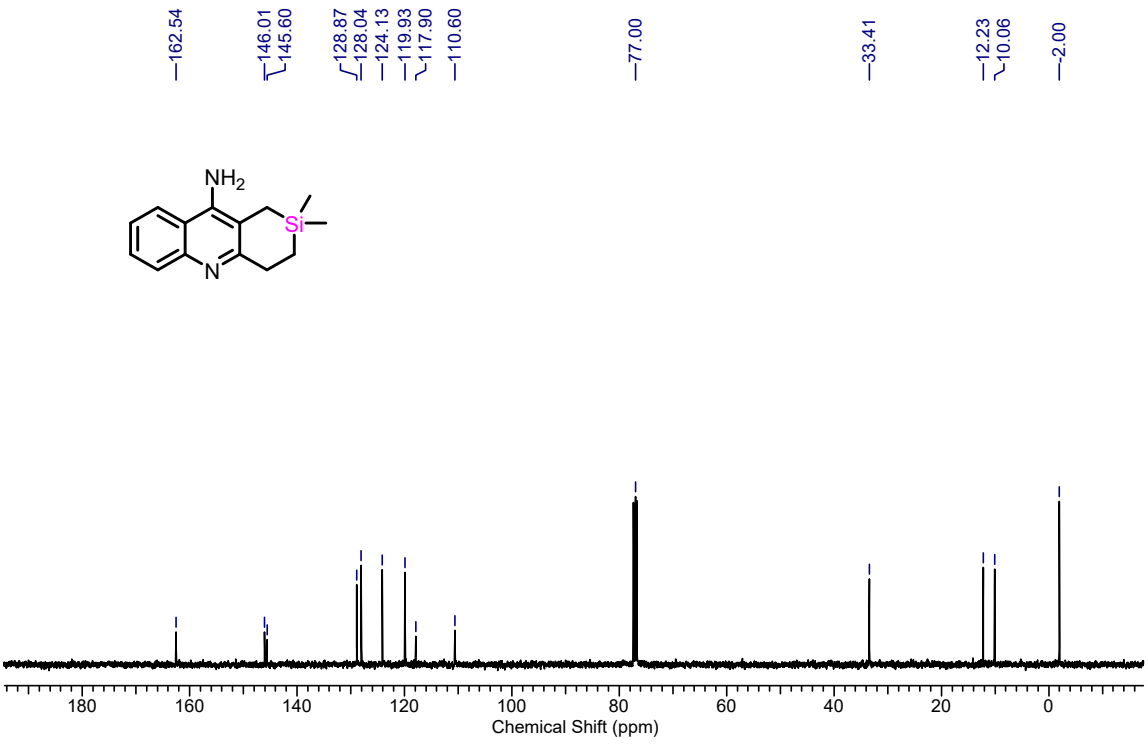
^{13}C NMR of 2 in $CDCl_3$ (100 MHz)



^{1}H NMR of 3 in $CDCl_3$ (400 MHz)



^{13}C NMR of 3 in $CDCl_3$ (100 MHz)



S3. DOSE-RESPONSE CURVES FOR INHIBITION OF CHOLINESTERASES BY COMPOUNDS 1-3