Electronic Supplementary Material (ESI) for RSC Advances.

Electronic Supplementary Information

New antimalarial 3-methoxy-1,2-dioxanes: optimization of cellular pharmacokinetic and pharmacodynamic properties by incorporation of amino and N-heterocyclic moieties at C4

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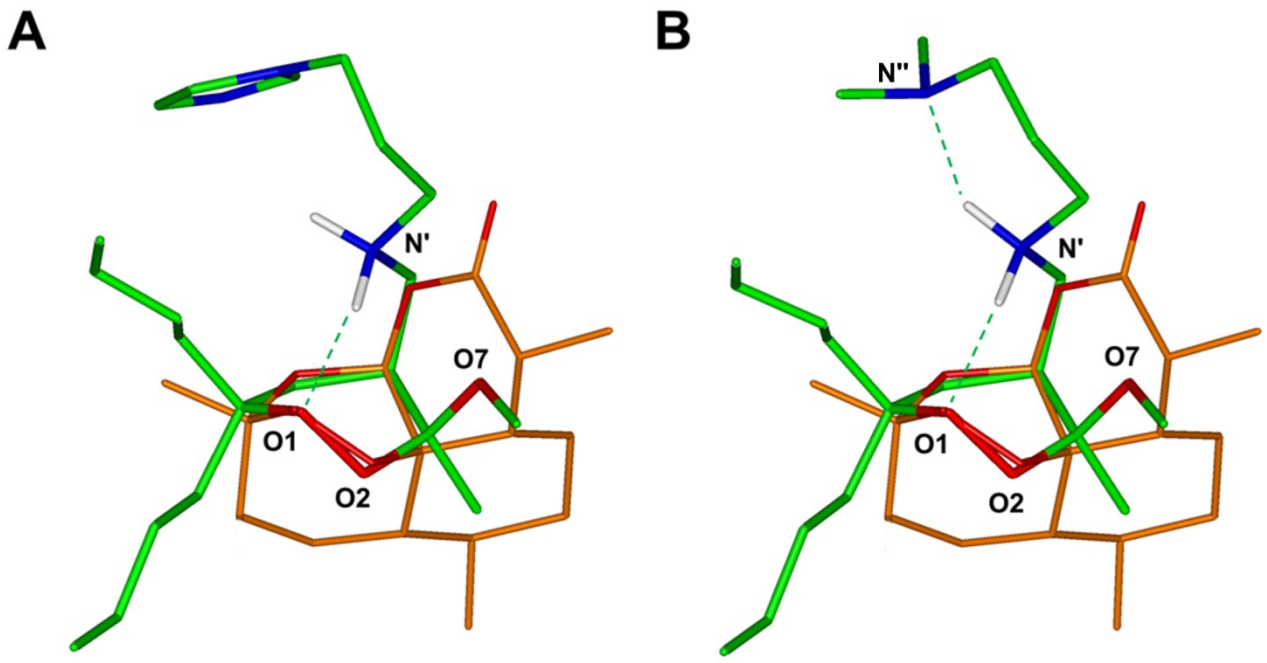


Figure 1SI. Superimposition of PM7 global minimum of **9b** (green; **A**) and **9e** (green; **B**) in protonated form on artemisinin X-ray structure (orange; CSDS code: QNGHSU). The molecules are colored by atom type (O = red, N = blue, and H = white). Hydrogens are omitted for sake of clarity, with the exception of those involved in the hydrogen bonds (highlighted by a green dashed line).

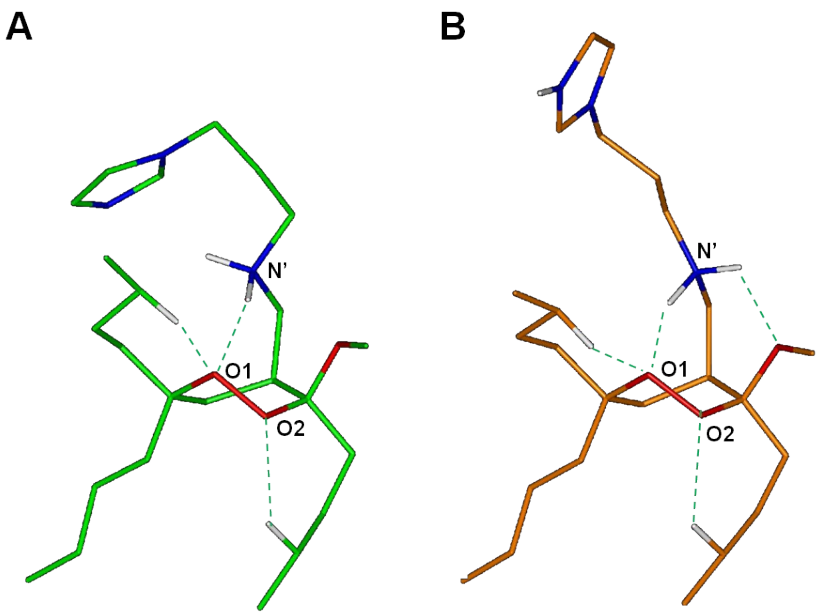


Figure 2SI. PM7 global minimum of **9c** presenting intramolecular distances suitable for the 1,5-H shift in protonated (green; **A**) and di-protonated (orange; **B**) form. Atoms are colored by atom type (O = red, N = blue, and H = white). Hydrogens are omitted for sake of clarity, with the exception of those involved as possible partners in a "through-space" intramolecular radical shift and in the hydrogen bonds (highlighted by a green dashed line).

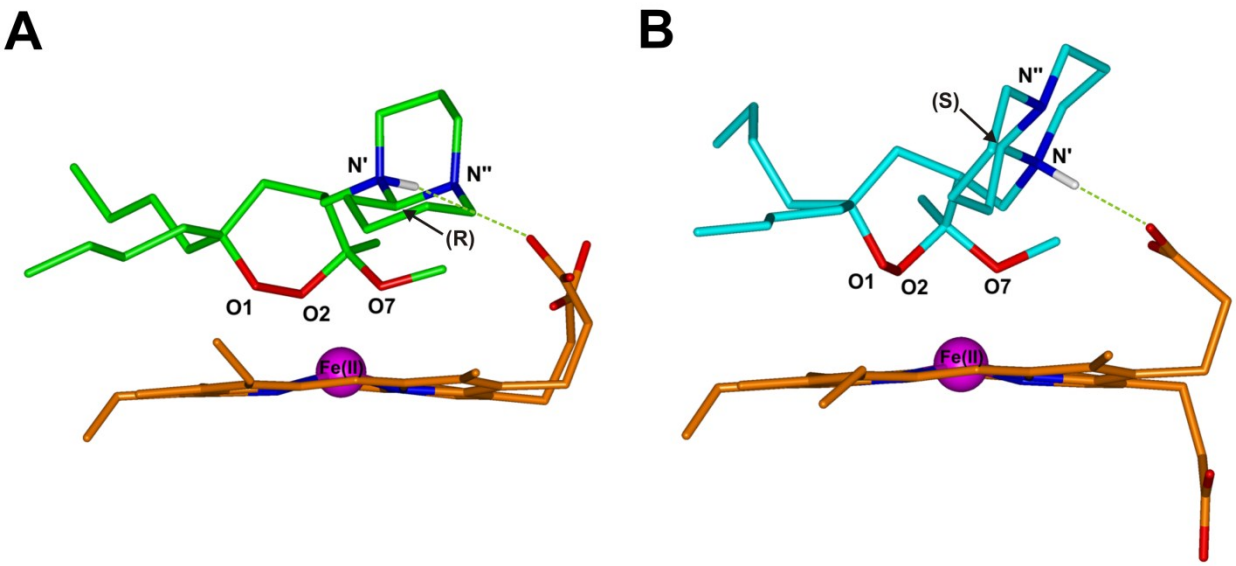


Figure 3SI. Docking results of **9h** diastereomers (A (green): (*R*)-configured stereocenter in the side-chain; B (cyan): (*S*)-configured stereocenter in the side-chain) in complex with heme (orange). The molecules are colored by atom type (O = red; N = blue; Fe = magenta and H = white). Iron atom vdW volume is shown (scaled by 70% for clarity of presentation). Hydrogens are omitted for sake of clarity, with the exception of those involved in hydrogen bonds (highlighted by a green dashed line).

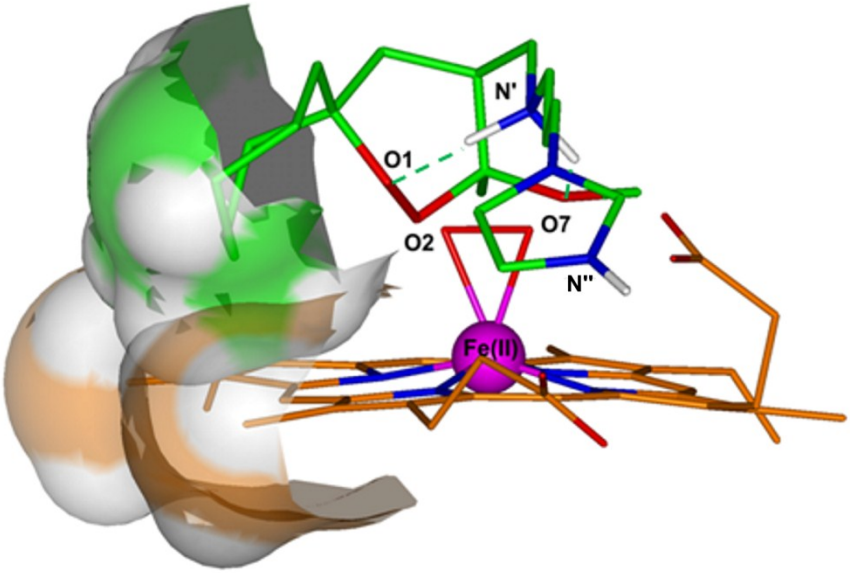


Figure 4SI. Di-protonated form of **9i** in complex wih heme superimposed (coordination O2/O7) on the X-ray structure of peroxo-bridged heme complex (CSD code UKACIS). The molecules are colored by atom type (C = green and orange for PM7 conformer and heme, respectively; O = red; N = blue; Fe = magenta and H = white). The solvent accessible surface of atoms responsible for steric hindrance between **9i** and heme is shown (transparency = 50%). Iron atom vdW volume is shown (scaled by 70% for clarity of presentation). Hydrogens are omitted for sake of clarity, with the exception of those involved in the intramolecular hydrogen bonds (highlighted by a green dashed line).

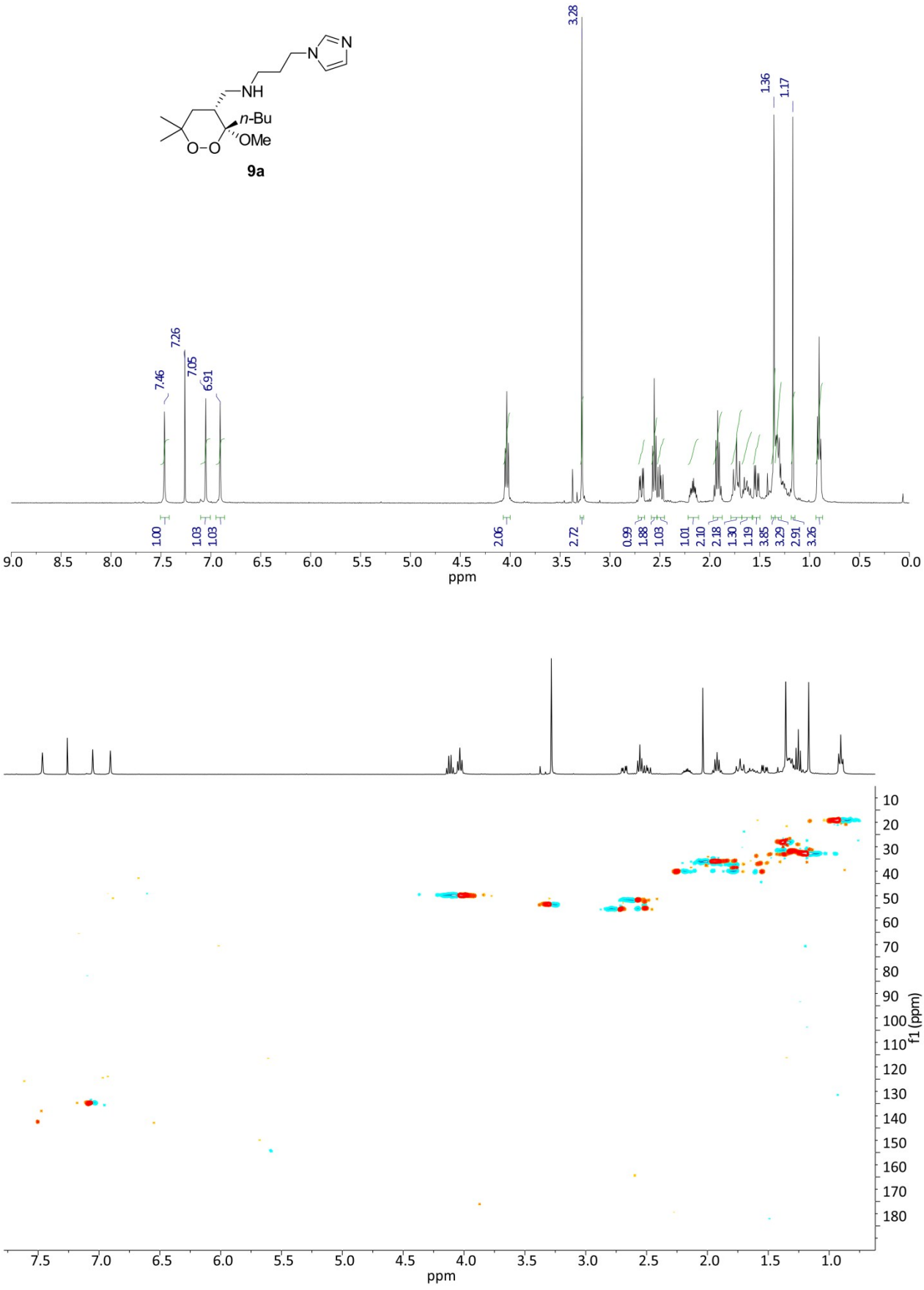


Figure 5SI. 1H-NMR and HSQC-NMR spectra of **9a**.

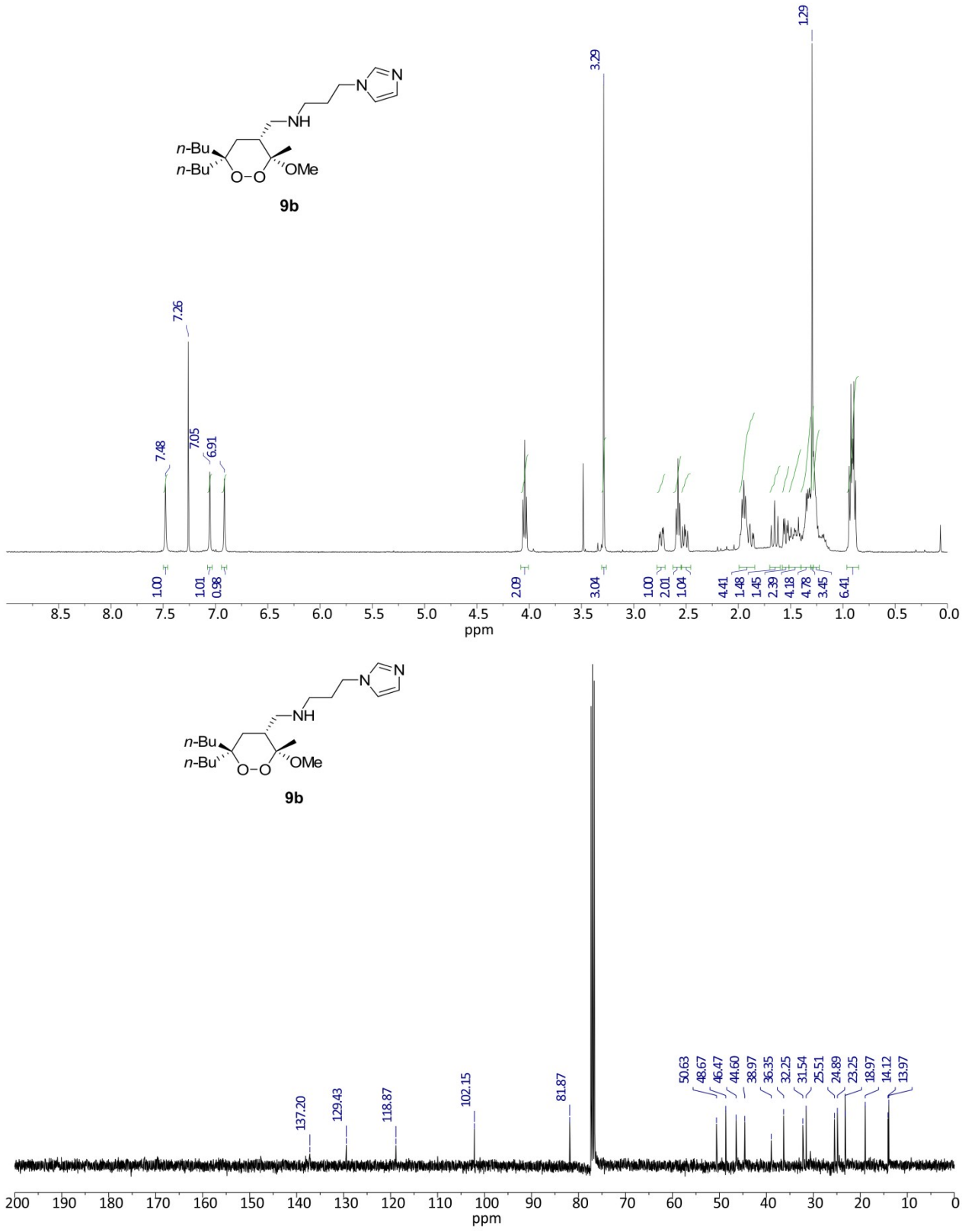


Figure 6SI. 1H-NMR and 13C-NMR spectra of **9b**.

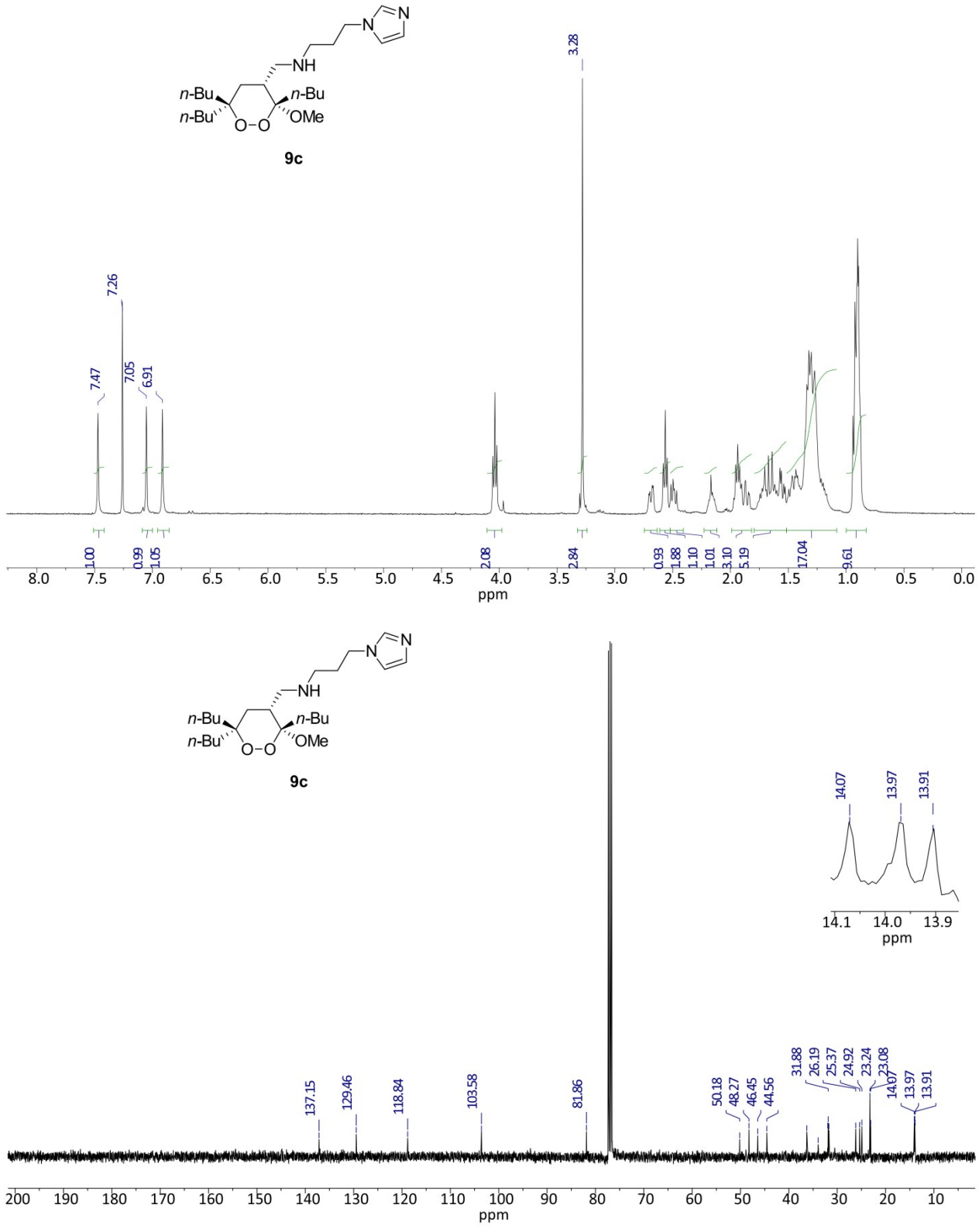


Figure 7SI. 1H-NMR and 13C-NMR spectra of **9c**.

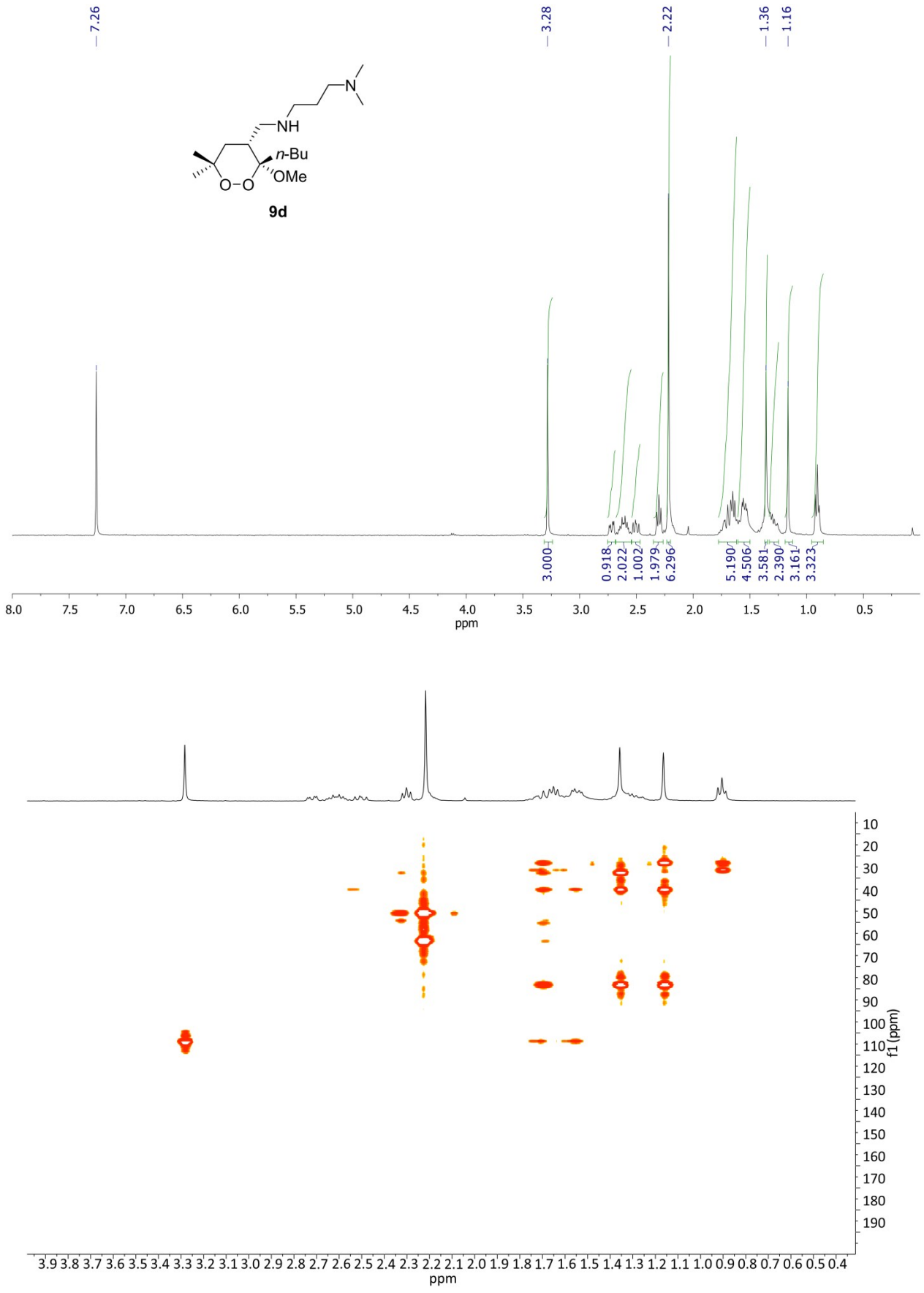


Figure 8SI. 1H-NMR and HMBC-NMR spectra of **9d**.

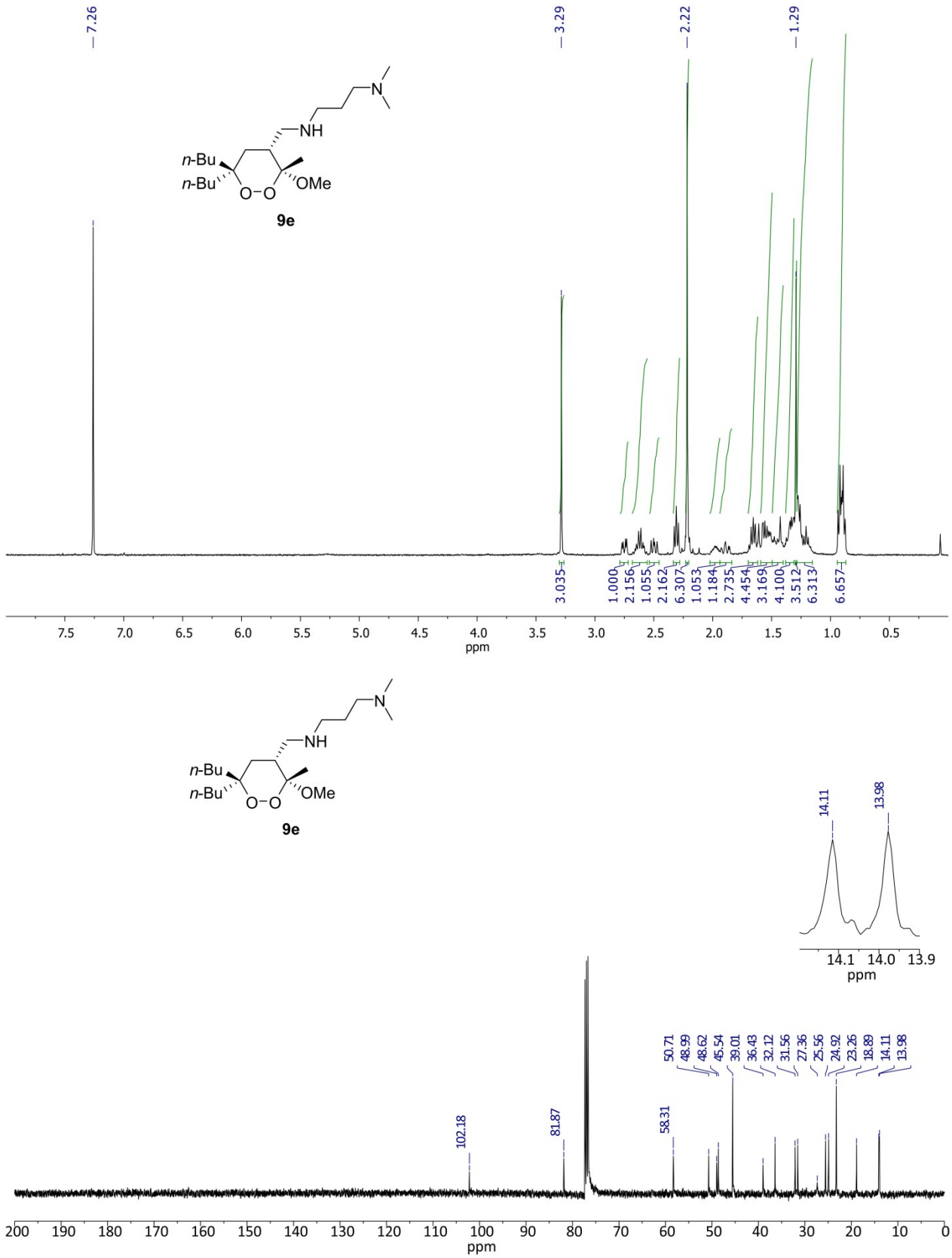


Figure 9SI. 1H-NMR and 13C-NMR spectra of **9e**.

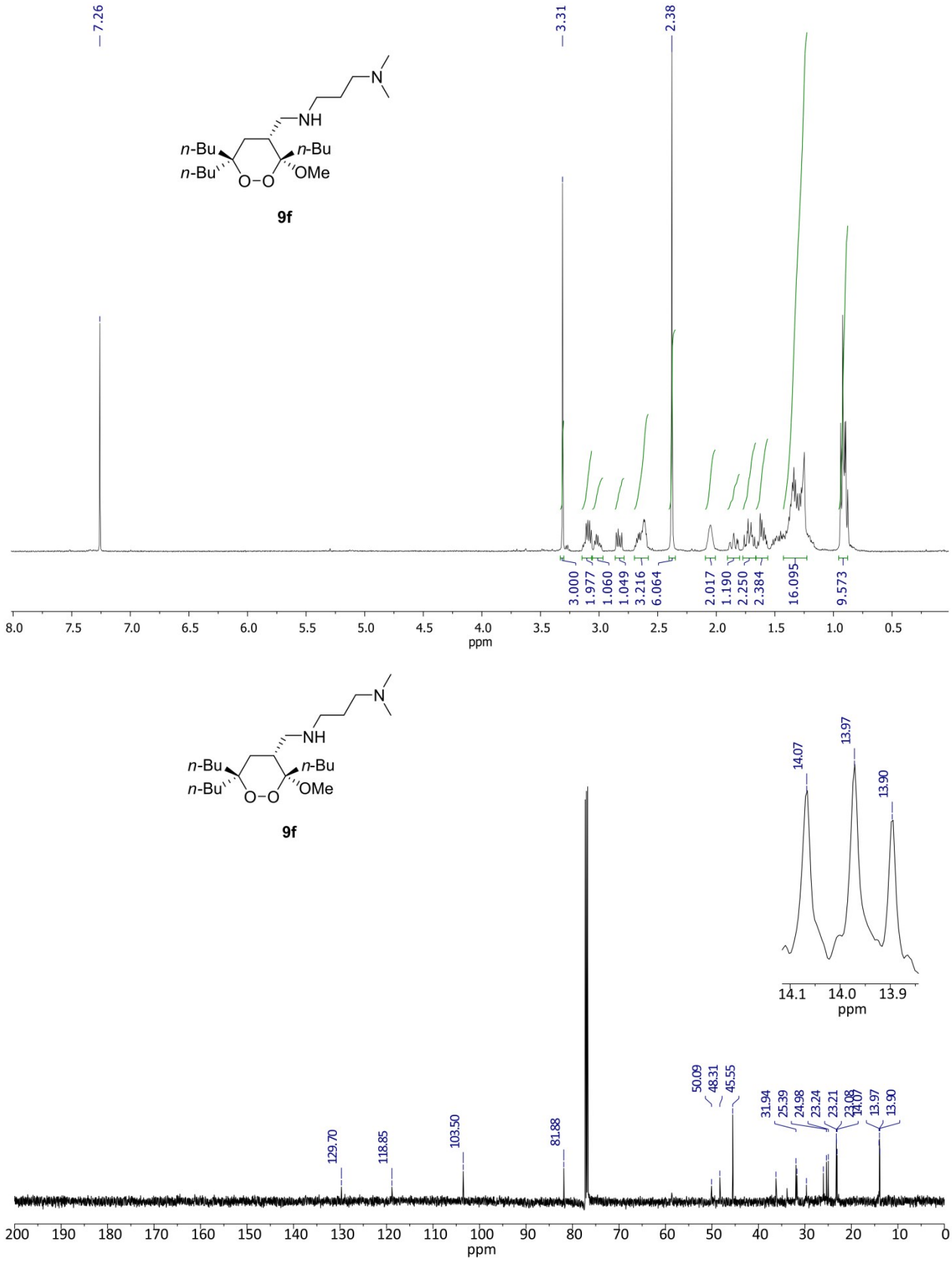


Figure 10SI. 1H-NMR and 13C-NMR spectra of **9f**.

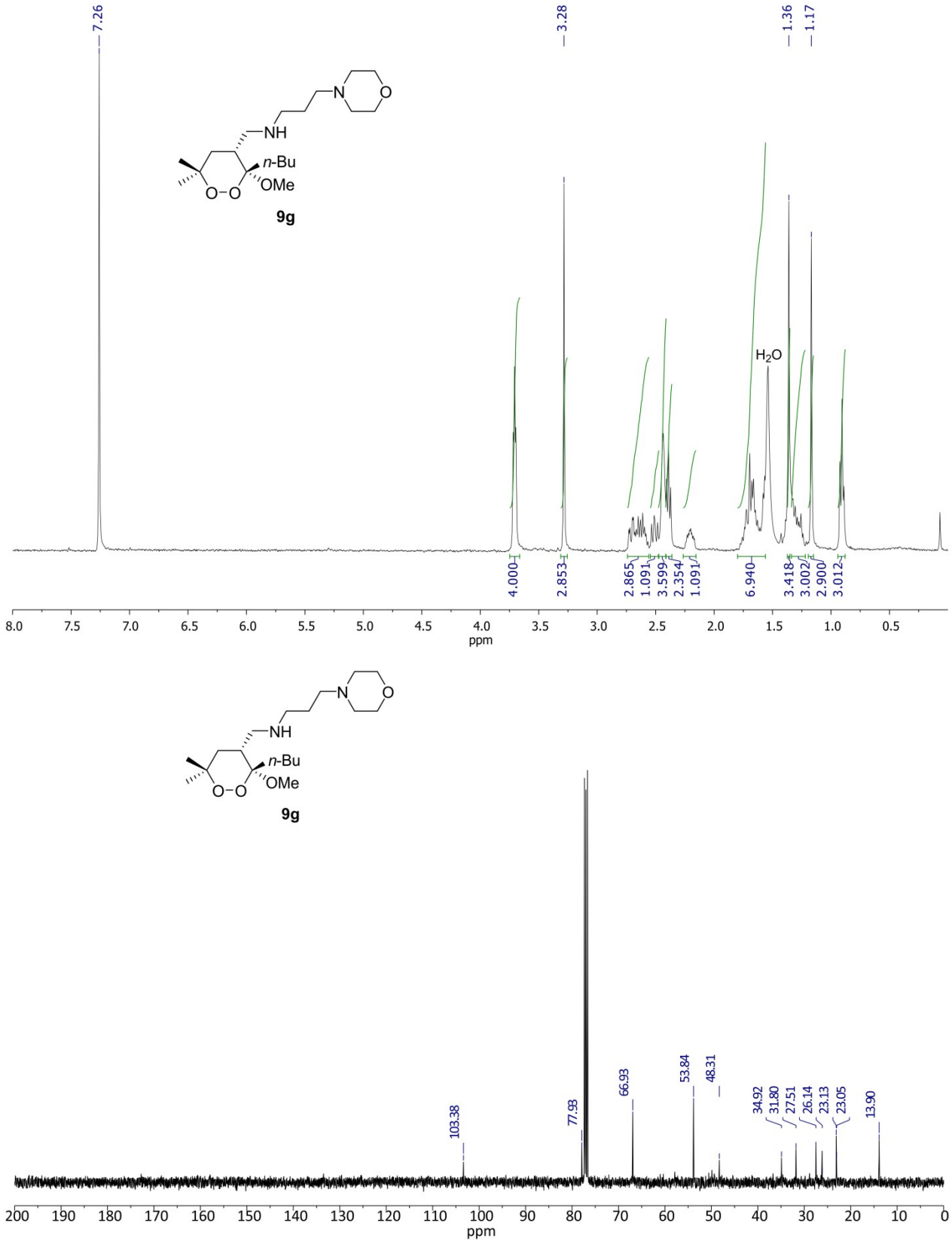


Figure 11SI. 1H-NMR and 13C-NMR spectra of **9g**.

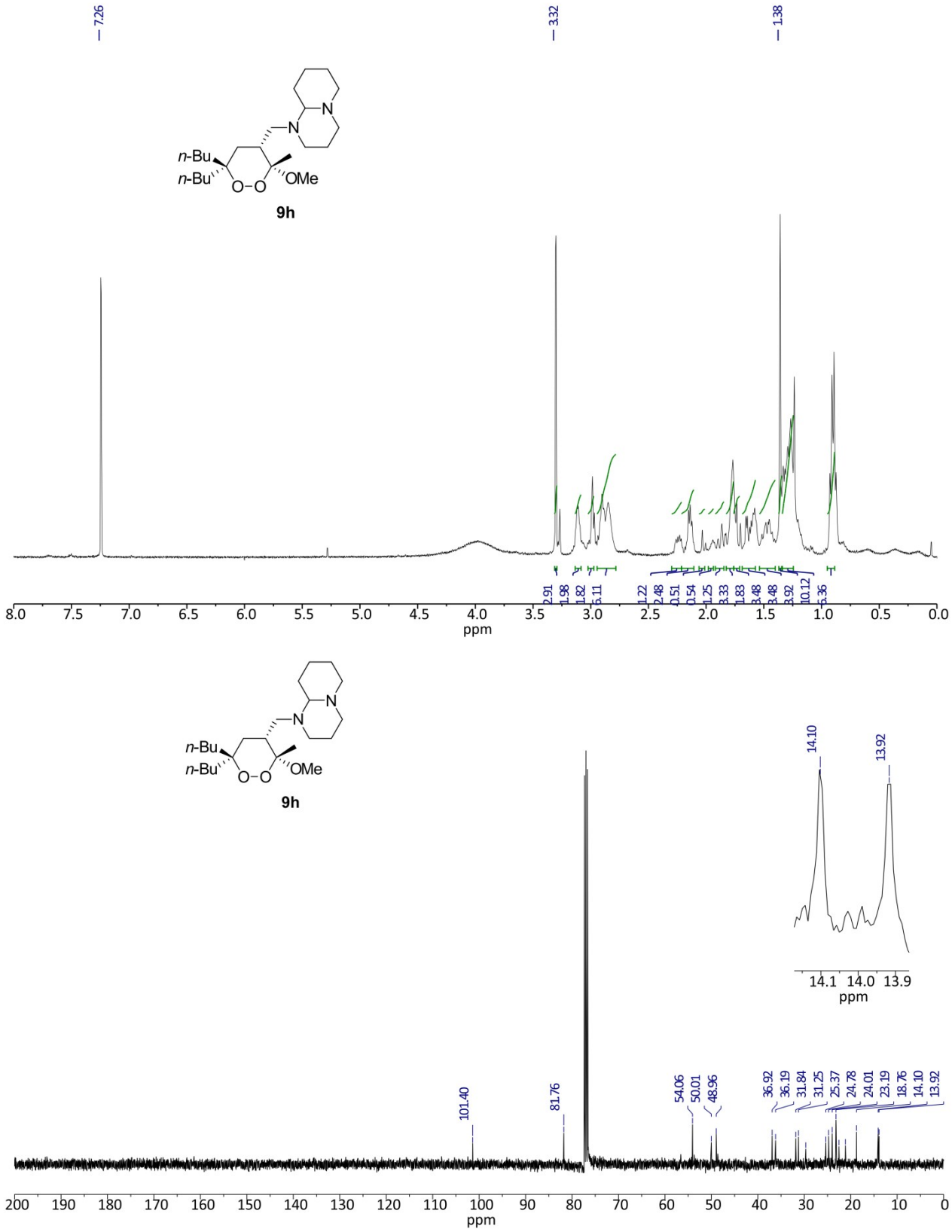


Figure 12SI. 1H-NMR and 13C-NMR spectra of **9h**.

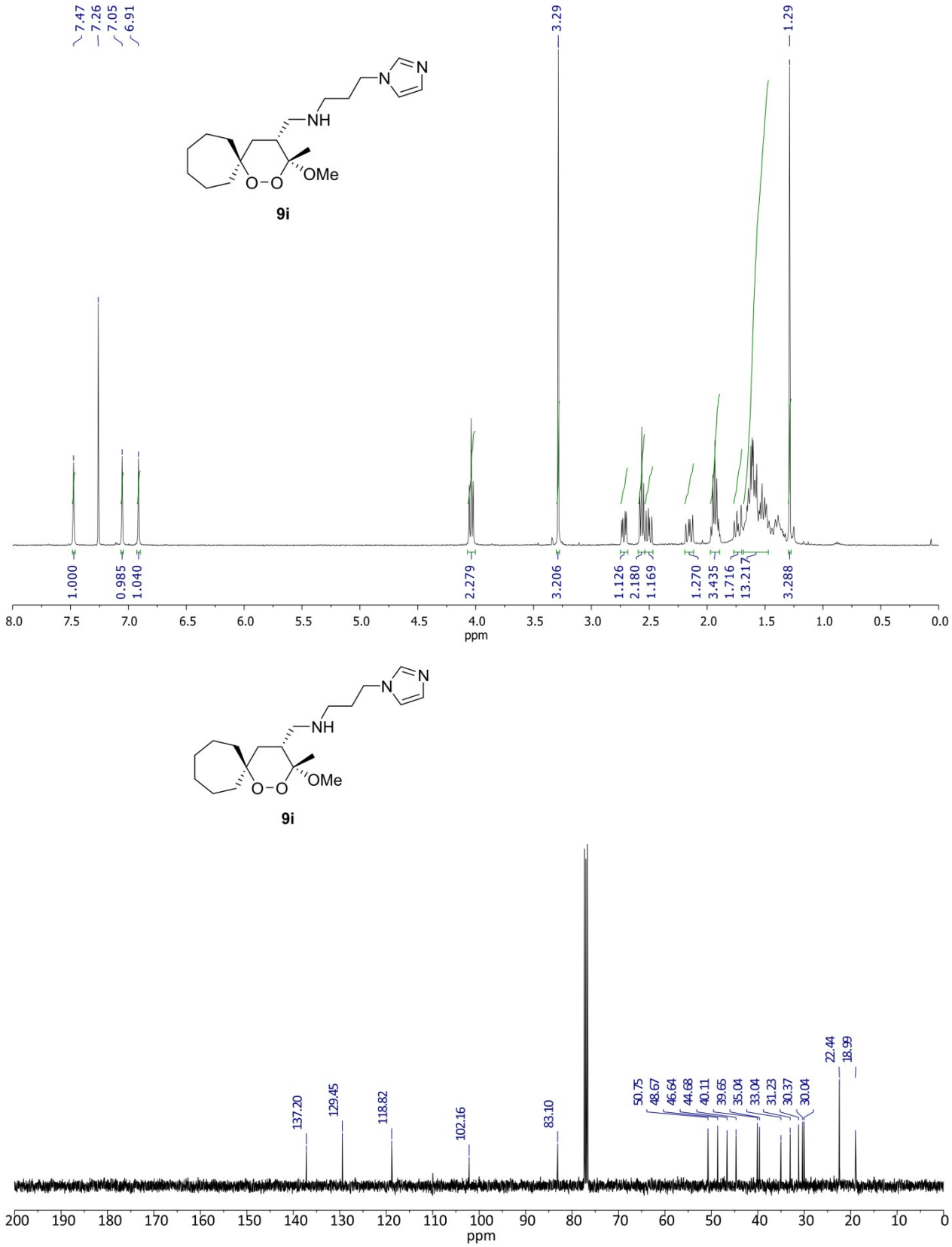


Figure 13SI. 1H-NMR and 13C-NMR spectra of **9i**.

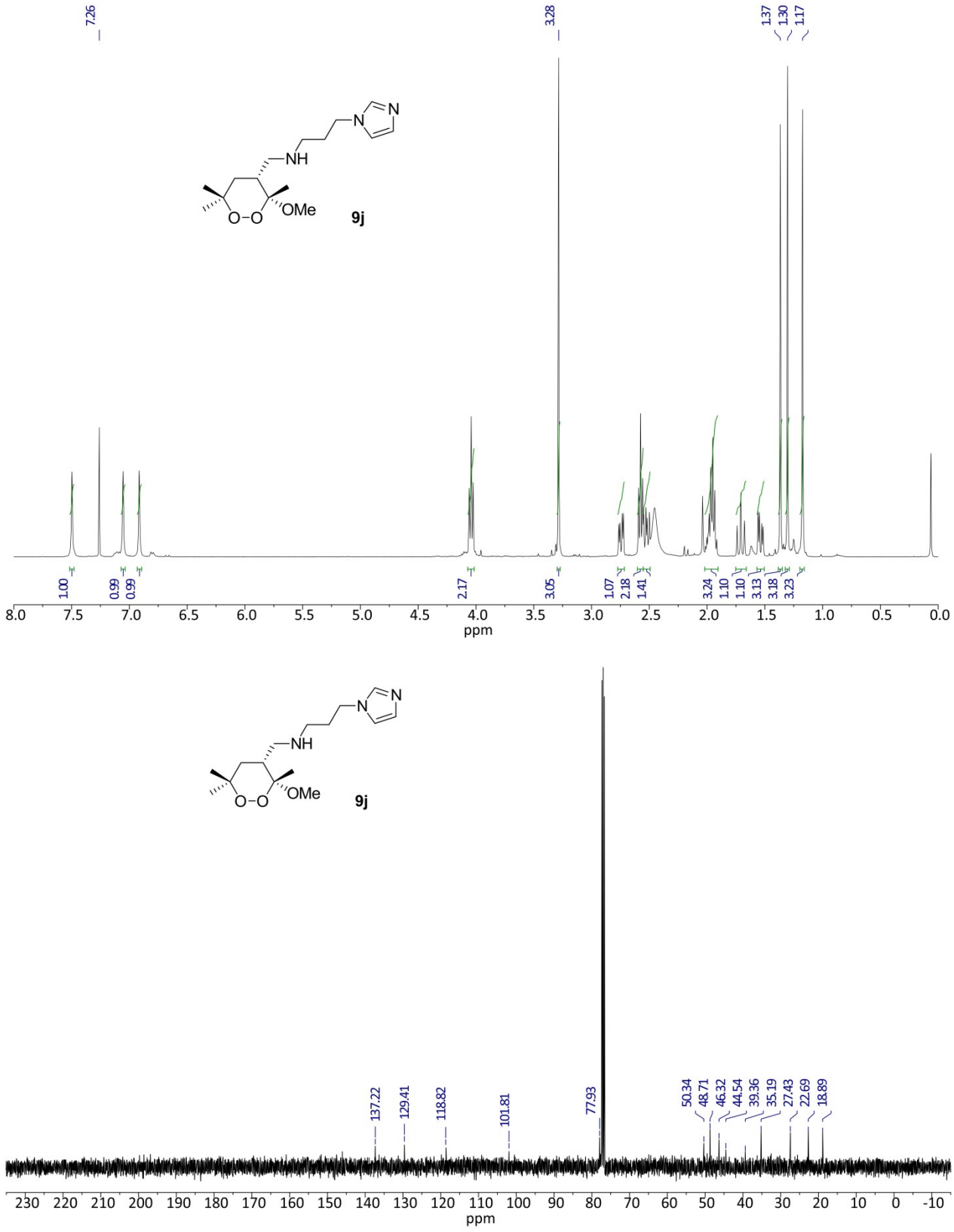


Figure 14SI. 1H-NMR and 13C-NMR spectra of **9j**.

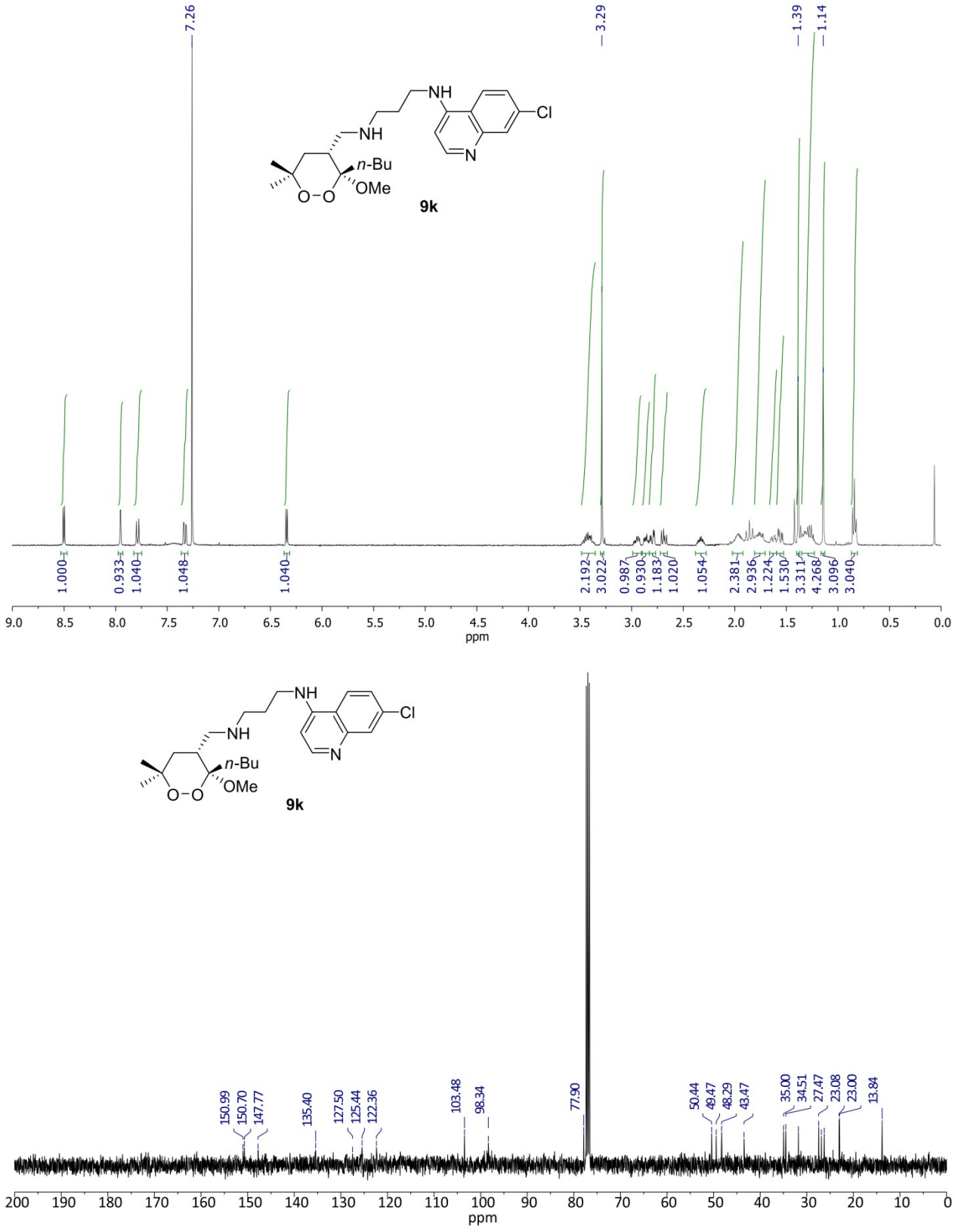


Figure 15SI. 1H-NMR and 13C-NMR spectra of **9k**.

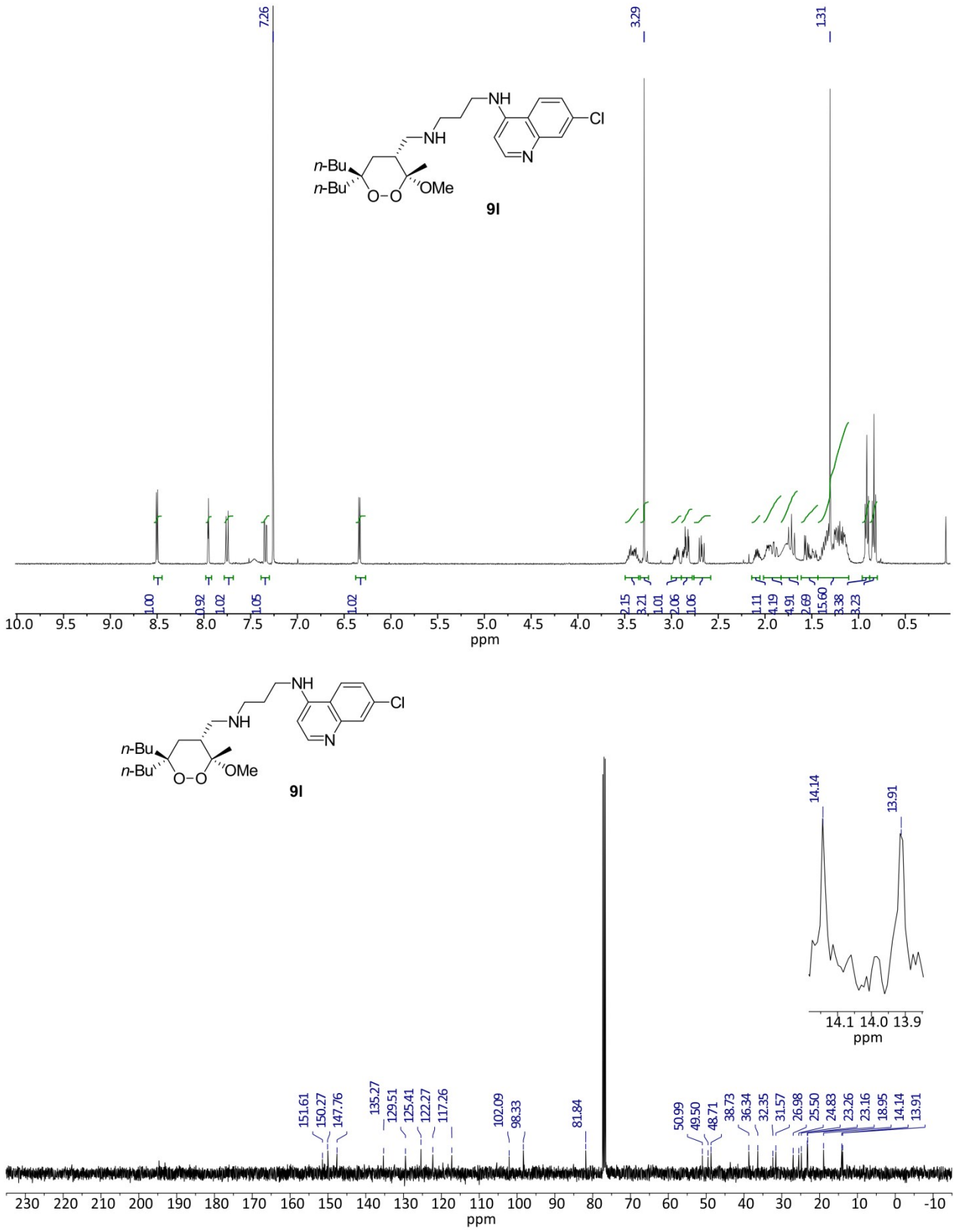


Figure 16SI. 1H-NMR and 13C-NMR spectra of **9l**.

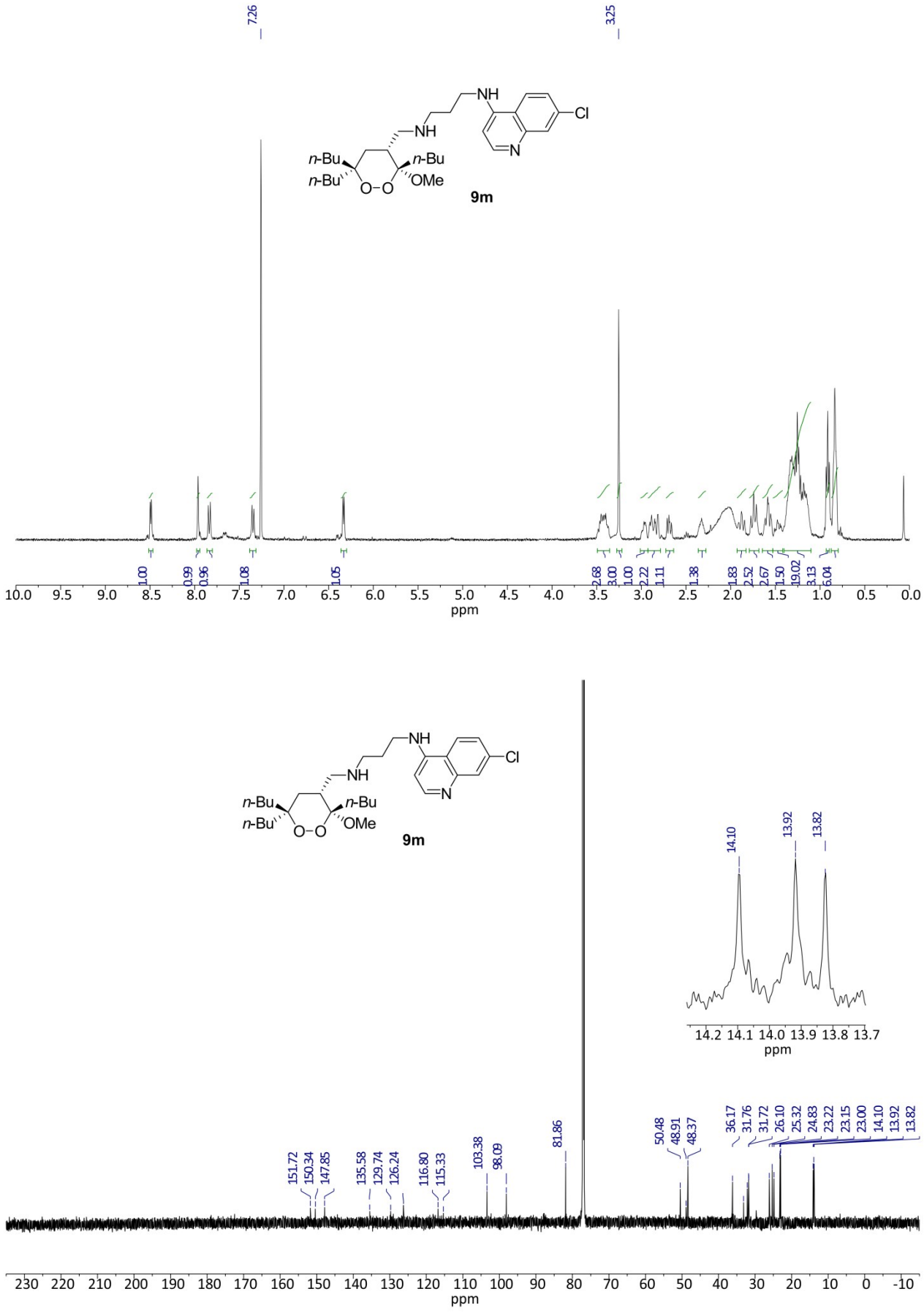


Figure 17SI. 1H-NMR and 13C-NMR spectra of **9m**.

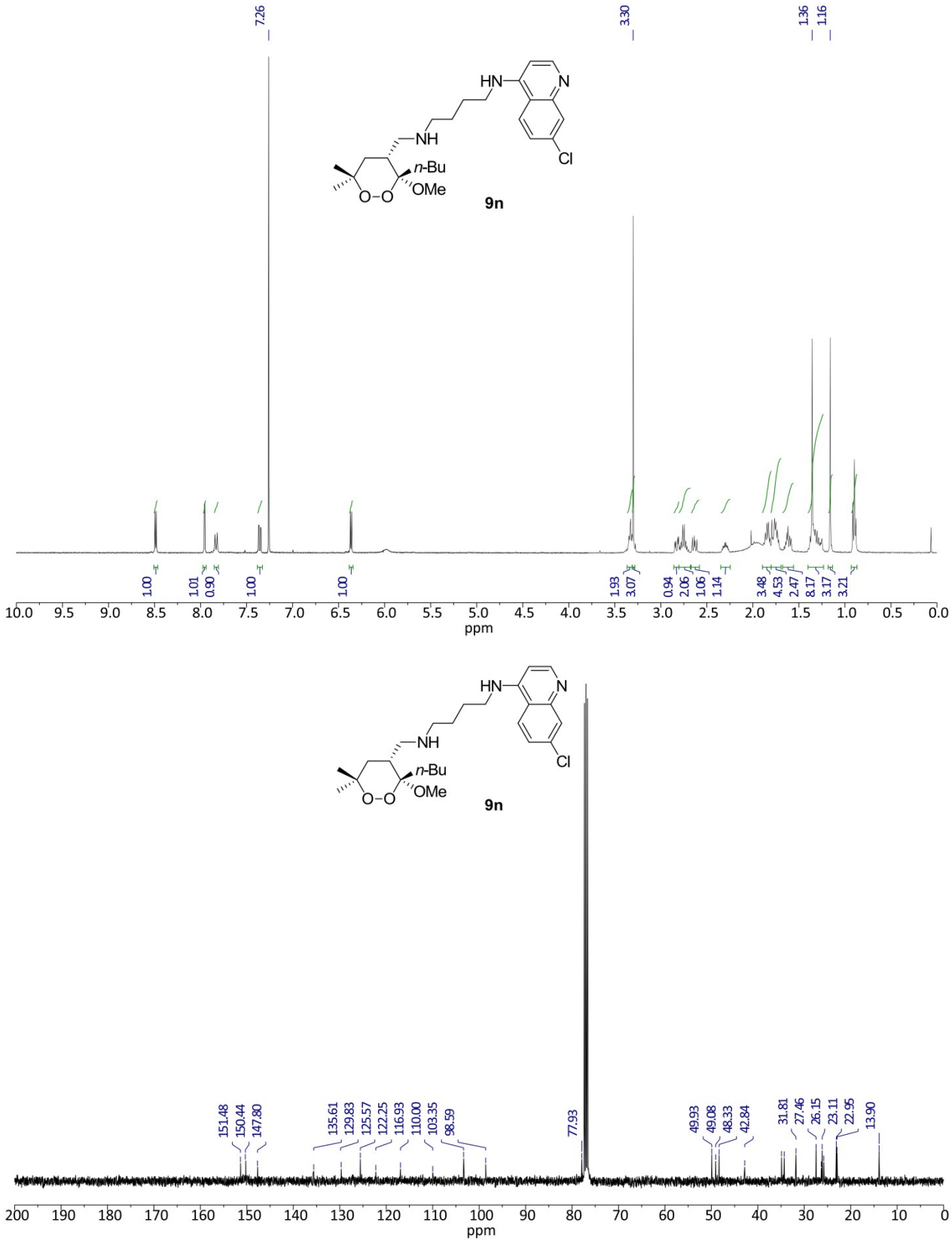


Figure 18SI. 1H-NMR and 13C-NMR spectra of **9n**.

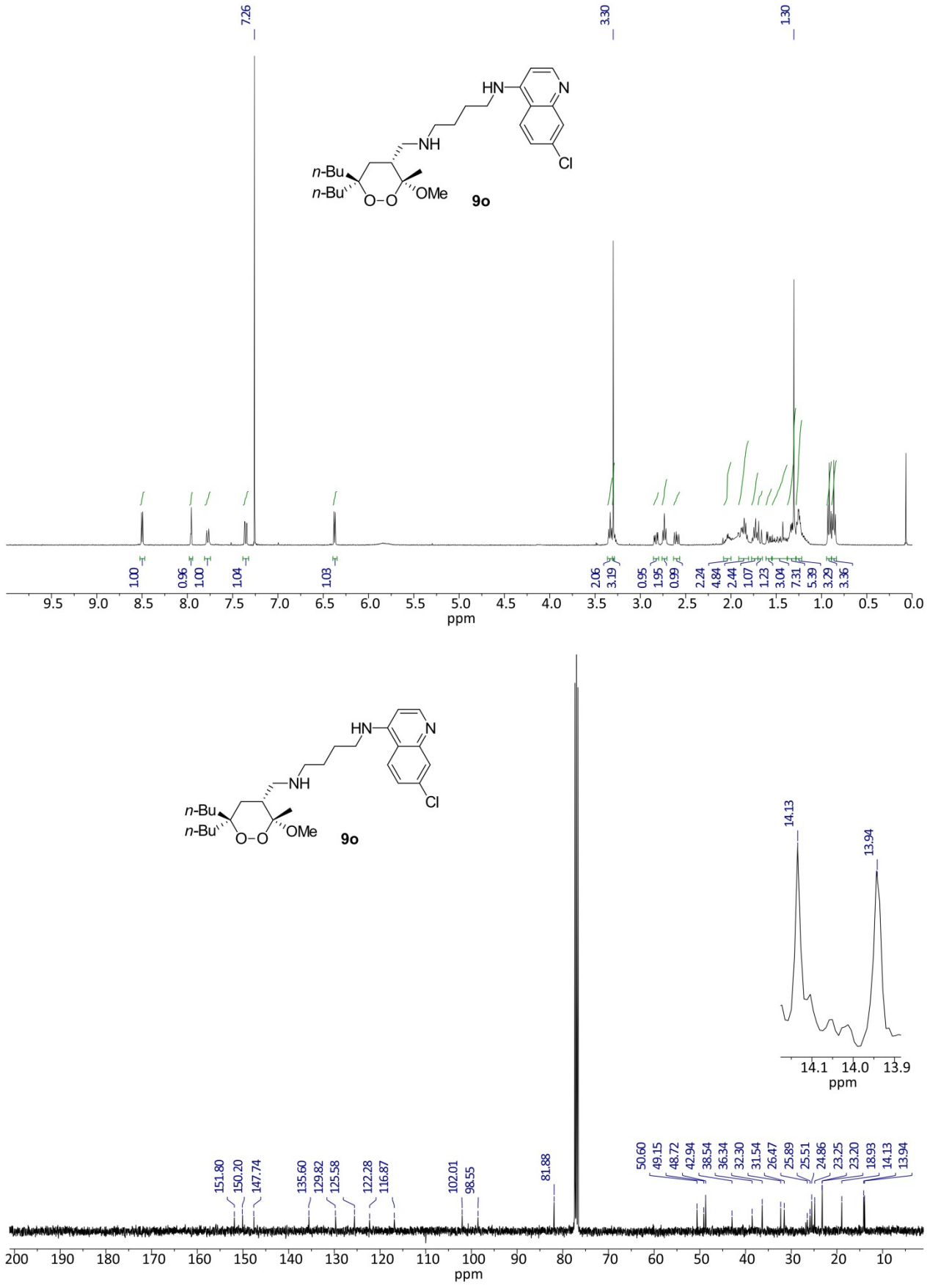


Figure 19SI. 1H-NMR and 13C-NMR spectra of **9o**.

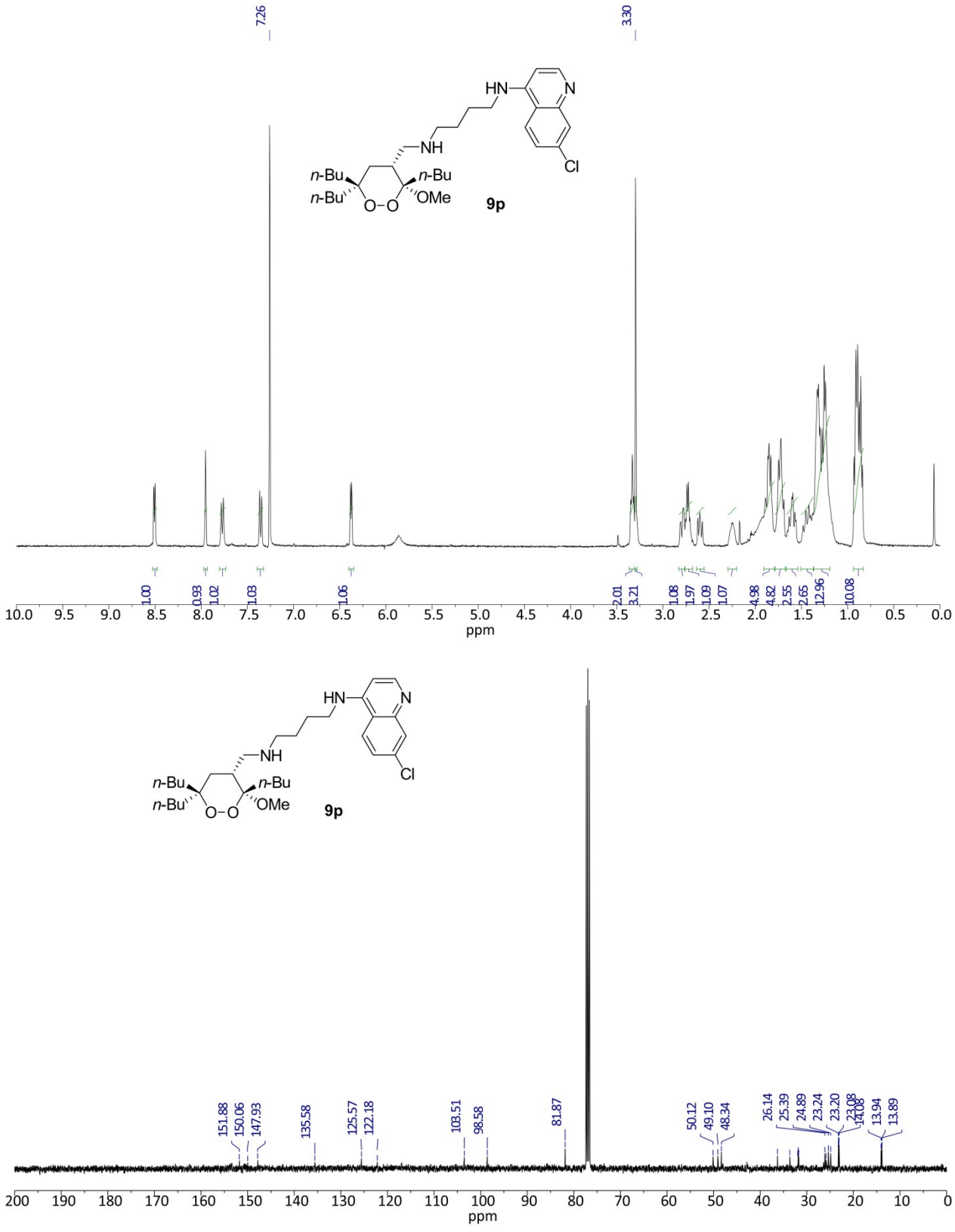


Figure 20SI. 1H-NMR and 13C-NMR spectra of **9p**.

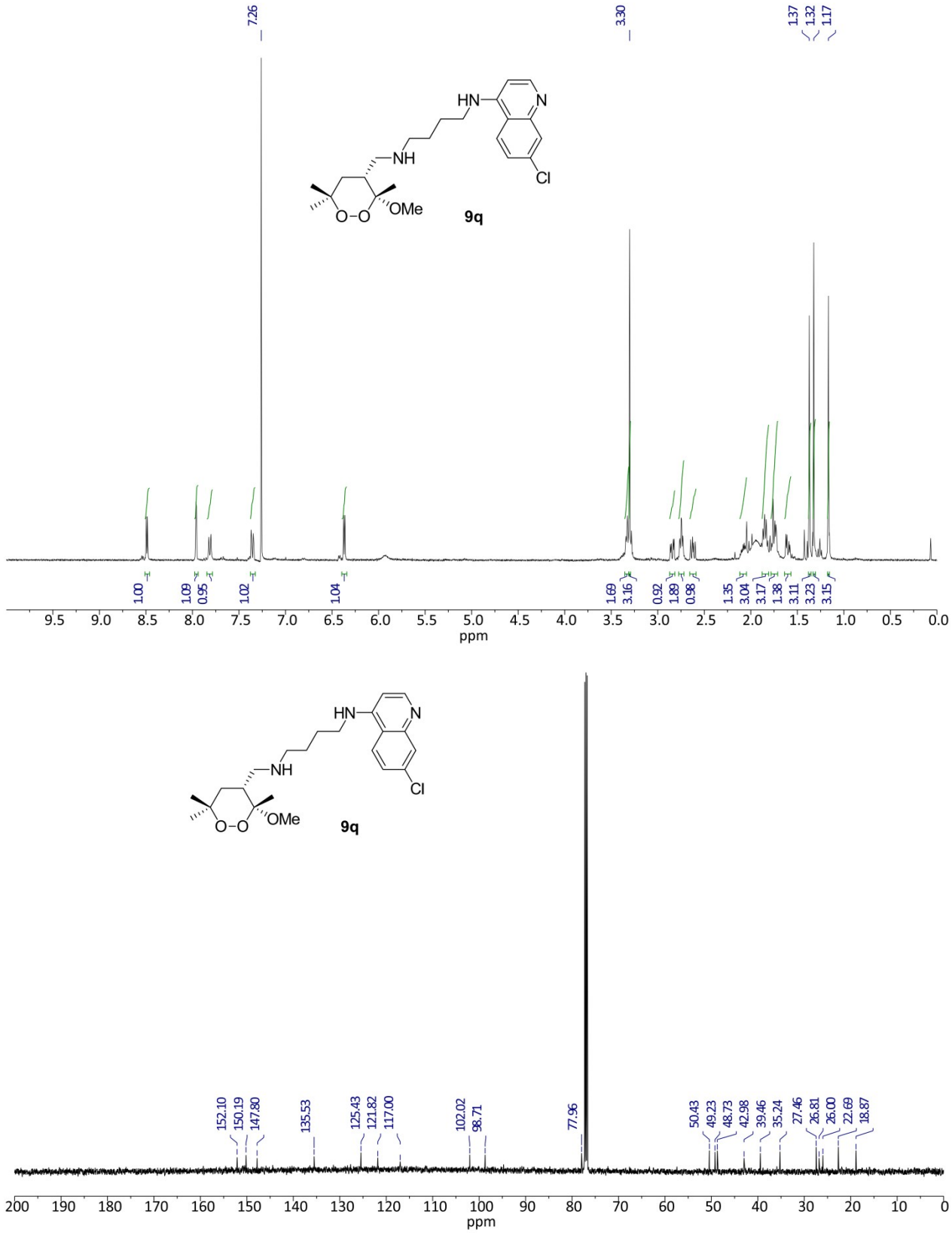


Figure 21SI. 1H-NMR and 13C-NMR spectra of **9q**.

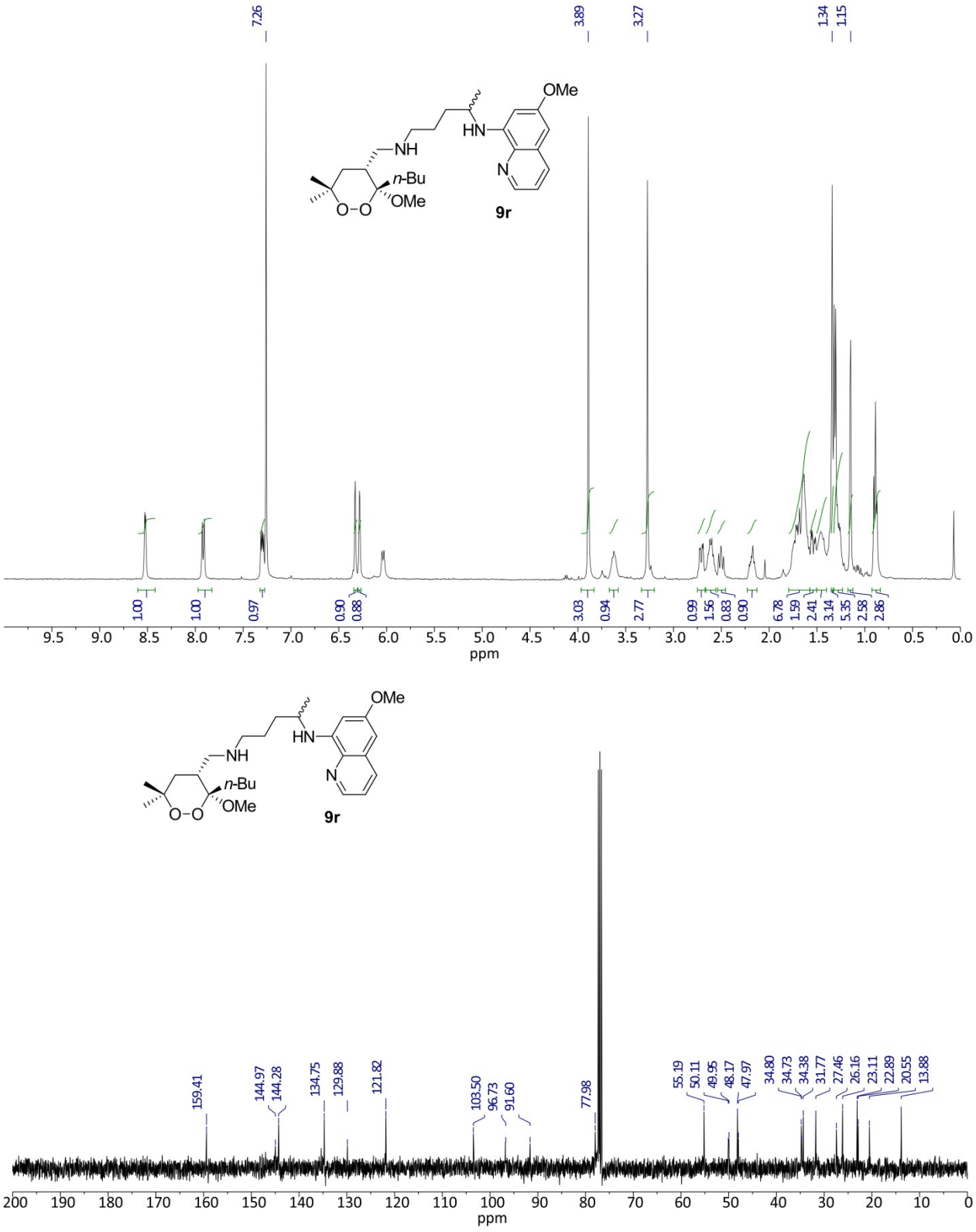


Figure 22SI. 1H-NMR and 13C-NMR spectra of **9r**.

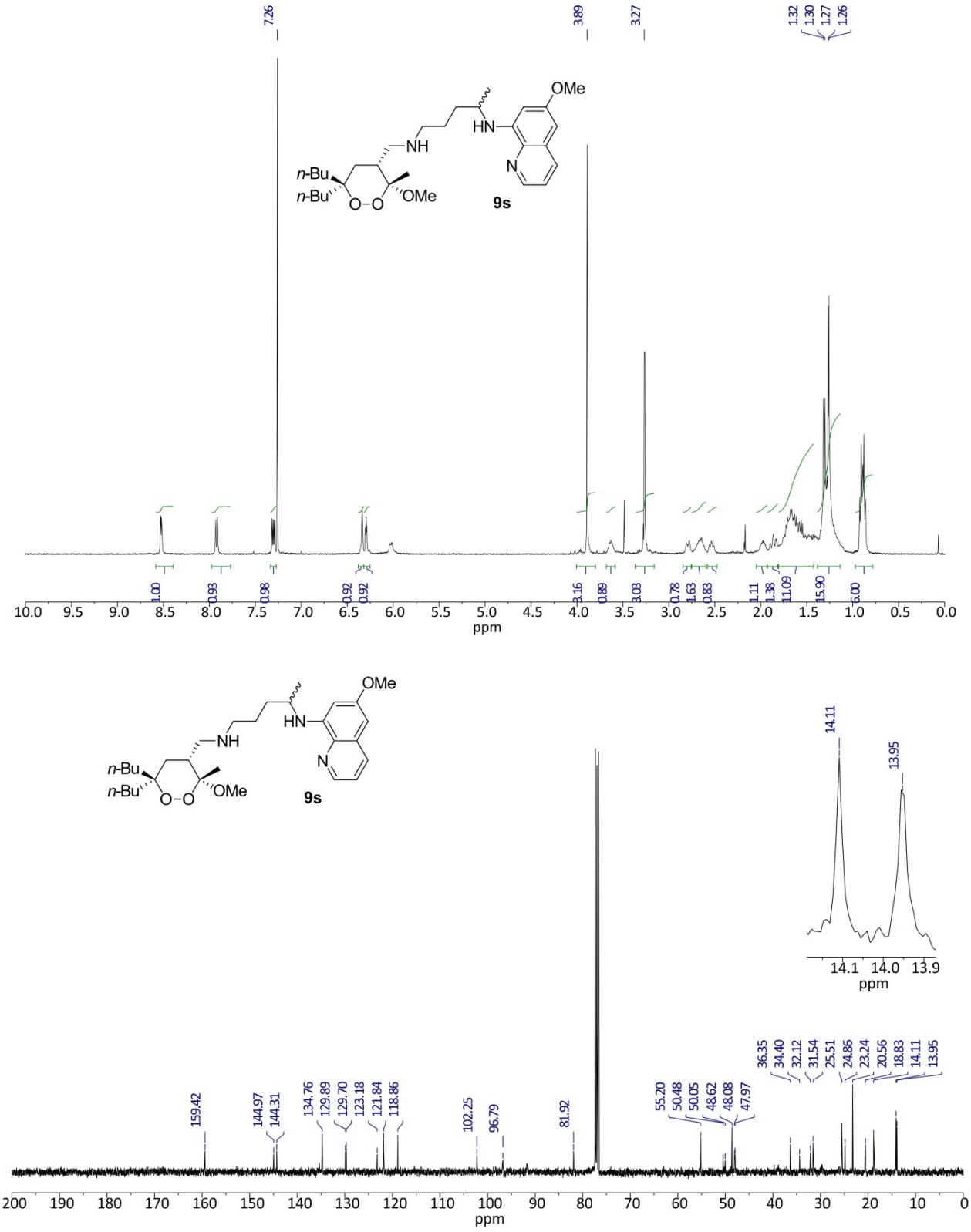


Figure 23SI. 1H-NMR and 13C-NMR spectra of **9s**.

Table 1SI. Calculated ionic forms.

	Ionic form (%)[a]		
Comp	**pH 7.4**	**pH 7.2**	**pH 5.5**
9a	DP(15) P(85)	DP(22) P(78)	DP(93) P(7)
9b	DP(15) P(85)	DP(22) P(78)	DP(93) P(7)
9c	DP(15) P(85)	DP(22) P(78)	DP(93) P(7)
9d	DP(80) P(20)	DP(86) P(14)	DP(100)
9e	DP(80) P(20)	DP(86) P(14)	DP(100)
9f	DP(80) P(20)	DP(86) P(14)	DP(100)
9g	DP(2) P(98)	DP(3) P(97)	DP(56) P(44)
9h	P(68) N(32)	P(77) N(23)	P(99) N(1)
9i	DP(15) P(85)	DP(22) P(78)	DP(93) P(7)
9j	DP(15) P(85)	DP(22) P(78)	DP(93) P(7)
9k	DP(14) P(86)	DP(21) P(79)	DP(100)
9l	DP(14) P(86)	DP(21) P(79)	DP(100)
9m	DP(14) P(86)	DP(21) P(79)	DP(100)
9n	DP(11) P(89)	DP(16) P(84)	DP(100)
9o	DP(11) P(89)	DP(16) P(84)	DP(100)
9p	DP(11) P(89)	DP(16) P(84)	DP(100)
9q	DP(11) P(89)	DP(16) P(84)	DP(100)
9r	P(100)	P(100)	P(100)
9s	P(100)	P(100)	P(100)

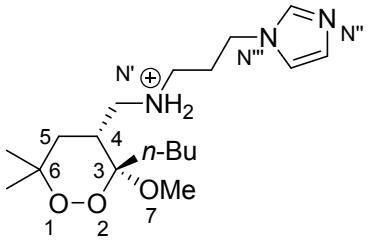
[a]Percentage of ionic form in brackets. P = protonated form; DP = di-protonated form. (ACD/Percepta software, version 14.0.0, Advanced Chemistry Development, Inc., Toronto, ON, Canada).

Table 2SI. Occurrence Rate (%) of PM7 conformers within 5 kcal mol^{-1} from the global minimum with interatomic distances suitable for a radical shift from O1 or O2 (≤ 3 Å).

Cmp	Ionic form[a]	C3 alkyl side chain	C6 alkyl side chains	C4 protonated amine group
9a	P	68	-	16
	DP	66	-	58
9b	P	-	100	83
	DP	-	100	100
9c	P	40	100	100
	DP	43	71	100
9d	P	65	-	10
	DP	100	-	100
9e	P	-	100	28.5
	DP	-	80	80
9f	P	100	88	22
	DP	80	100	80
9g	P	70	-	11
	DP	100	-	100
9h[b]	P	-	91	9
9h[c]	P	-	94	6
9i	P	-	74	16
	DP	-	86	100
9j	P	-	-	18
	DP	-	-	44
9k	P	70	-	21
	DP	50	-	25
9l	P	-	50	20
	DP	-	100	33
9m	P	100	100	43
	DP	50	100	50
9n	P	56	-	9
	DP	67	-	17
9o	P	-	100	25
	DP	-	75	-
9p	P	100	75	25
	DP	0	-	-
9q	P	-	-	10
	DP	-	-	60
9r[b]	P	76	-	9
9r[c]	P	72	-	17
9s[b]	P	-	100	33
9s[c]	P	-	100	22

[a]DP = di-protonated form, P = protonated form. [b]Diastereomer with (*R*)-configured stereocenter in the side-chain. [c]Diastereomer with (*S*)-configured stereocenter in the side-chain.

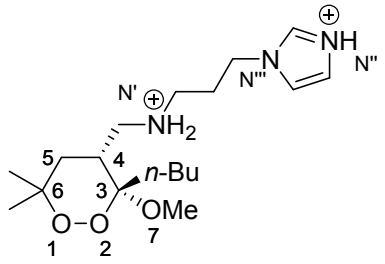
Table 3SI. PM7 conformers within 5 kcal mol^{-1} from the global minimum of **9a** protonated form.



Cnf	ΔE	1,2-dioxane ring conformation	Intramolecular interactions	H-shift[a]
9a_001	0	Skew Boat B	N'-O1; N'-IMID (cat-π)	N', C3
9a_002	2.478	Skew Boat B	N'-O1; N'-IMID (cat-π)	N', C3
9a_003	2.5924	Skew Boat B	N'-O1; N'-IMID (cat-π)	N'
9a_004	2.7539	Chair A	N'-O7; N'-IMID (cat-π)	-
9a_005	2.755	Chair A	N'-O7; N'-IMID (cat-π)	C3
9a_006	2.8339	Chair A	N'-O7; N'-IMID (cat-π)	C3
9a_007	2.9663	Chair A	N'-O7; N'-IMID (cat-π)	C3
9a_008	3.0093	Chair A	N'-O7; N'-IMID (cat-π)	C3
9a_009	3.4844	Chair A	N'-O7; N'-IMID (cat-π)	C3
9a_010	3.6091	Chair A	N'-O7; N'-IMID (cat-π)	C3
9a_011	3.7333	Chair A	N'-O7; N'-IMID (cat-π)	-
9a_012	3.9003	Chair A	N'-O7; N'-IMID (cat-π)	C3
9a_013	3.9946	Chair A	N'-O7; N'-IMID (cat-π)	C3
9a_014	4.3414	Skew Boat B	N'-O7; N'-IMID (cat-π)	-
9a_015	4.3557	Skew Boat B	N'-O7; N'-IMID (cat-π)	-
9a_016	4.4909	Chair A	N'-O7; N'-IMID (cat-π)	C3
9a_017	4.5195	Chair A	N'-O7; N'-IMID (cat-π)	-
9a_018	4.5953	Chair A	N'-O7; N'-IMID (cat-π)	C3
9a_019	4.7757	Skew Boat B	N'-O7; N'-IMID (cat-π)	C3

[a]Putative partners for a "through space" intramolecular radical shift from O1 or O2 (≤ 3 Å; *i.e.* amine nitrogen (N') and C3 alkyl chain).

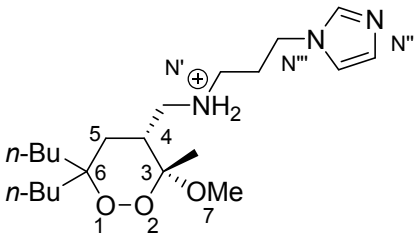
Table 4SI. PM7 conformers within 5 kcal mol^{-1} from the global minimum of **9a** di-protonated form.



Cnf	ΔE	1,2-dioxane ring conformation	Intramolecular interactions	H-shift[a]
9a_001	0	Skew Boat B	N'-O1; N'-O7;	N'
9a_002	0.340	Skew Boat B	N'-O1; N'-O7;	N', C3
9a_003	0.354	Skew Boat B	N'-O1; N'-O7;	N', C3
9a_004	0.471	Skew Boat B	N'-O1; N'-O7;	N', C3
9a_005	2.319	Skew Boat B	N'-O1; N'-O7;	N', C3
9a_006	2.365	Skew Boat B	N'-O7	-
9a_007	3.395	Skew Boat B	N'-O1; N'-O7;	N'
9a_008	3.717	Skew Boat B	N'-O7	C3
9a_009	3.76	Skew Boat B	N'-O1; N'-O7;	N', C3
9a_010	4.512	Chair A	N'-O7	C3
9a_011	4.894	Chair A	N'-O7	C3
9a_012	4.939	Skew Boat B	N'-O7	-

[a]Putative partners for a "through space" intramolecular radical shift from O1 or O2 (≤ 3 Å; *i.e.* amine nitrogen (N') and C3 alkyl chain).

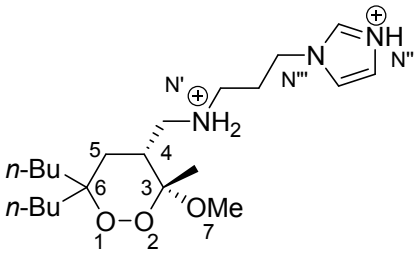
Table 5SI. PM7 conformers within 5 kcal mol^{-1} from the global minimum of **9b** protonated form.



Cnf	ΔE	1,2-dioxane ring conformation	Intramolecular interactions	H-shift[a]
9b_001	0	Skew Boat B	N'-O1; N'-IMID (cat-π)	N', C6
9b_002	0.62518	Skew Boat B	N'-O1; N'-IMID (cat-π)	N', C6
9b_003	1.89011	Skew Boat B	N'-O1; N'-O7; N'-IMID (cat-π)	N', C6
9b_004	1.97564	Skew Boat B	N'-O1; N'-O7;N'-IMID (cat-π)	N', C6
9b_005	4.37518	Skew Boat B	N'-O1; N'-O7;N'-IMID (cat-π)	N', C6
9b_006	4.63141	Chair A	N'-O7; N'-IMID (cat-π)	C6

[a]Putative partners for a "through space" intramolecular radical shift from O1 or O2 (≤ 3 Å; *i.e.* amine nitrogen (N') and C6 alkyl chain(s)).

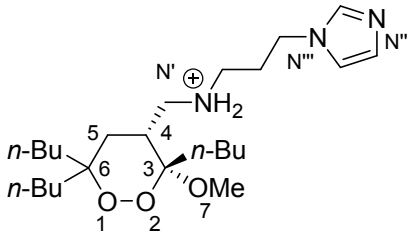
Table 6SI. PM7 conformers within 5 kcal mol^{-1} from the global minimum of **9b** di-protonated form.



Cnf	ΔE	1,2-dioxane ring conformation	Intramolecular interactions	H-shift[a]
9b_001	0	Skew Boat B	N'-O1; N'-O7	N', C6
9b_002	2.3397	Skew Boat B	N'-O1; N'-O7	N', C6

[a]Putative partners for a "through space" intramolecular radical shift from O1 or O2 (≤ 3 Å; *i.e.* amine nitrogen (N') and C6 alkyl chain(s)).

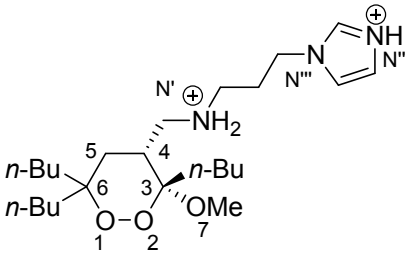
Table 7SI. PM7 conformers within 5 kcal mol^{-1} from the global minimum of **9c** protonated form.



Cnf	ΔE	1,2-dioxane ring conformation	Intramolecular interactions	H-shift[a]
9c_001	0	Skew Boat B	N'-O1; N'-O7	N', C3, C6
9c_002	1.62172	Skew Boat B	N'-O1; N'-IMID (cat-π)	N', C6
9c_003	4.74081	Skew Boat B	N'-O1; N'-IMID (cat-π)	N', C6
9c_004	4.75471	Skew Boat B	N'-O1; N'-O7	N', C3, C6
9c_005	4.95111	Skew Boat B	N'-O1; N'-O7	N', C6

[a]Putative partners for a "through space" intramolecular radical shift from O1 or O2 (≤ 3 Å; *i.e.* amine nitrogen (N') and C3 or C6 alkyl chain(s)).

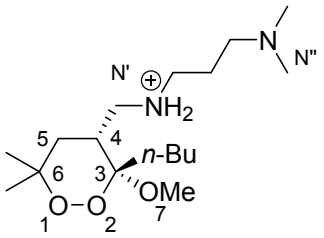
Table 8SI. PM7 conformers within 5 kcal mol^{-1} from the global minimum of **9c** di-protonated form.



Cnf	ΔE	1,2-dioxane ring conformation	Intramolecular interactions	H-shift[a]
9c_001	0	Skew Boat B	N'-O1; N'-O7	N', C3, C6
9c_002	0.49355	Skew Boat B	N'-O1; N'-O7	N', C6
9c_003	2.16355	Skew Boat B	N'-O1; N'-O7	N', C6
9c_004	2.45555	Skew Boat B	N'-O1; N'-O7	N', C3, C6
9c_005	2.80055	Skew Boat B	N'-O1; N'-O7	N'
9c_006	4.14755	Skew Boat B	N'-O1; N'-O7	N'
9c_007	4.73455	Skew Boat B	N'-O1	N', C3, C6

[a]Putative partners for a "through space" intramolecular radical shift from O1 or O2 (≤ 3 Å; *i.e.* amine nitrogen (N') and C3 or C6 alkyl chain(s)).

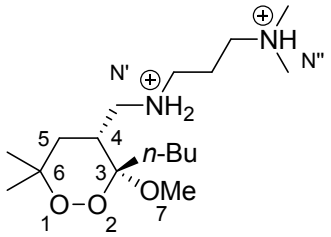
Table 9SI. PM7 conformers within 5 kcal mol^{-1} from the global minimum of **9d** protonated form.



Cnf	ΔE	1,2-dioxane ring conformation	Intramolecular interactions	H-shift[a]
9d_001	0	Skew BoatB	N'-O1; N'-N''	N', C3
9d_002	0.08702	Skew BoatB	N'-O1; N'-N''	N', C3
9d_003	0.31069	Skew BoatB	N'-O1; N'-O7; N'-N''	N'
9d_004	1.29656	Chair A	N'-O7; N'-N''	-
9d_005	1.51038	Chair A	N'-O7; N'-N''	C3
9d_006	1.59382	Chair A	N'-O7; N'-N''	-
9d_007	2.00094	Skew Boat B	N'-O7; N'-N''	-
9d_008	2.1994	Chair A	N'-O7; N'-N''	C3
9d_009	2.2606	Chair A	N'-O7; N'-N''	C3
9d_010	2.30568	Skew Boat B	N'-O7; N'-N''	C3
9d_011	2.31513	Chair A	N'-O7; N'-N''	C3
9d_012	2.58078	Chair A	N'-O7; N'-N''	C3
9d_013	2.97134	Chair A	N'-O7; N'-N''	-
9d_014	3.09399	Chair A	N'-O7; N'-N''	C3
9d_015	3.3254	Chair A	N'-O7; N'-N''	-
9d_016	3.45957	Chair A	N'-O7; N'-N''	C3
9d_017	3.83284	Chair A	N'-O7; N'-N''	C3
9d_018	4.27183	Skew Boat B	N'-O7; N'-N''	C3
9d_019	4.35059	Chair A	N'-O7; N'-N''	-
9d_020	4.51544	Skew Boat B	N'-O7; N'-N''	C3

[a]Putative partners for a "through space" intramolecular radical shift from O1 or O2 (≤ 3 Å; *i.e.* amine nitrogen (N') and C3 alkyl chain).

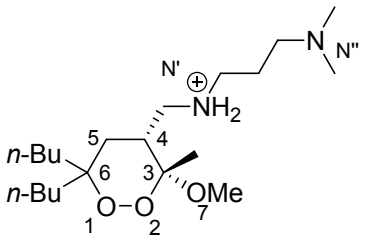
Table 10SI. PM7 conformers within 5 kcal mol^{-1} from the global minimum of **9d** di-protonated form.



Cnf	ΔE	1,2-dioxane ring conformation	Intramolecular interactions	H-shift[a]
9d_001	0	Skew Boat B	N'-O1; N''-O7	N', C3
9d_002	0.23591	Skew Boat B	N'-O1; N''-O7	N', C3

[a]Putative partners for a "through space" intramolecular radical shift from O1 or O2 (≤ 3 Å; *i.e.* amine nitrogen (N') and C3 alkyl chain).

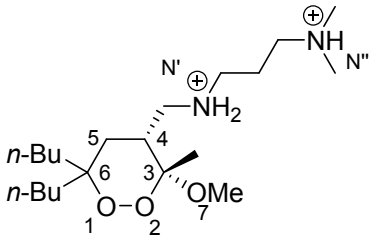
Table 11SI. PM7 conformers within 5 kcal mol^{-1} from the global minimum of **9e** protonated form.



Cnf	ΔE	1,2-dioxane ring conformation	Intramolecular interactions	H-shift[a]
9e_001	0	Skew Boat B	N'-O1; N'-N''	N', C6
9e_002	1.18442	Skew Boat B	N'-O1; N'-N''	N', C6
9e_003	3.26327	Chair A	N'-O7; N'-N''	C6
9e_004	3.30462	Chair A	N'-O7; N'-N''	C6
9e_005	3.71147	Chair A	N'-O7; N'-N''	C6
9e_006	4.23654	Chair A	N'-O7; N'-N''	C6
9e_007	4.86989	Chair A	N'-O7; N'-N''	C6

[a]Putative partners for a "through space" intramolecular radical shift from O1 or O2 (≤ 3 Å; *i.e.* amine nitrogen (N') and C6 alkyl chain(s)).

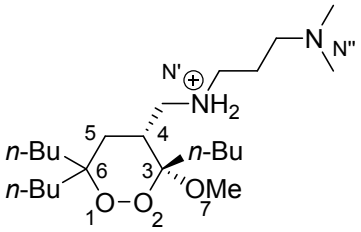
Table 12SI. PM7 conformers within 5 kcal mol^{-1} from the global minimum of **9e** di-protonated form.



Cnf	ΔE	1,2-dioxane ring conformation	Intramolecular interactions	H-shift[a]
9e_001	0	Skew Boat B	N'-O1; N''-O7	N', C6
9e_002	1.37128	Skew Boat B	N'-O1; N''-O7	N', C6
9e_003	3.71528	Skew Boat B	N'-O1; N'-O7	N', C6
9e_004	4.42928	Skew Boat B	N'-O7; N''-O7	-
9e_005	4.94928	Skew Boat B	N'-O7; N''-O7	N', C6

[a]Putative partners for a "through space" intramolecular radical shift from O1 or O2 (≤ 3 Å; *i.e.* amine nitrogen (N') and C6 alkyl chain(s)).

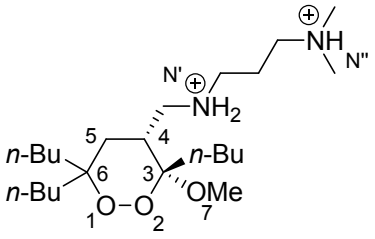
Table 13SI. PM7 conformers within 5 kcal mol^{-1} from the global minimum of **9f** protonated form.



Cnf	ΔE	1,2-dioxane ring conformation	Intramolecular interactions	H-shift[a]
9f_001	0	Skew Boat B	N'-O1; N'-N''	N', C3, C6
9f_002	1.85195	Chair A	N'-O7; N'-N''	C3, C6
9f_003	2.43713	Skew Boat B	N'-O1; N'-N''	N', C3, C6
9f_004	2.84788	Chair A	N'-O7; N'-N''	C3, C6
9f_005	4.00041	Chair A	N'-O7; N'-N''	C3
9f_006	4.12054	Chair A	N'-O7; N'-N''	C3, C6
9f_007	4.36199	Chair A	N'-O7; N'-N''	C3, C6
9f_008	4.57456	Chair A	N'-O7; N'-N''	C3, C6
9f_009	4.95301	Chair A	N'-O7; N'-N''	C3, C6

[a]Putative partners for a "through space" intramolecular radical shift from O1 or O2 (≤ 3 Å; *i.e.* amine nitrogen (N') and C3 or C6 alkyl chain(s)).

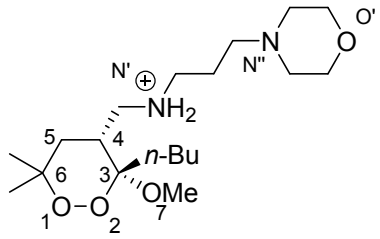
Table 14SI. PM7 conformers within 5 kcal mol-1 from the global minimum of **9f** di-protonated form.



Cnf	ΔE	1,2-dioxane ring conformation	Intramolecular interactions	H-shift[a]
9f_001	0	Skew Boat B	N'-O1; N''-O7	N', C3 , C6
9f_002	0.51721	Skew Boat B	N'-O1; N''-O7	N', C3 , C6
9f_003	1.02301	Skew Boat B	N'-O1; N''-O7	N', C3 , C6
9f_004	4.47601	Skew Boat B	N'-O1; N'-O7	N', C3 , C6
9f_005	4.83371	Skew Boat B	N'-O7	C6

[a]Putative partners for a "through space" intramolecular radical shift from O1 or O2 (≤ 3 Å; *i.e.* amine nitrogen (N') and C3 or C6 alkyl chain(s)).

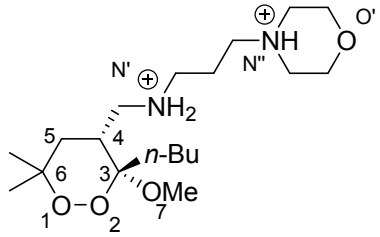
Table 15SI. PM7 conformers within 5 kcal mol-1 from the global minimum of **9g** protonated form.



Cnf	ΔE	1,2-dioxane ring conformation	Intramolecular interactions	H-shift[a]
9g_001	0	Skew Boat B	N'-O7; N'-O'; N'-N''	C3
9g_002	0.2116	Chair A	N'-O7; N'-N''	C3
9g_003	0.3882	Chair A	N'-O7; N'-N''	C3
9g_004	0.84045	Chair A	N'-O7; N'-N''	-
9g_005	0.85292	Skew Boat B	N'-O1; N'-N''	N', C3
9g_006	1.0702	Skew Boat B	N'-O7; N'-N''	-
9g_007	1.0843	Chair A	N'-O7; N'-N''	C3
9g_008	1.0843	Chair A	N'-O7; N'-N''	C3
9g_009	1.1683	Chair A	N'-O7; N'-N''	C3
9g_010	1.3192	Skew Boat B	N'-O7; N'-N''	-
9g_011	1.4997	Chair A	N'-O7; N'-O'; N'-N''	C3
9g_012	1.694	Skew Boat B	N'-O7; N'-N''	-
9g_013	1.775	Chair A	N'-O7; N'-N''	C3
9g_014	1.778	Chair A	N'-O7; N'-O'; N'-N''	C3
9g_015	1.9685	Chair A	N'-O7; N'-N''	C3
9g_016	2.007	Skew Boat B	N'-O1; N'-N''	N', C3
9g_017	2.8524	Skew Boat B	N'-O7; N'-N''	-
9g_018	2.8524	Skew Boat B	N'-O7; N'-N''	-
9g_019	3.0808	Skew Boat B	N'-O7; N'-O'; N'-N''	C3
9g_020	3.4106	Skew Boat B	N'-O1; N'-O7; N'-N''	N', C3
9g_021	3.4802	Skew Boat B	N'-O7; N'-N''	-
9g_022	3.5235	Skew Boat A	N'-O7; N'-O'; N'-N''	-
9g_023	3.5825	Chair A	N'-O7; N'-O'; N'-N''	C3
9g_024	3.8389	Chair A	N'-O'; N'-N''	C3
9g_025	4.1697	Skew Boat A	N'-O7; N'-O'; N'-N''	C3
9g_026	4.2985	Skew Boat B	N'-O7; N'-O'; N'-N''	C3
9g_027	4.3793	Chair A	N'-O'; N'-N''	C3

[a]Putative partners for a "through space" intramolecular radical shift from O1 or O2 (≤ 3 Å; *i.e.* amine nitrogen (N') and C3 alkyl chain).

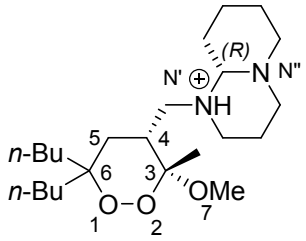
Table 16SI. PM7 conformers within 5 kcal mol-1 from the global minimum of **9g** di-protonated form.



Cnf	ΔE	1,2-dioxane ring conformation	Intramolecular interactions	H-shift[a]
9g_001	0	Skew Boat B	N'-O1; N''-O7	N', C3
9g_002	0.28722	Skew Boat B	N'-O1; N''-O7	N', C3

[a]Putative partners for a "through space" intramolecular radical shift from O1 or O2 (≤ 3 Å; *i.e.* amine nitrogen (N') and C3 alkyl chain).

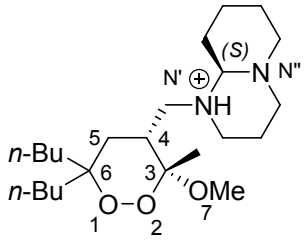
Table 17SI. PM7 conformers within 5 kcal mol^{-1} from the global minimum of **9h** diastereomer characterized by (*R*)-configured stereocenter on the side-chain.



Cnf	ΔE	1,2-dioxane ring conformation	Intramolecular interactions	H-shift[a]
9h_R_001	0	Skew Boat B	N'-O7; N'-N''	C6
9h_R_002	0.84698	Skew Boat B	N'-O7; N'-N''	C6
9h_R_003	2.21771	Chair A	N'-O7; N'-N''	C6
9h_R_004	2.85726	Skew Boat B	N'-O7	C6
9h_R_005	3.40775	Skew Boat B	N'-O7; N'-N''	C6
9h_R_006	3.73302	Skew Boat B	N'-O7	C6
9h_R_007	3.91828	Skew Boat B	N'-O7	C6
9h_R_008	3.93578	Skew Boat B	N'-O7	C6
9h_R_009	4.31695	Skew Boat B	N'-O7	C6
9h_R_010	4.50223	Skew Boat B	N'-O1; N'-N''	N', C6
9h_R_011	4.74022	Skew Boat A	N'-O7; N'-N''	-

[a]Putative partners for a "through space" intramolecular radical shift from O1 or O2 (≤ 3 Å; *i.e.* amine nitrogen (N') and C6 alkyl chain(s)).

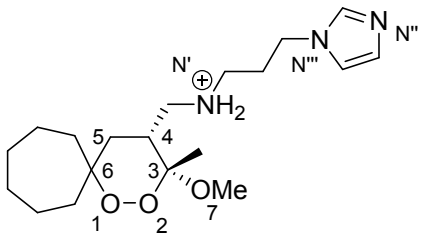
Table 18SI. PM7 conformers within 5 kcal mol^{-1} from the global minimum of **9h** diastereomer characterized by (*S*)-configured stereocenter on the side-chain.



Cnf	ΔE	1,2-dioxane ring conformation	Intramolecular interactions	H-shift[a]
9h_S_001	0	Chair A	N'-O7	C6
9h_S_002	1.26352	Chair A	N'-O7	C6
9h_S_003	2.05469	Chair B	N'-O7	C6
9h_S_004	2.05629	Skew Boat B	N'-O7; N'-N''	C6
9h_S_005	2.10045	Skew Boat B	N'-O7; N'-N''	C6
9h_S_006	2.96992	Skew Boat B	N'-O7; N'-N''	C6
9h_S_007	2.98875	Skew Boat B	N'-O7; N'-N''	C6
9h_S_008	3.41519	Chair A	N'-O7	C6
9h_S_009	3.43039	Skew Boat B	N'-O7; N'-N''	C6
9h_S_010	3.93215	Skew Boat B	N'-O1	N', C6
9h_S_011	3.94311	Skew Boat B	N'-O7; N'-N''	C6
9h_S_012	4.16923	Skew Boat B	N'-O7; N'-N''	C6
9h_S_013	4.17988	Skew Boat B	N'-O7; N'-N''	C6
9h_S_014	4.2843	Skew Boat B	N'-O7; N'-N''	C6
9h_S_015	4.45925	Skew Boat B	N'-O7; N'-N''	C6
9h_S_016	4.69094	Chair A	N'-O7; N'-N''	-
9h_S_017	4.99081	Skew Boat B	N'-O7	C6

[a]Putative partners for a "through space" intramolecular radical shift from O1 or O2 (≤ 3 Å; *i.e.* amine nitrogen (N') and C6 alkyl chain(s)).

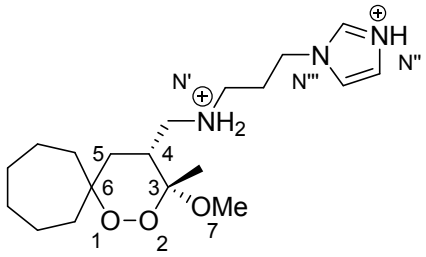
Table 19SI. PM7 conformers within 5 kcal mol^{-1} from the global minimum of **9i** protonated form.



Cnf	ΔE	1,2-dioxane ring conformation	Intramolecular interactions	H-shift[a]
9i_001	0	Chair A	N'-O7; N'-IMID (cat-π)	C6
9i_002	0.9783	Chair A	N'-O7; N'-IMID (cat-π)	C6
9i_003	1.2881	Chair A	N'-O7; N'-IMID (cat-π)	C6
9i_004	1.7616	Skew Boat B	N'-O7; N'-O1	N', C6
9i_005	1.8290	Skew Boat B	N'-O1; N'-IMID (cat-π)	N', C6
9i_006	1.9222	Chair A	N'-O7; N'-IMID (cat-π)	C6
9i_007	3.1157	Chair A	N'-O7; N'-IMID (cat-π)	C6
9i_008	3.1822	Skew Boat B	N'-O7; N'-IMID (cat-π)	C6
9i_009	3.1822	Skew Boat B	N'-O7; N'-IMID (cat-π)	C6
9i_010	3.2704	Chair A	N'-O7; N'-IMID (cat-π)	C6
9i_011	3.4762	Chair A	N'-O7; N'-IMID (cat-π)	-
9i_012	3.9009	Skew Boat B	N'-O7; N'-IMID (cat-π)	C6
9i_013	4.1282	Chair A	N'-O7; N'-IMID (cat-π)	-
9i_014	4.3837	Chair A	N'-O7; N'-IMID (cat-π)	-
9i_015	4.586	Chair A	N'-O7; N'-IMID (cat-π)	-
9i_016	4.586	Chair A	N'-O7; N'-IMID (cat-π)	-
9i_017	4.6976	Chair B	N'-O7; N'-O2; N'-IMID (cat-π)	N', C6
9i_018	4.8139	Skew Boat B	N'-O7; N'-IMID (cat-π)	C6
9i_019	4.9612	Chair A	N'-O7	C6

[a]Putative partners for a "through space" intramolecular radical shift from O1 or O2 (≤ 3 Å; *i.e.* amine nitrogen (N') and C6 alkyl chain(s)).

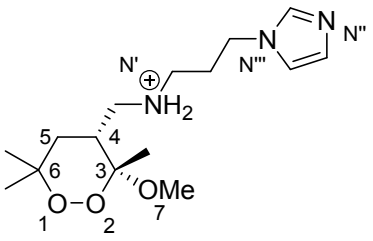
Table 20SI. PM7 conformers within 5 kcal mol^{-1} from the global minimum of **9i** di-protonated form.



Cnf	ΔE	1,2-dioxane ring conformation	Intramolecular interactions	H-shift[a]
9i_001	0	Skew Boat B	N'-O1; N'-O7	N', C6
9i_002	0.166	Skew Boat B	N'-O1; N'-O7	N', C6
9i_003	0.78	Skew Boat B	N'-O1; N'-O7	N', C6
9i_004	0.823	Skew Boat B	N'-O1; N'-O7	N', C6
9i_005	1.001	Skew Boat B	N'-O1; N'-O7	N', C6
9i_006	1.611	Skew Boat B	N'-O1; N'-O7	N', C6
9i_007	1.874	Skew Boat B	N'-O1; N'-O7	N'

[a]Putative partners for a "through space" intramolecular radical shift from O1 or O2 (≤ 3 Å; *i.e.* amine nitrogen (N') and C6 alkyl chain(s)).

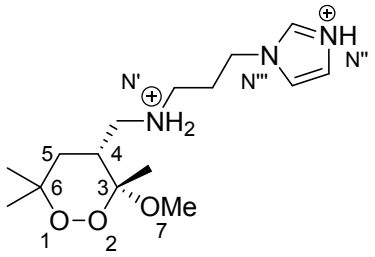
Table 21SI. PM7 conformers within 5 kcal mol^{-1} from the global minimum of **9j** protonated form.



Cnf	ΔE	1,2-dioxane ring conformation	Intramolecular interactions	H-shift[a]
9j_001	0	Skew Boat B	N'-O1; N'-O7; N'-IMID (cat-π)	N'
9j_002	0.00003	Skew Boat B	N'-O1; N'-O7; N'-IMID (cat-π)	N'
9j_003	0.3328	Skew Boat B	N'-O1; N'-O7; N'-IMID (cat-π)	N'
9j_004	0.90164	Chair A	N'-O7; N'-IMID (cat-π)	-
9j_005	1.99161	Chair A	N'-O7; N'-IMID (cat-π)	-
9j_006	1.99164	Chair A	N'-O7; N'-IMID (cat-π)	-
9j_007	1.99196	Chair A	N'-O7; N'-IMID (cat-π)	-
9j_008	2.26023	Chair A	N'-O7; N'-IMID (cat-π)	-
9j_009	2.90036	Skew Boat B	N'-O7; N'-IMID (cat-π)	-
9j_010	2.90036	Skew Boat B	N'-O7; N'-IMID (cat-π)	-
9j_011	2.90036	Skew Boat B	N'-O7; N'-IMID (cat-π)	-
9j_012	3.05464	Chair A	N'-O7; N'-IMID (cat-π)	-
9j_013	3.13459	Skew Boat B	N'-O7; N'-IMID (cat-π)	-
9j_014	3.18739	Chair A	N'-O7; N'-IMID (cat-π)	-
9j_015	3.43661	Skew Boat B	N'-O7; N'-IMID (cat-π)	-
9j_016	4.37751	Skew Boat B	N'-O7; N'-IMID (cat-π)	-
9j_017	4.83828	Skew Boat B	N'-O7; N'-IMID (cat-π)	-

[a]Putative partners for a "through space" intramolecular radical shift from O1 or O2 (≤ 3 Å; *i.e.* amine nitrogen (N')).

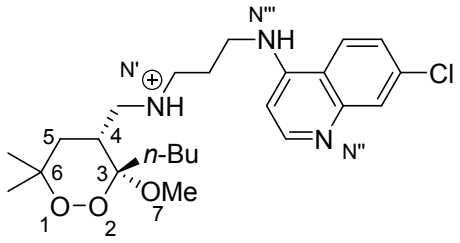
Table 22SI. PM7 conformers within 5 kcal mol^{-1} from the global minimum of **9j** di-protonated form.



Cnf	ΔE	1,2-dioxane ring conformation	Intramolecular interactions	H-shift[a]
9j_001	0	Skew Boat B	N'-O1; N'-O7	N'
9j_002	0	Skew Boat B	N'-O1; N'-O7	N'
9j_003	0.06664	Skew Boat B	N'-O1; N'-O7	N'
9j_004	1.988	Skew Boat B	N'-O1; N'-O7	N'
9j_005	2.88347	Skew Boat B	N'-O7	-
9j_006	2.88353	Skew Boat B	N'-O7	-
9j_007	2.88355	Skew Boat B	N'-O7	-
9j_008	3.47998	Skew Boat B	N'-O7	-
9j_009	3.48	Skew Boat B	N'-O7	-

[a]Putative partners for a "through space" intramolecular radical shift from O1 or O2 (≤ 3 Å; *i.e.* amine nitrogen (N')).

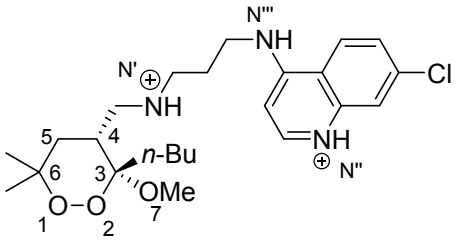
Table 23SI. PM7 conformers within 5 kcal mol^{-1} from the global minimum of **9k** protonated form.



Cnf	ΔE	1,2-dioxane ring conformation	Intramolecular interactions	H-shift[a]
9k_001	0	Skew Boat B	N'-O1; N'-O7; N'-N'''	N'
9k_002	1.31217	Chair A	N'-O7; N'-N'''	C3
9k_003	1.70707	Chair A	N'-O7; N'-N'''	-
9k_004	1.87956	Skew Boat B	N'-O7; N'-N'''	C3
9k_005	2.18244	Skew Boat B	N'-O7; N'-N'''	C3
9k_006	2.28255	Skew Boat B	N'-O7; N'-N'''	C3
9k_007	2.48338	Skew Boat B	N'-O1; N'-O7; N'-N'''	N', C3
9k_008	2.56506	Chair A	N'-O7; N'-N'''	-
9k_009	2.58526	Chair A	N'-O7; N'-N'''	C3
9k_010	2.71551	Chair A	N'-O7; N'-N'''	C3
9k_011	2.79428	Chair B	N'-O7; N'-N'''	-
9k_012	2.82351	Chair A	N'-O7; N'-N'''	C3
9k_013	2.89685	Skew Boat B	N'-O1; N'-N'''	N', C3
9k_014	3.43495	Chair A	N'-O7; N'-N'''	C3
9k_015	3.44424	Skew Boat B	N'-O7; N'-N'''	C3
9k_016	3.53674	Skew Boat B	N'-O1; N'-O7; N'-N'''	N', C3
9k_017	3.60823	Skew Boat B	N'-O7; N'-N'''	C3
9k_018	3.64853	Skew Boat B	N'-O7; N'-N'''	C3
9k_019	3.65937	Chair B	N'-O2; N'-O7; N'-N'''	N', C3
9k_020	3.78698	Chair A	N'-O7; N'-N'''	C3
9k_021	4.18539	Chair A	N'-O7; N'-N'''	-
9k_022	4.26164	Skew Boat B	N'-O7; N'-N'''	C3
9k_023	4.27064	Chair A	N'-O7; N'-N'''	-
9k_024	4.36193	Chair A	N'-O7; N'-N'''	-
9k_025	4.37127	Skew Boat A	N'-O7; N'-N'''	C3
9k_026	4.62724	Chair A	N'-O7; N'-N'''	-
9k_027	4.71695	Skew Boat B	N'-O7; N'-N'''	C3
9k_028	4.78915	Skew Boat A	N'-O7; N'-N'''	C3
9k_029	4.79564	Chair B	N'-O2; N'-O7; N'-N'''	-
9k_030	4.83182	Chair B	N'-O2; N'-O7; N'-N'''	N', C3
9k_031	4.83182	Chair B	N'-O2; N'-O7; N'-N'''	N', C3
9k_032	4.87345	Skew Boat A	N'-O7; N'-N'''	C3
9k_033	4.92585	Skew Boat A	N'-O7; N'-N'''	-

[a]Putative partners for a "through space" intramolecular radical shift from O1 or O2 (≤ 3 Å; *i.e.* amine nitrogen (N') and C3 alkyl chain).

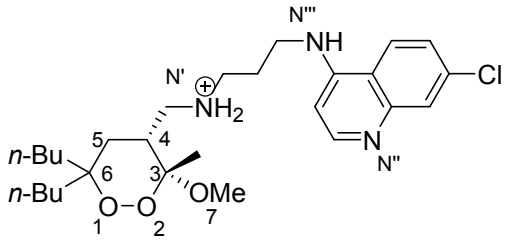
Table 24SI. PM7 conformers within 5 kcal mol^{-1} from the global minimum of **9k** di-protonated form.



Cnf	ΔE	1,2-dioxane ring conformation	Intramolecular interactions	H-shift[a]
9k_001	0	Skew Boat B	N'-O1; N'-N'''; N'''-O1; N'''-O2; N'''-O7	N'
9k_002	3.03625	Skew Boat B	N'-O7; N'''-O1; N'''-O2; N'''-O7	-
9k_003	4.95597	Chair A	N'-O7; N'''-O7	C3
9k_004	4.95872	Chair A	N'-O1; N'-O7	C3

[a]Putative partners for a "through space" intramolecular radical shift from O1 or O2 (≤ 3 Å; *i.e.* amine nitrogen (N') and C3 alkyl chain).

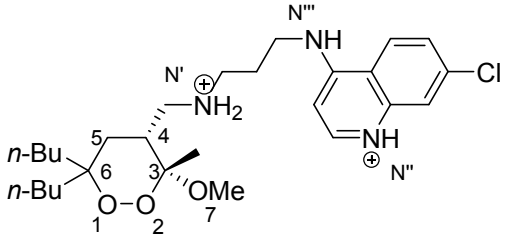
Table 25SI. PM7 conformers within 5 kcal mol^{-1} from the global minimum of **9l** protonated form.



Cnf	ΔE	1,2-dioxane ring conformation	Intramolecular interactions	H-shift[a]
9l_001	0	Skew Boat B	N'-O1; N'-N'''	N', C6
9l_002	0.80406	Skew Boat B	N'-O1; N'-N'''	N', C6
9l_003	2.6654	Chair A	N'-O7; N'-N'''	-
9l_004	3.04073	Chair A	N'-O7; N'-N'''	-
9l_005	3.71538	Skew Boat B	N'-O7; N'-N'''	C6
9l_006	3.90508	Chair A	N'-O7; N'-N'''	C6
9l_007	4.31964	Chair A	N'-O7; N'-N'''	-
9l_008	4.51176	Skew Boat A	N'-O7; N'-N'''	-
9l_009	4.56214	Chair A	N'-O7; N'-N'''	C6
9l_010	4.63751	Skew Boat A	N'-O7; N'-N'''	-

[a]Putative partners for a "through space" intramolecular radical shift from O1 or O2 (≤ 3 Å; *i.e.* amine nitrogen (N') and C6 alkyl chain(s)).

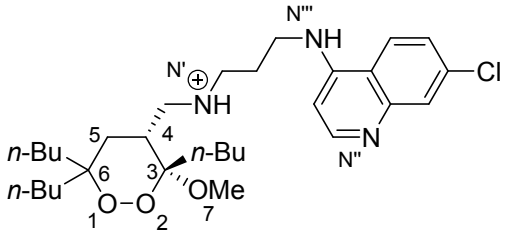
Table 26SI. PM7 conformers within 5 kcal mol^{-1} from the global minimum of **9l** di-protonated form.



Cnf	ΔE	1,2-dioxane ring conformation	Intramolecular interactions	H-shift[a]
9l_001	0	Skew Boat B	N'-O1; N'-N'''; N'''-O1; N'''-O2; N'''-O7	N', C6
9l_002	3.84718	Skew Boat B	N'-O7; N'''-O1; N'''-O2; N'''-O7	C6
9l_003	3.84718	Skew Boat B	N'-O7; N'''-O1; N'''-O2; N'''-O7	C6

[a]Putative partners for a "through space" intramolecular radical shift from O1 or O2 (≤ 3 Å; *i.e.* amine nitrogen (N') and C6 alkyl chain(s)).

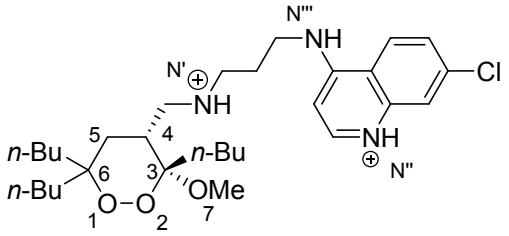
Table 27SI. PM7 conformers within 5 kcal mol^{-1} from the global minimum of **9m** protonated form.



Cnf	ΔE	1,2-dioxane ring conformation	Intramolecular interactions	H-shift[a]
9m_001	0	Skew Boat B	N'-O1; N'-N'''	N', C3, C6
9m_002	0.92417	Skew Boat B	N'-O1; N'-N'''	N', C3, C6
9m_003	1.61772	Chair B	N'-O1; N'-O7; N'-N'''	N', C3, C6
9m_004	3.80672	Skew Boat A	N'-O7; N'-N'''	C3, C6
9m_005	4.15564	Skew Boat A	N'-O7; N'-N'''	C3, C6
9m_006	4.72119	Chair A	N'-O7; N'-N'''	C3, C6
9m_007	4.96856	Chair A	N'-O7; N'-N'''	C3, C6

[a]Putative partners for a "through space" intramolecular radical shift from O1 or O2 (≤ 3 Å; *i.e.* amine nitrogen (N') and C3 or C6 alkyl chain(s)).

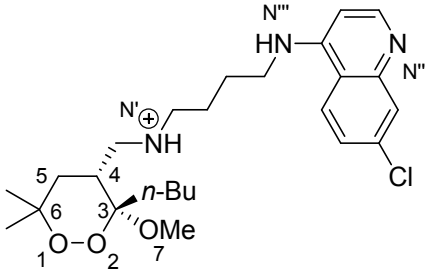
Table 28SI. PM7 conformers within 5 kcal mol^{-1} from the global minimum of **9m** di-protonated form.



Cnf	ΔE	1,2-dioxane ring conformation	Intramolecular interactions	H-shift[a]
9m_001	0	Skew Boat B	N'-O1; N'-N'''; N'''-O1; N'''-O2; N'''-O7	N', C6
9m_002	2.96876	Skew Boat B	N'-O7; N'''-O1; N'''-O2; N'''-O7	C6
9m_003	4.44829	Skew Boat B	N'-O1; N'-O7	N', C3, C6
9m_004	4.60592	Skew Boat B	N'-O7; N'''-O1; N'''-O2; N'''-O7	C3, C6

[a]Putative partners for a "through space" intramolecular radical shift from O1 or O2 (≤ 3 Å; *i.e.* amine nitrogen (N') and C3 or C6 alkyl chain(s)).

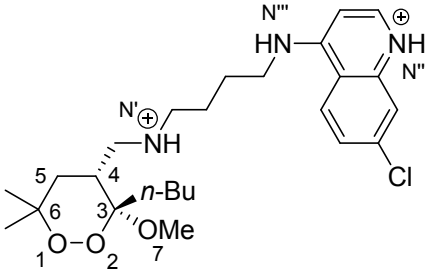
Table 29SI. PM7 conformers within 5 kcal mol^{-1} from the global minimum of **9n** protonated form.



Cnf	ΔE	1,2-dioxane ring conformation	Intramolecular interactions	H-shift[a]
9n_001	0	Skew Boat B	N'-O1; N'-O7; N'-N'''	N'
9n_002	0.28277	Skew Boat B	N'-O1; N'-O7; N'-N'''	N', C3
9n_003	0.74905	Chair A	N'-O7; N'-N'''	-
9n_004	0.90658	Chair A	N'-O7; N'-N'''	C3
9n_005	1.98877	Chair A	N'-O7; N'-N'''	C3
9n_006	2.15295	Chair B	N'-O7; N'-N'''	-
9n_007	2.32528	Chair A	N'-O7; N'-N'''	-
9n_08	2.40036	Chair A	N'-O7; N'-N''	C3
9n_09	2.75453	Skew Boat B	N'-O1; N'-O7	N'
9n_010	2.89621	Chair A	N'-O7; N'-N''	C3
9n_011	2.92254	Chair A	N'-O7; N'-N'''	-
9n_012	3.03778	Skew Boat A	N'-O7; N'-N'''	-
9n_013	3.2515	Skew Boat B	N'-O7	-
9n_014	3.26457	Chair A	N'-O7; N'-N'''	C3
9n_015	3.34474	Chair A	N'-O7; N'-N'''	-
9n_016	3.44486	Skew Boat A	N'-O7; N'-N'''	C3
9n_017	3.46663	Chair A	N'-O7	C3
9n_018	3.53071	Chair A	N'-O7; N'-N'''	-
9n_019	3.86941	Skew Boat A	N'-O7; N'-N'''	C3
9n_020	4.01321	Chair A	N'-N'''	C3
9n_021	4.12714	Chair A	N'-O7	-
9n_022	4.14181	Chair A	N'-O7; N'-N'''	C3
9n_023	4.14182	Chair A	N'-O7; N'-N'''	C3
9n_024	4.27832	Chair A	N'-N'''	C3
9n_025	4.34109	Skew Boat A	N'-O7; N'-N'''	-
9n_026	4.34806	Skew Boat A	N'-O7; N'-N'''	C3
9n_027	4.55981	Skew Boat A	N'-O7; N'-N'''	C3
9n_028	4.68717	Skew Boat B	N'-N'''	-
9n_029	4.85337	Chair B	N'-O7; N'-N'''	C3
9n_030	4.90891	Skew Boat B	N'-O7	C3

[a]Putative partners for a "through space" intramolecular radical shift from O1 or O2 (≤ 3 Å; *i.e.* amine nitrogen (N') and C3 alkyl chain).

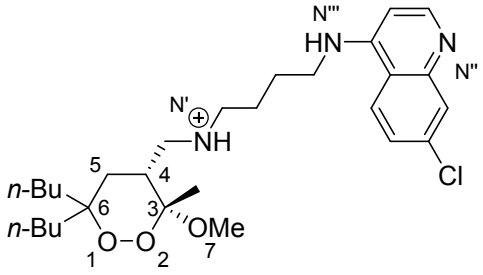
Table 30SI. PM7 conformers within 5 kcal mol^{-1} from the global minimum of **9n** di-protonated form.



Cnf	ΔE	1,2-dioxane ring conformation	Intramolecular interactions	H-shift[a]
9n_001	0	Skew Boat B	N'-O7; N'''-O1; N'''-O2; N'''-O7	-
9n_002	2.25218	Chair A	N'-O7; N'''-O7	C3
9n_003	3.28288	Skew Boat B	N'-O1; N'-O7	N', C3
9n_004	3.91965	Skew Boat B	N'-O7; N'''-O1	C3
9n_005	4.12757	Chair A	N'-O7; N'''-O7	C3
9n_006	4.54611	Chair B	N'-O7; N'''-O2	-

[a]Putative partners for a "through space" intramolecular radical shift from O1 or O2 (≤ 3 Å; *i.e.* amine nitrogen (N') and C3 alkyl chain).

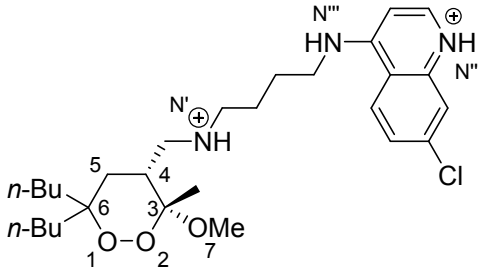
Table 31SI. PM7 conformers within 5 kcal mol^{-1} from the global minimum of **9o** protonated form.



Cnf	ΔE	1,2-dioxane ring conformation	Intramolecular interactions	H-shift[a]
9o_001	0	Skew Boat B	N'-O1; N'-N'''	N'; C6
9o_002	2.57719	Skew Boat A	N'-O7; N'-N'''	C6
9o_003	3.28876	Chair A	N'-O7; N'-N'''	C6
9o_004	3.59017	Skew Boat B	N'-O7; N'-N'''	C6
9o_005	3.78403	Skew Boat B	N'-O1; N'-O7; N'-N'''	N', C6
9o_006	3.86242	Skew Boat B	N'-O7; N'-N'''	C6
9o_007	4.74913	Skew Boat B	N'-O7	C6
9o_008	4.95156	Chair A	N'-O7; N'-N'''	C6

[a]Putative partners for a "through space" intramolecular radical shift from O1 or O2 (≤ 3 Å; *i.e.* amine nitrogen (N') and C6 alkyl chain(s)).

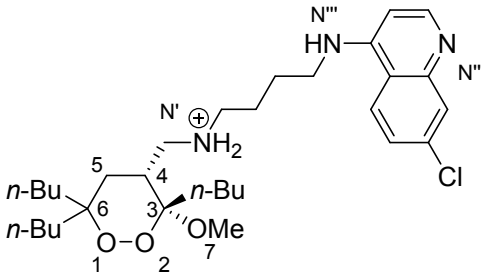
Table 32SI. PM7 conformers within 5 kcal mol^{-1} from the global minimum of **9o** di-protonated form.



Cnf	ΔE	1,2-dioxane ring conformation	Intramolecular interactions	H-shift[a]
9o_001	0	Skew Boat B	N'-O7; N'''-O1; N'''-O2; N'''-O7	-
9o_002	2.47221	Chair B	N'-O7; N'''-O2; N'''-O7	C6
9o_003	2.64306	Chair B	N'-O7; N'''-O2	C6
9o_004	4.88133	Skew Boat B	N'-O7; N'''-O1; N'''-O7	C6

[a]Putative partners for a "through space" intramolecular radical shift from O1 or O2 (≤ 3 Å; *i.e.* C6 alkyl chain(s)).

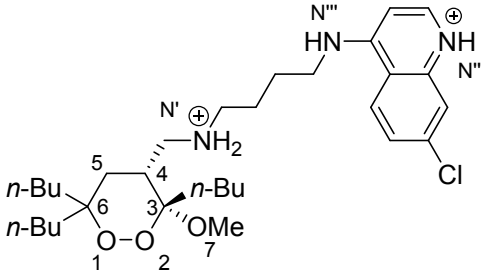
Table 33SI. PM7 conformers within 5 kcal mol^{-1} from the global minimum of **9p** protonated form.



Cnf	ΔE	1,2-dioxane ring conformation	Intramolecular interactions	H-shift[a]
9p_001	0	Skew Boat B	N'-O1; N'-N'''	N', C3, C6
9p_002	2.35263	Chair A	N'-O7; N'-N'''	C3, C6
9p_003	4.13439	Skew Boat B	N'-O7; N'-N'''	C3
9p_004	4.31063	Skew Boat B	N'-O7; N'-N'''	C3, C6

[a]Putative partners for a "through space" intramolecular radical shift from O1 or O2 (≤ 3 Å; *i.e.* amine nitrogen (N') and C3 or C6 alkyl chain(s)).

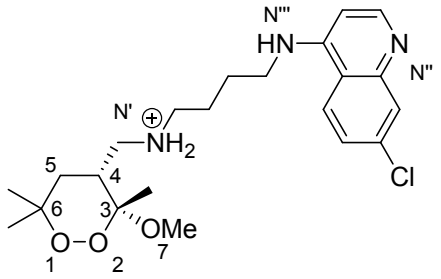
Table 34SI. PM7 conformers within 5 kcal mol^{-1} from the global minimum of **9p** di-protonated form.



Cnf	ΔE	1,2-dioxane ring conformation	Intramolecular interactions	H-shift[a]
9p_001	0	Skew Boat B	N'-O7; N'''-O1; N'''-O2; N'''-O7	-

[a]Putative partners for a "through space" intramolecular radical shift from O1 or O2 (≤ 3 Å).

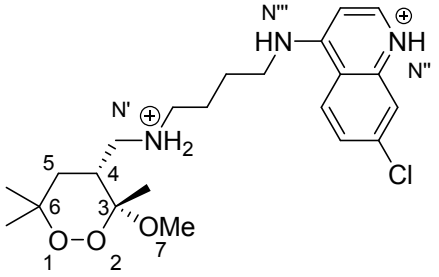
Table 35SI. PM7 conformers within 5 kcal mol^{-1} from the global minimum of **9q** protonated form.



Cnf	ΔE	1,2-dioxane ring conformation	Intramolecular interactions	H-shift[a]
9q_001	0	Skew Boat B	N'-O1; N'-N'''	N'
9q_002	0.48893	Skew Boat B	N'-O7; N'-N'''	-
9q_003	0.48893	Skew Boat B	N'-O7; N'-N'''	-
9q_004	1.75392	Chair A	N'-O7; N'-N'''	-
9q_005	1.8727	Chair A	N'-O7; N'-N'''	-
9q_006	2.18248	Skew Boat B	N'-O1; N'-O7	N'
9q_007	2.4224	Skew Boat B	N'-O7; N'-N''	-
9q_008	2.4224	Skew Boat B	N'-O7; N'-N''	-
9q_009	2.65543	Skew Boat B	N'-O7; N'-N'''	-
9q_010	2.65543	Skew Boat B	N'-O7; N'-N'''	-
9q_011	2.8506	Skew Boat A	N'-O7 N'-N'''	-
9q_012	3.15456	Skew Boat B	N'-O7; N'-N'''	-
9q_013	3.35279	Chair A	N'-O7; N'-N''	-
9q_014	3.5134	Skew Boat B	N'-O1; N'-O7	N'
9q_015	3.53631	Chair B	N'-O7; N'-N'''	-
9q_016	3.60151	Chair A	N'-O7; N'-N'''	-
9q_017	3.60724	Chair A	N'-O7; N'-N'''	-
9q_018	3.62951	Chair A	N'-O7; N'-N'''	-
9q_019	3.88029	Chair A	N'-O7	-
9q_020	3.9104	Chair A	N'-O7	-
9q_021	3.91115	Chair A	N'-O7	-
9q_022	3.91115	Chair A	N'-O7	-
9q_023	4.42857	Skew Boat A	N'-O7; N'-N'''	-
9q_024	4.65552	Chair A	N'-O7; N'-N'''	-
9q_025	4.65552	Chair A	N'-O7; N'-N'''	-
9q_026	4.78641	Chair B	N'-O7; N'-N'''	-
9q_027	4.85055	Chair A	N'-O7; N'-N''	-
9q_028	4.91916	Chair A	N'-O7; N'-N'''	-
9q_029	4.93329	Skew Boat B	N'-O7; N'-N''	-
9q_030	4.96186	Skew Boat A	N'-O7; N'-N'''	-
9q_031	4.96187	Skew Boat A	N'-O7; N'-N'''	-

[a]Putative partners for a "through space" intramolecular radical shift from O1 or O2 (≤ 3 Å; i.e. amine nitrogen (N')).

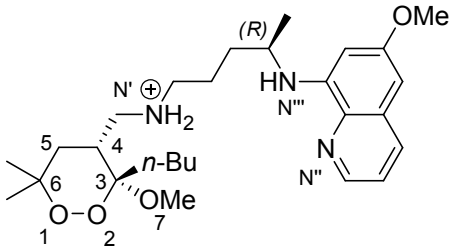
Table 36SI. PM7 conformers within 5 kcal mol^{-1} from the global minimum of **9q** di-protonated form.



Cnf	ΔE	1,2-dioxane ring conformation	Intramolecular interactions	H-shift[a]
9q_001	0	Skew Boat B	N'-O7; N'''-O1; N'''-O2; N'''-O7	-
9q_002	2.31115	Skew Boat B	N'-O1; N'-O7	N'
9q_003	2.68405	Skew Boat B	N'-O1; N'-O7	N'
9q_004	3.27742	Chair A	N'-O7; N'''-O1; N'''-O7	-
9q_005	4.19502	Skew Boat B	N'-O1; N'-O7	N'

[a]Putative partners for a "through space" intramolecular radical shift from O1 or O2 (≤ 3 Å; *i.e.* amine nitrogen (N')).

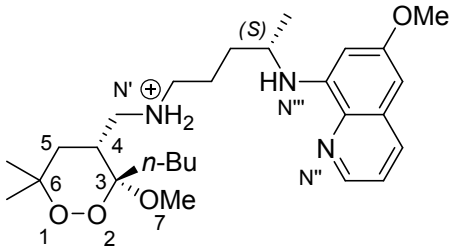
Table 37SI. PM7 conformers within 5 kcal mol^{-1} from the global minimum of **9r** diastereomer characterized by (*R*)-configured stereocenter in the side-chain.



Cnf	ΔE	1,2-dioxane ring conformation	Intramolecular interactions	H-shift[a]
9r_R_001	0	Skew Boat B	N'-O7; N'-N'''	-
9r_R_002	0.11712	Skew Boat B	N'-O1; N'-O7; N'-N'''	N'
9r_R_003	0.21525	Chair A	N'-O7; N'-N'''; N'-N''	C3
9r_R_004	0.64192	Chair A	N'-O7; N'-N'''; N'-N''	C3
9r_R_005	0.74439	Chair A	N'-O7; N'-N'''; N'-N''	C3
9r_R_006	1.08291	Skew Boat B	N'-O7; N'-N'''	C3
9r_R_007	1.21872	Skew Boat B	N'-O1; N'-O7; N'-N'''	N', C3
9r_R_008	1.42073	Chair A	N'-O7; N'-N'''	C3
9r_R_009	1.67992	Chair A	N'-O7; N'-N'''; N'-N''	C3
9r_R_010	1.83679	Chair A	N'-O7; N'-N'''; N'-N''	C3
9r_R_011	1.88754	Chair A	N'-O7; N'-N'''	C3
9r_R_012	2.01228	Chair A	N'-O7; N'-N'''; N'-N''	C3
9r_R_013	2.08448	Skew Boat B	N'-O7; N'-N'''	-
9r_R_014	2.15125	Chair A	N'-N'''; N'-N''	C3
9r_R_015	2.58582	Skew Boat B	N'-O1; N'-O7; N'-N'''	N', C3
9r_R_016	2.74147	Chair A	N'-O7; N'-N'''	-
9r_R_017	2.83568	Chair A	N'-O7; N'-N'''; N'-N''	C3
9r_R_018	2.91553	Skew Boat B	N'-O7; N'-N'''; N'-N''	C3
9r_R_019	2.97808	Chair A	N'-O7; N'-N''; N'-N'''; N''-O7	C3
9r_R_020	3.23051	Chair A	N'-O7; N'-N'''; N'-N''	C3
9r_R_021	3.51391	Chair B	N'-O7; N'-N'''; N'-N''	-
9r_R_022	3.60965	Chair A	N'-N'''; N'-N''	C3
9r_R_023	3.92056	Chair A	N'-O7; N'-N'''; N'-N''	C3
9r_R_024	4.11536	Chair A	N'-O7; N'-N'''; N'-N'''	C3
9r_R_025	4.25029	Chair A	N'-N'''; N'-N''	C3
9r_R_026	4.43214	Chair A	N'-N'''; N'-N''	C3
9r_R_027	4.51052	Skew Boat A	N'-O7; N'-N'''; N'-N''	-
9r_R_028	4.52653	Chair A	N'-O7; N'-N'''	C3
9r_R_029	4.67495	Chair A	N'-N'''; N'-N''	C3
9r_R_030	4.79969	Chair B	N'-O7; N'-N'''; N'-N''	-
9r_R_031	4.79971	Chair B	N'-O7; N'-N'''; N'-N''	-
9r_R_032	4.8579	Chair B	N'-O7; N'-N'''; N'-N''	C3
9r_R_033	4.99459	Chair A	N'-O7; N'-N'''	C3

[a]Putative partners for a "through space" intramolecular radical shift from O1 or O2 (≤ 3 Å; *i.e.* amine nitrogen (N') and C3 alkyl chain).

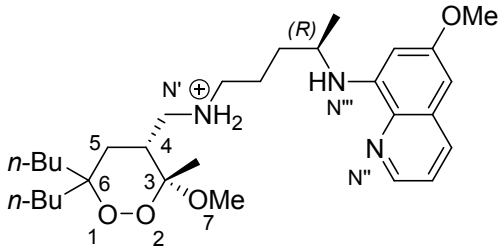
Table 38SI. PM7 conformers within 5 kcal mol^{-1} from the global minimum of **9r** diastereomer characterized by (*S*)-configured stereocenter in the side-chain.



Cnf	ΔE	1,2-dioxane ring conformation	Intramolecular interactions	H-shift[a]
9r_S_001	0	Skew Boat B	N'-O7; N'-N'''; N'-N''	C3
9r_S_002	1.41799	Chair A	N'-O7; N'-N'''; N'-N''	C3
9r_S_003	2.141	Chair A	N'-N'''; N'-N''	C3
9r_S_004	2.40006	Skew Boat B	N'-O7; N'-N'''; N'-N''	-
9r_S_005	2.9691	Skew Boat B	N'-O1; N'-N'''	N'; C3
9r_S_006	3.44775	Chair A	N'-O7; N'-N'''; N'-N''	C3
9r_S_007	3.57025	Chair A	N'-O7; N'-N'''	-
9r_S_008	3.66844	Chair A	N'-O7; N'-N'''; N'-N''	C3
9r_S_009	3.75913	Chair B	N'-O7; N'-N'''; N'-N''	-
9r_S_010	3.83217	Skew Boat B	N'-O1; N'-O7; N'-N'''	N', C3
9r_S_011	3.95899	Chair A	N'-N'''; N'-N''	-
9r_S_012	4.28249	Chair B	N'-O7; N'-N'''; N'-N''	-
9r_S_013	4.32915	Chair A	N'-N'''; N'-N''	C3
9r_S_014	4.45719	Chair A	N'-O7; N'-N'''; N'-N''	C3
9r_S_015	4.8583	Skew Boat B	N'-O1; N'-O7; N'-N'''	N', C3
9r_S_016	4.86629	Chair A	N'-O7; N'-N'''	C3
9r_S_017	4.91553	Chair B	N'-O7; N'-N'''; N'-N''	C3
9r_S_018	4.99927	Chair A	N'-O7; N'-N'''	C3

[a]Putative partners for a "through space" intramolecular radical shift from O1 or O2 (≤ 3 Å; *i.e.* amine nitrogen (N') and C3 alkyl chain).

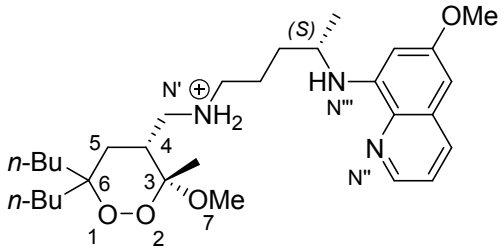
Table 39SI. PM7 conformers within 5 kcal mol^{-1} from the global minimum of **9s** diastereomer characterized by (*R*)-configured stereocenter in the side-chain.



Cnf	ΔE	1,2-dioxane ring conformation	Intramolecular interactions	H-shift[a]
9s_R_001	0	Skew Boat B	N'-O1; N'-N'''; N'-N''	N'; C6
9s_R_002	3.40321	Chair A	N'-O7; N'-N'''; N'-N''	C6
9s_R_003	3.43878	Chair A	N'-O7; N'-N'''; N'-N''	C6
9s_R_004	4.10335	Skew Boat B	N'-O1; N'-O7; N'-N'''	N', C6
9s_R_005	4.20996	Chair A	N'-N'''; N'-N''	C6
9s_R_006	4.49473	Skew Boat B	N'-N'''; N'-N''	C6

[a]Putative partners for a "through space" intramolecular radical shift from O1 or O2 (≤ 3 Å; *i.e.* amine nitrogen (N') and C6 alkyl chain(s)).

Table 40SI. PM7 conformers within 5 kcal mol^{-1} from the global minimum of **9s** diastereomer characterized by (*S*)-configured stereocenter in the side-chain.



Cnf	ΔE	1,2-dioxane ring conformation	Intramolecular interactions	H-shift[a]
9s_S_001	0	Skew Boat B	N'-O1; N'-N'''	N'; C6
9s_S_002	0.21788	Chair A	N'-O7; N'-N'''	C6
9s_S_003	0.89765	Chair A	N'-O7; N'-N'''	C6
9s_S_004	2.35565	Chair A	N'-N'''; N'-N''	C6
9s_S_005	2.45095	Chair A	N'-O7; N'-N'''	C6
9s_S_006	2.64368	Skew Boat B	N'-O1; N'-O7; N'-N'''	N', C6
9s_S_007	3.10563	Skew Boat B	N'-O7; N'-N'''	C6
9s_S_008	4.01158	Chair A	N'-O7; N'-N'''; N'-N''	C6
9s_S_009	4.02489	Skew Boat B	N'-O7; N'-N'''	C6

[a]Putative partners for a "through space" intramolecular radical shift from O1 or O2 (≤ 3 Å; *i.e.* amine nitrogen (N') and C6 alkyl chain(s)).