Supporting Information

Novel 2- and 4-Substituted 1*H*-Imidazo[4,5-*c*]quinolin-4-amine Derivatives as Allosteric Modulators of the A_3 Adenosine Receptor

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NOTES ON TAUTOMERIC RESOLUTION BY NOESY

Since the synthesized heterocyclic ligands were insoluble in water, the equilibrium structures of selected compounds were roughly estimated in dimethyl sulfoxide-d_6 by 2D NOESY experiments (see Figures S4, S5, and S7). For compounds **10** and **11**, somewhat intense NOE cross-peaks were observed between the imidazole NH proton (ca. 13.3 ppm) and the aniline (i.e., aryl) NH proton (ca. 10.1 ppm), but no NOE was found between the imidazole NH and H_9 (see proton labeling in Table 1 of the main text), suggesting the 3*H*-tautomer as an exclusive form. Structural analysis of **14** by NMR was atypical from the outset. Despite the numerous purification attempts to isolate the major compound under different chromatographic conditions, a minor isomer consistently appeared in the 1D proton NMR spectrum (major/minor ≈ 88:12 by NMR integration in DMSO-d_6). In fact these two isomers were found correlated by NOE cross-peaks–i.e., 1*H*- and 3*H*-tautomers through proton exchange. Here, the imidazole NH of the major tautomer at 13.16 ppm showed weak NOE cross-peaks with H_9, suggesting 1*H* as a major form.

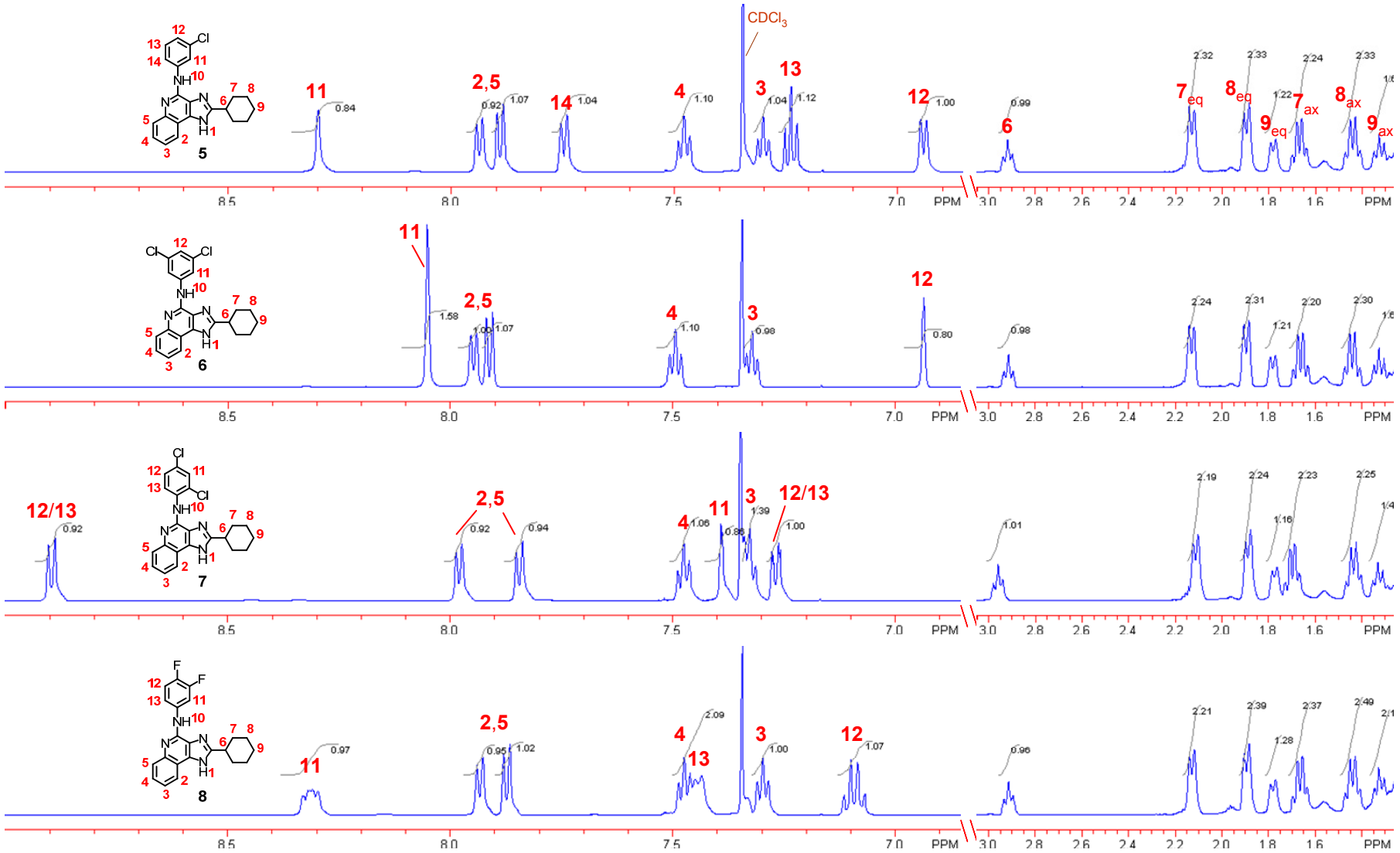

Figure S1. ^{1}H NMR spectra of compounds **5**, **6**, **7**, and **8** in 4:1 $CDCl_3/CD_3OD$.

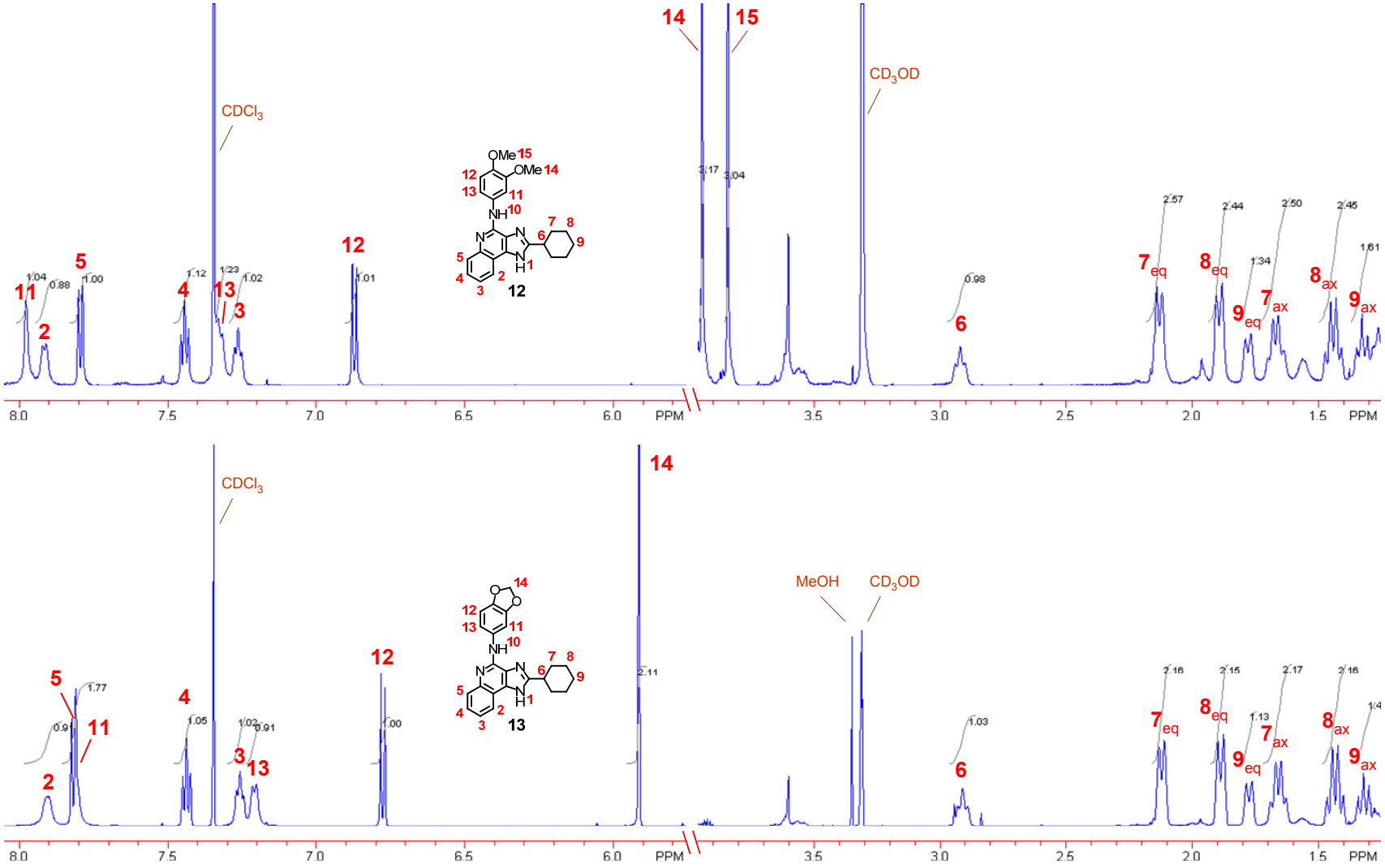

Figure S2. ^{1}H NMR spectra of compounds **12** and **13** in 4:1 $CDCl_3/CD_3OD$.

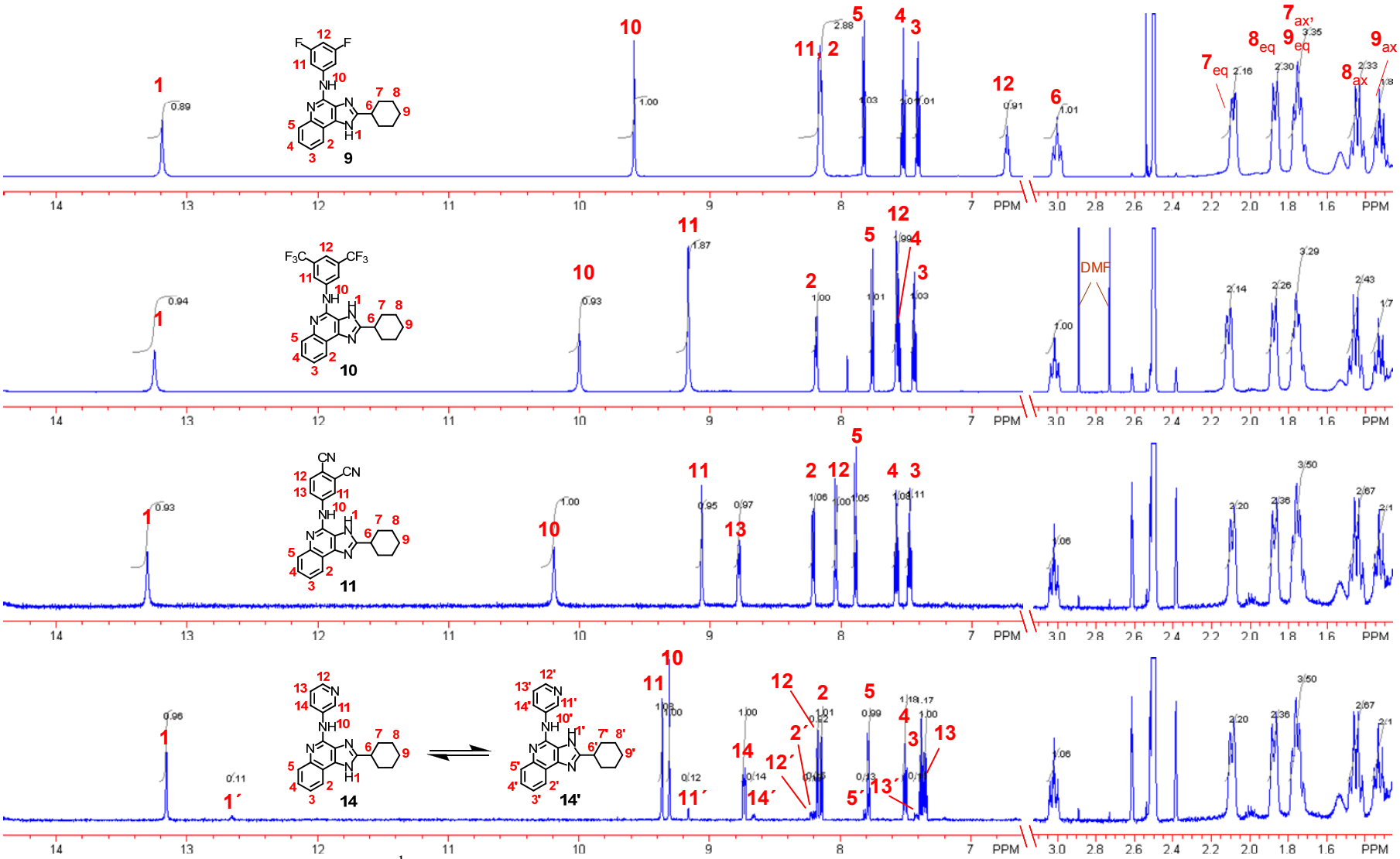

Figure S3. ^{1}H NMR spectra of compounds compounds **9**, **10**, **11**, and **14** in DMSO-d_6.

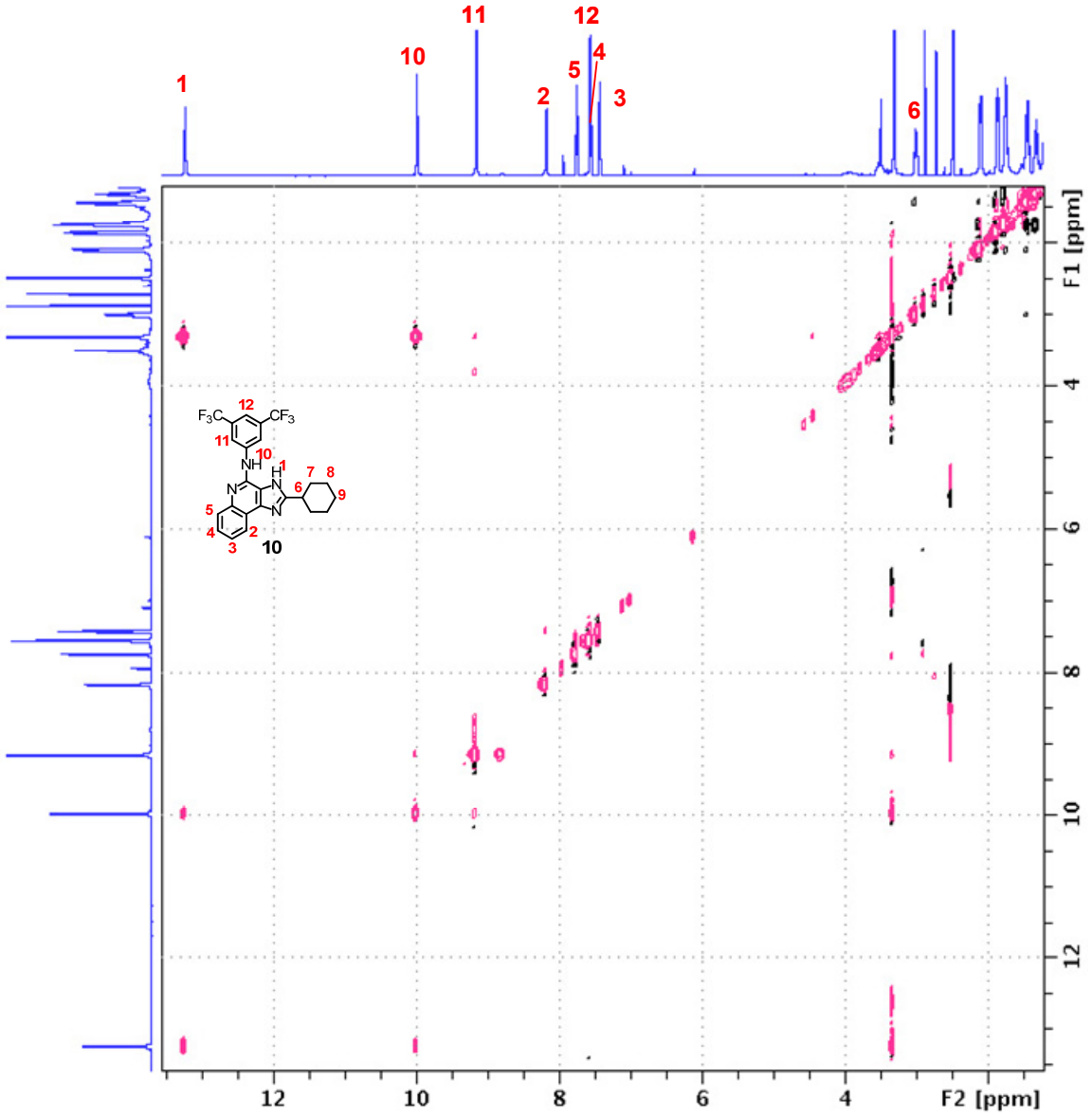

Figure S4. NOESY spectrum of **10** in DMSO-d_6.

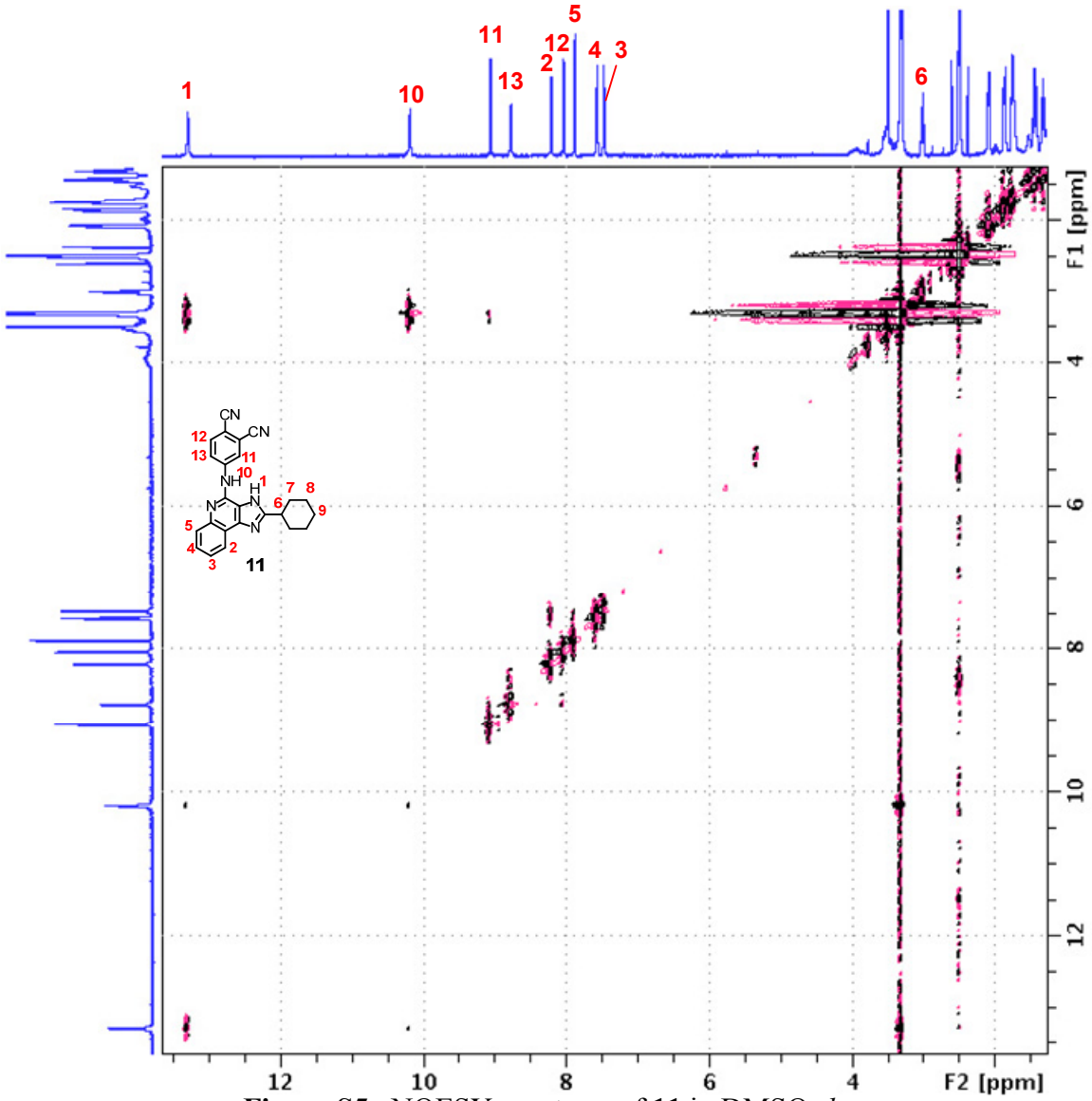

Figure S5. NOESY spectrum of **11** in DMSO-d_6.

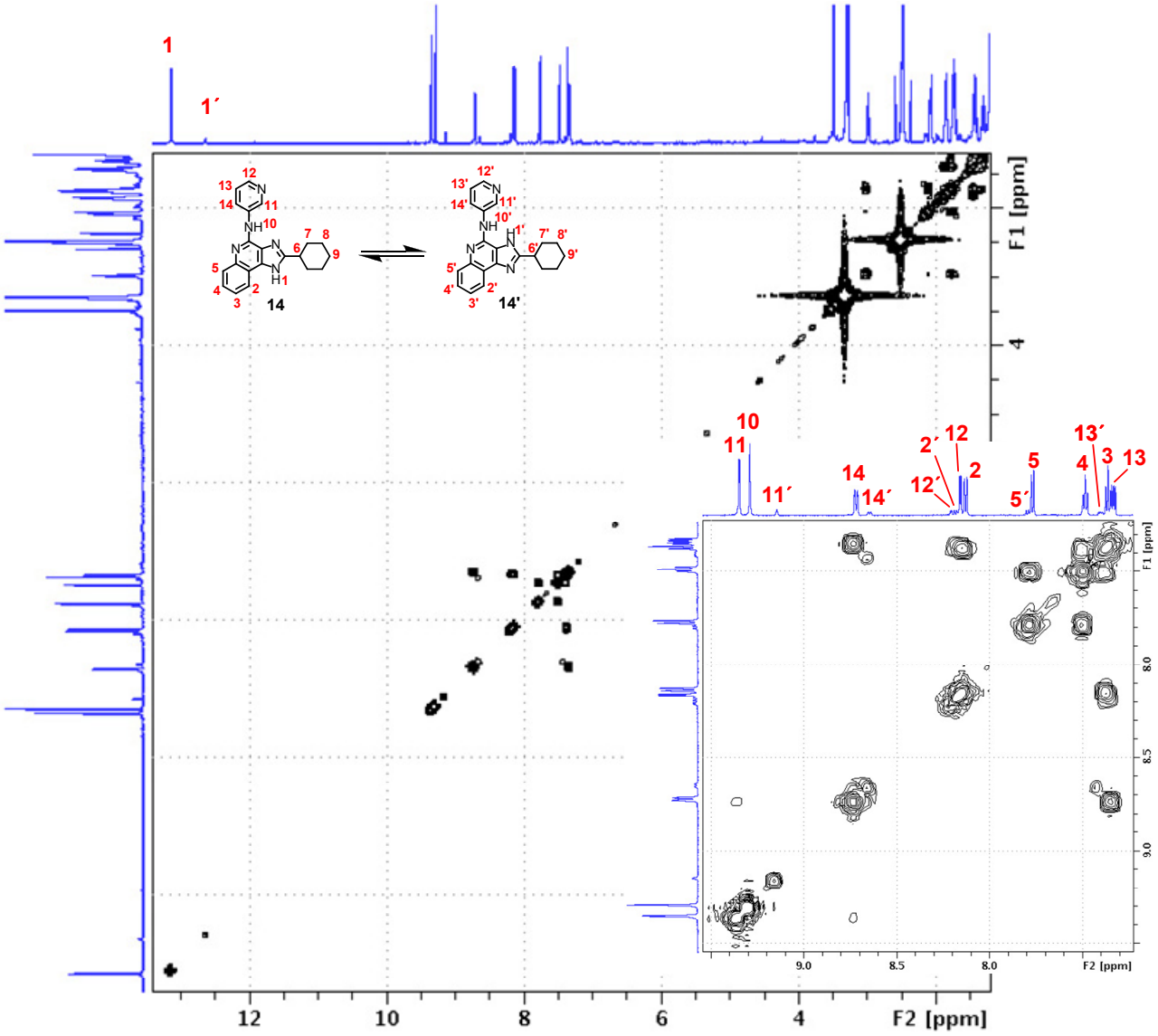

Figure S6. COSY spectrum of **14** in DMSO-d_6.

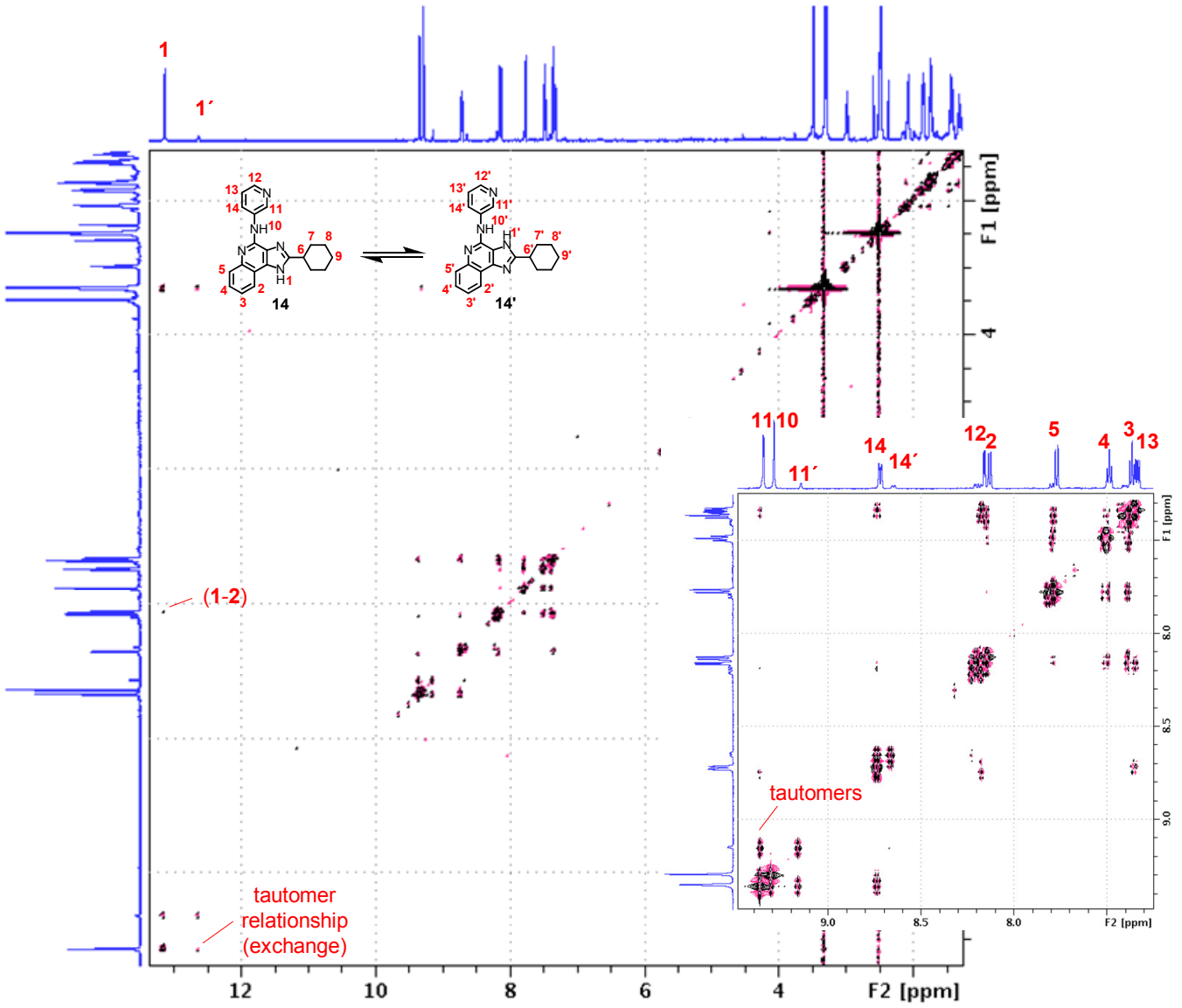

Figure S7. NOESY spectrum of **14** in DMSO-d_6.

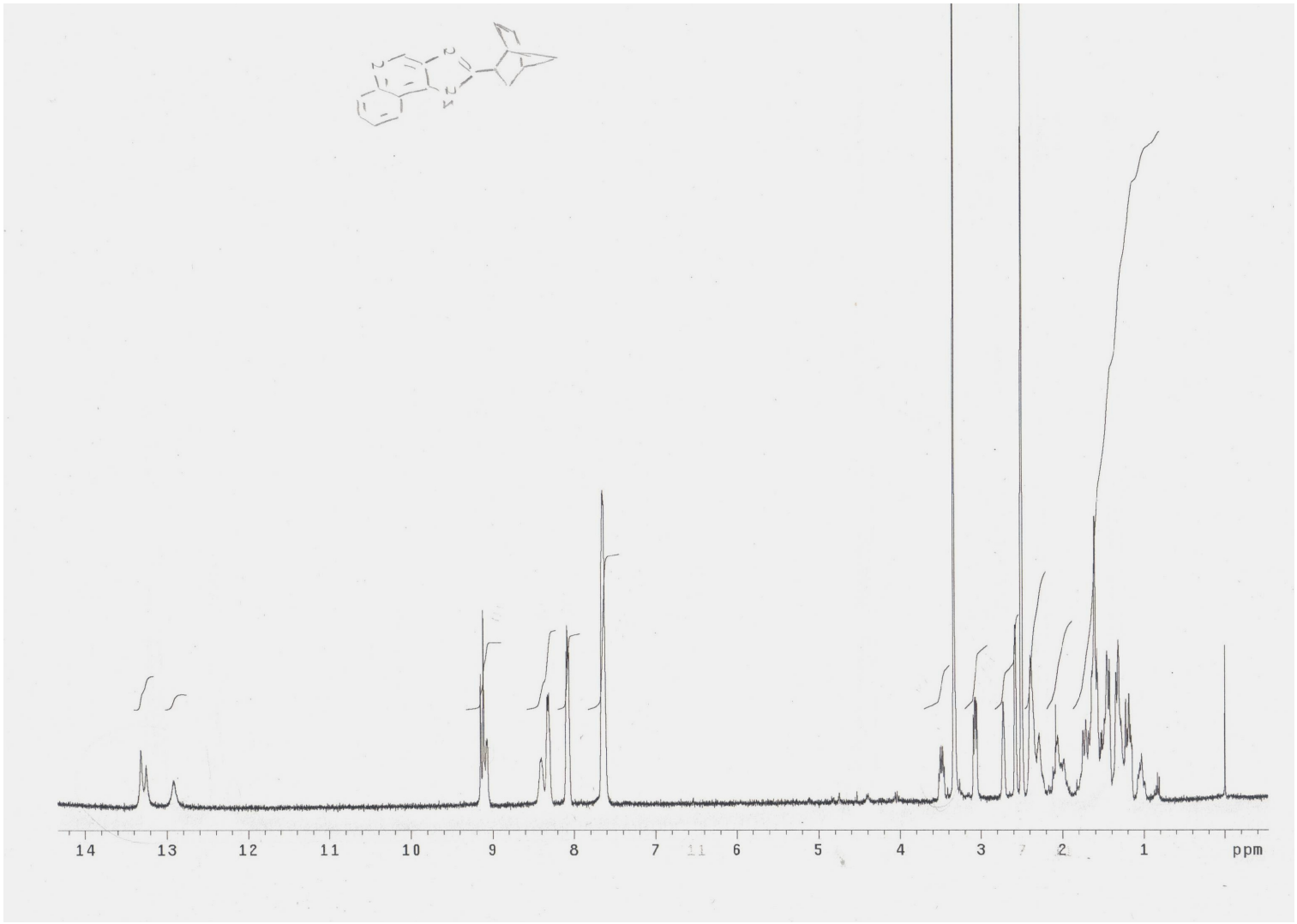

Figure S8. ^{1}H NMR spectra of compound **31b** in $CD_3OD/CDCl_3$.

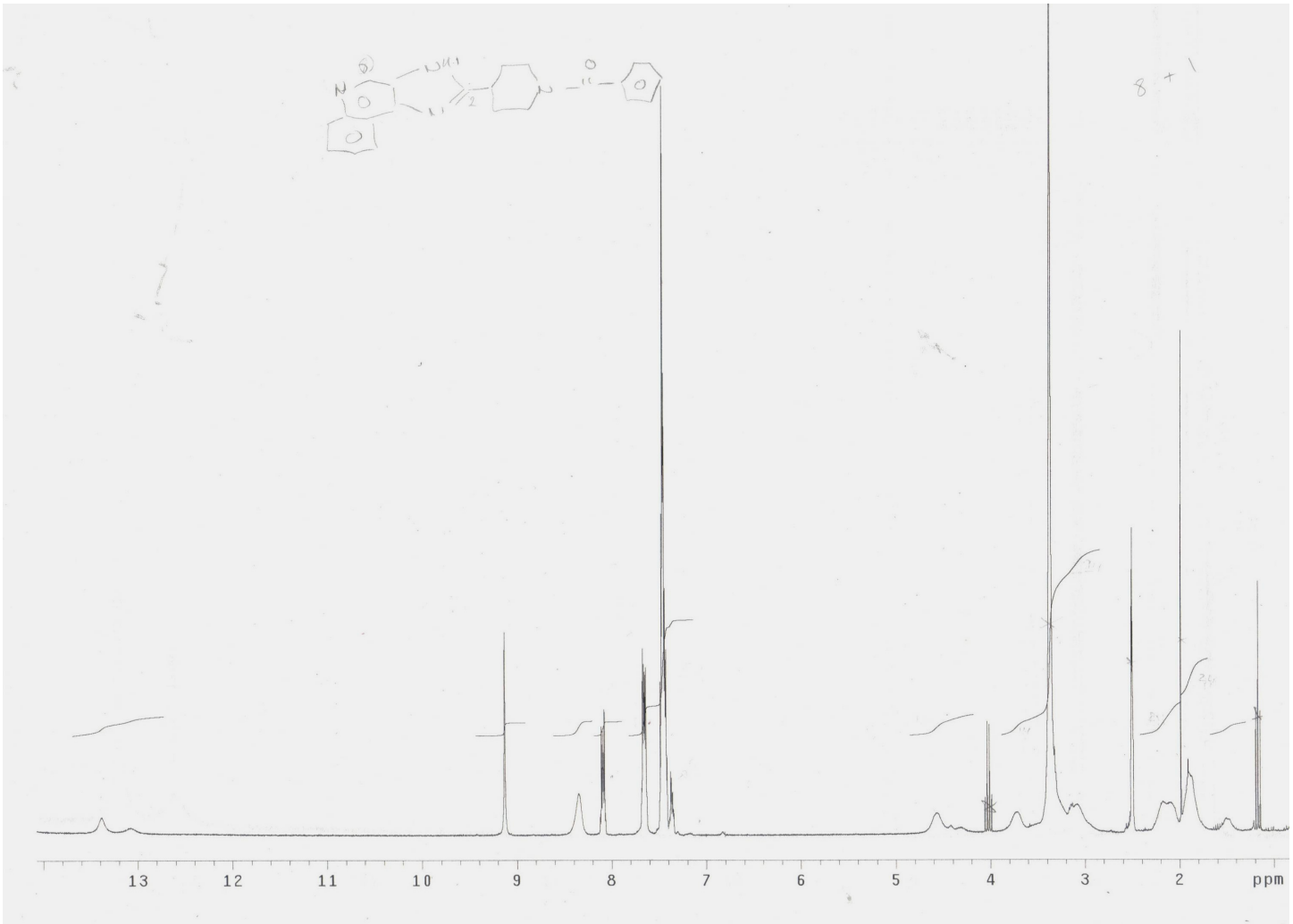

Figure S9. ^{1}H NMR spectra of compound **31d** in $CD_3OD/CDCl_3$.

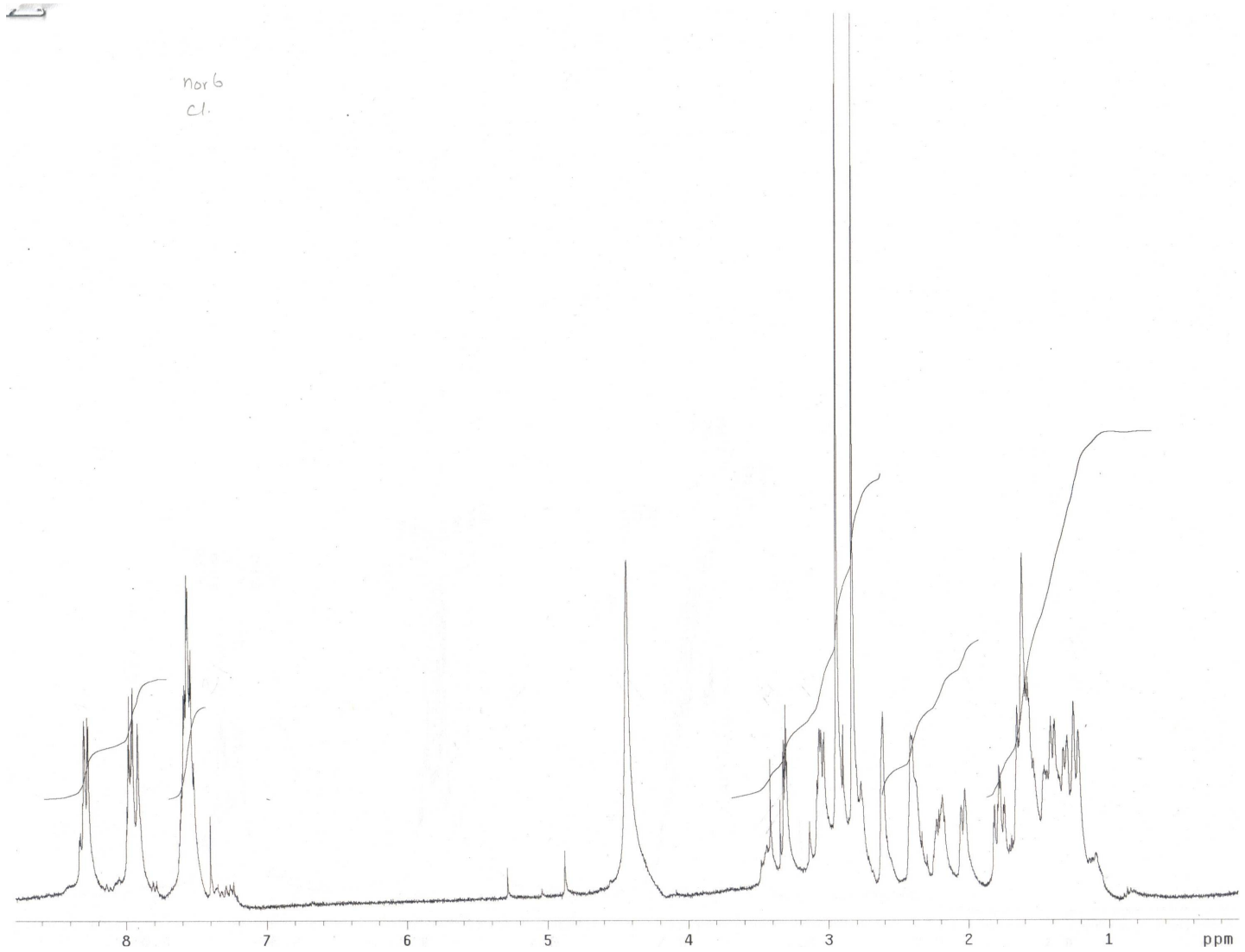

Figure S10. ^{1}H NMR spectra of compound **33b** in $CD_3OD/CDCl_3$.

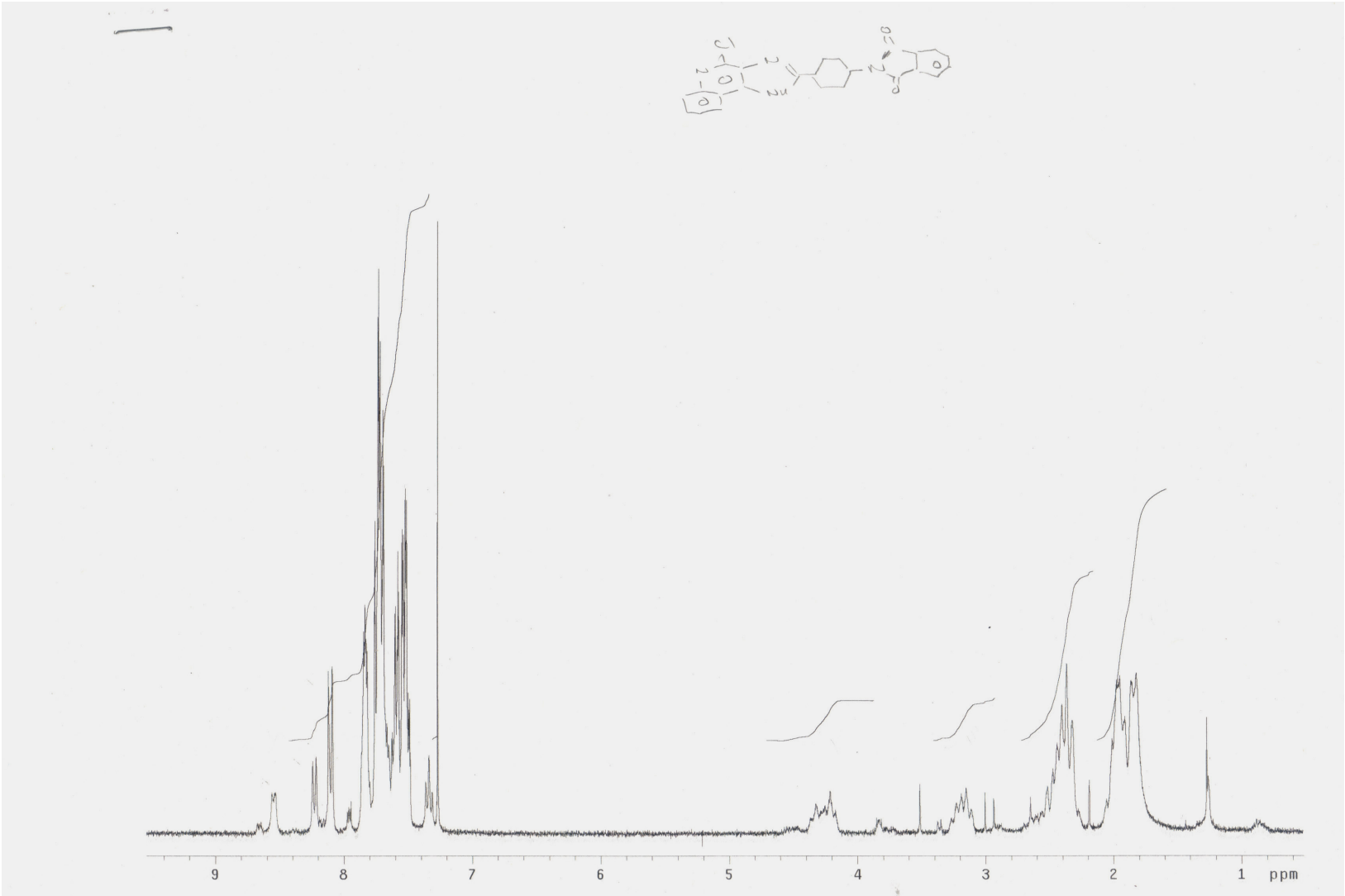

Figure S11. ^{1}H NMR spectra of compound **33c** in $CD_3OD/CDCl_3$.

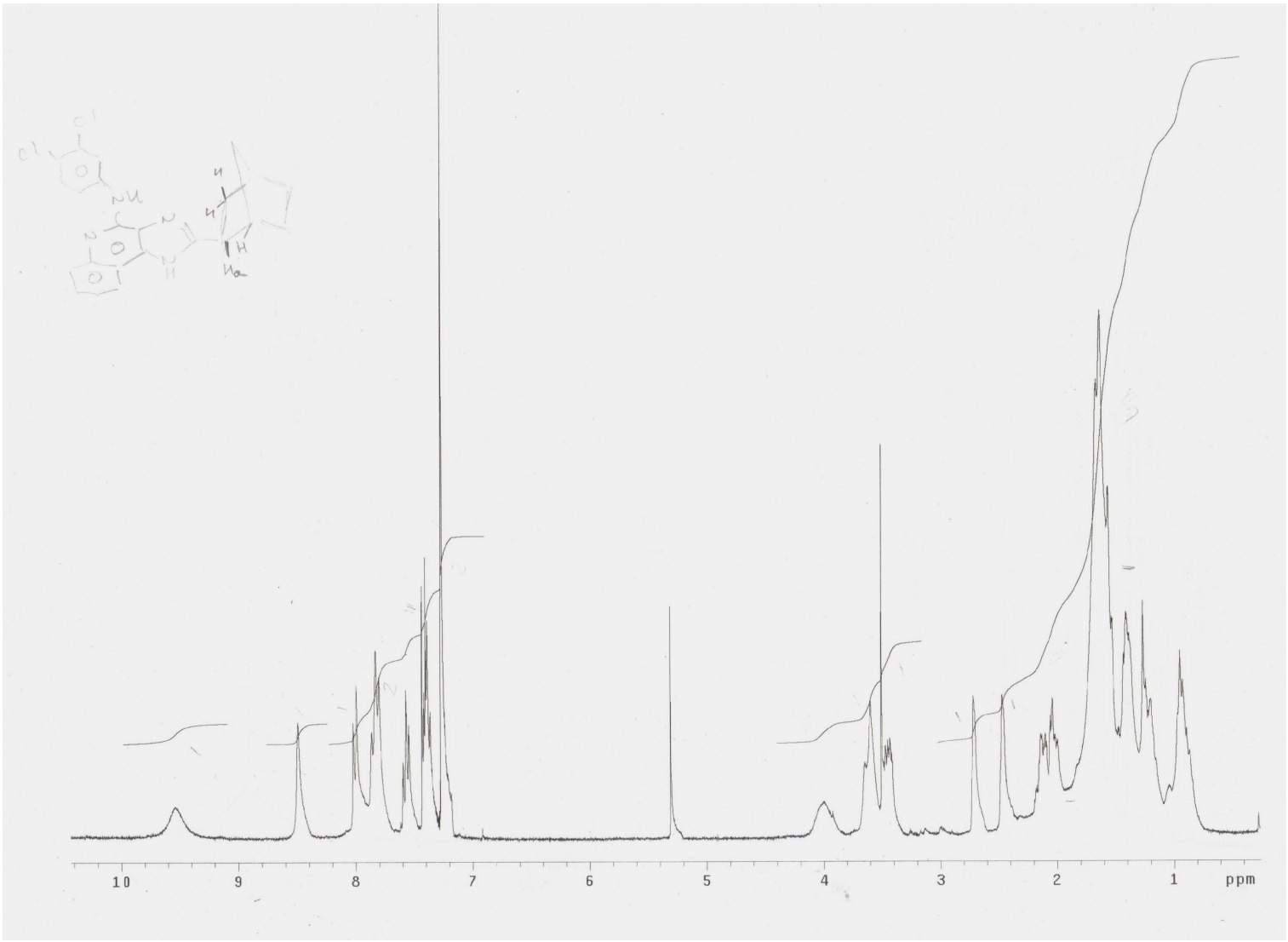

Figure S12. ^{1}H NMR spectra of compound **17** in $CD_3OD/CDCl_3$.

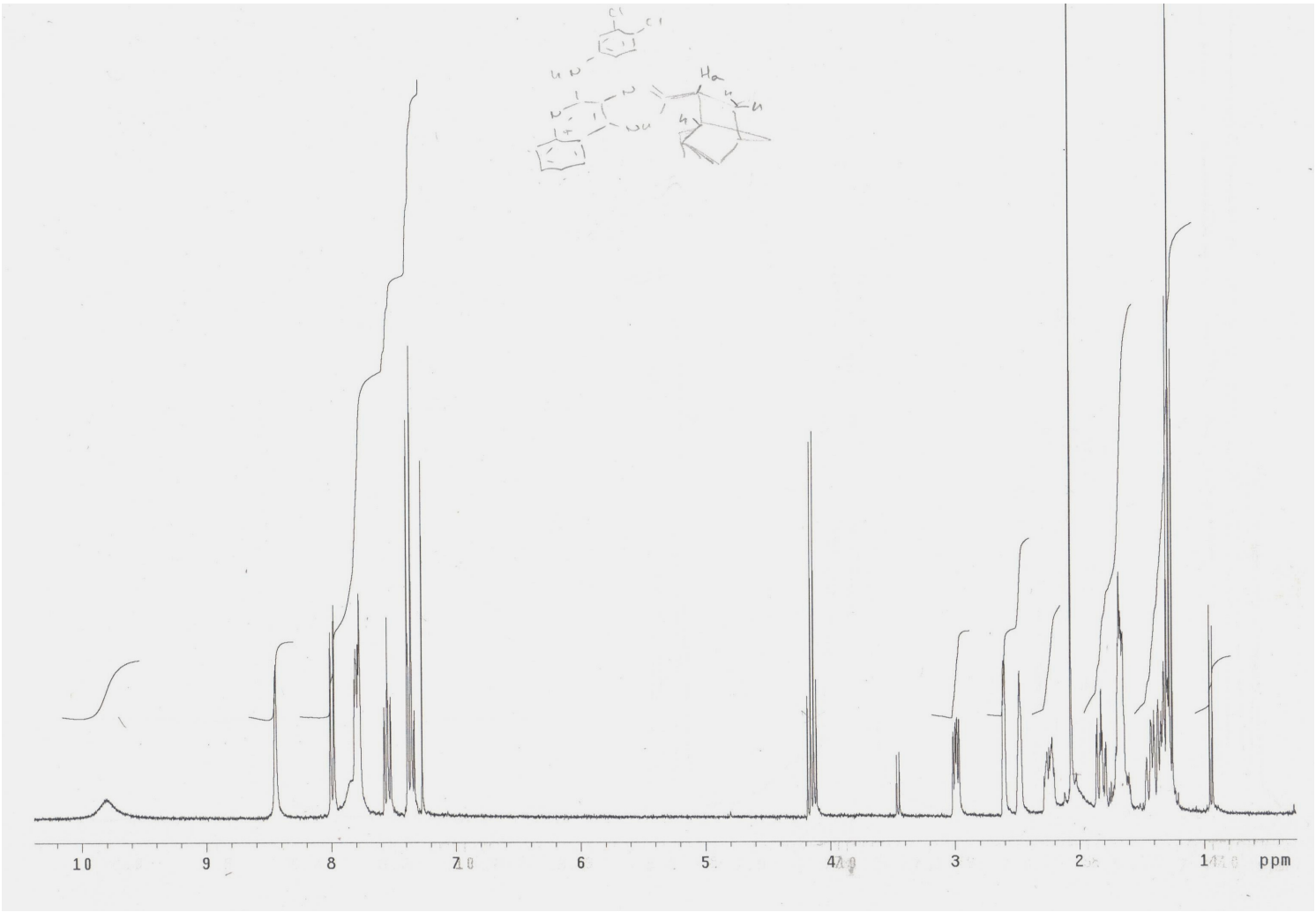

Figure S13. ^{1}H NMR spectra of compound **18** in $CD_3OD/CDCl_3$.

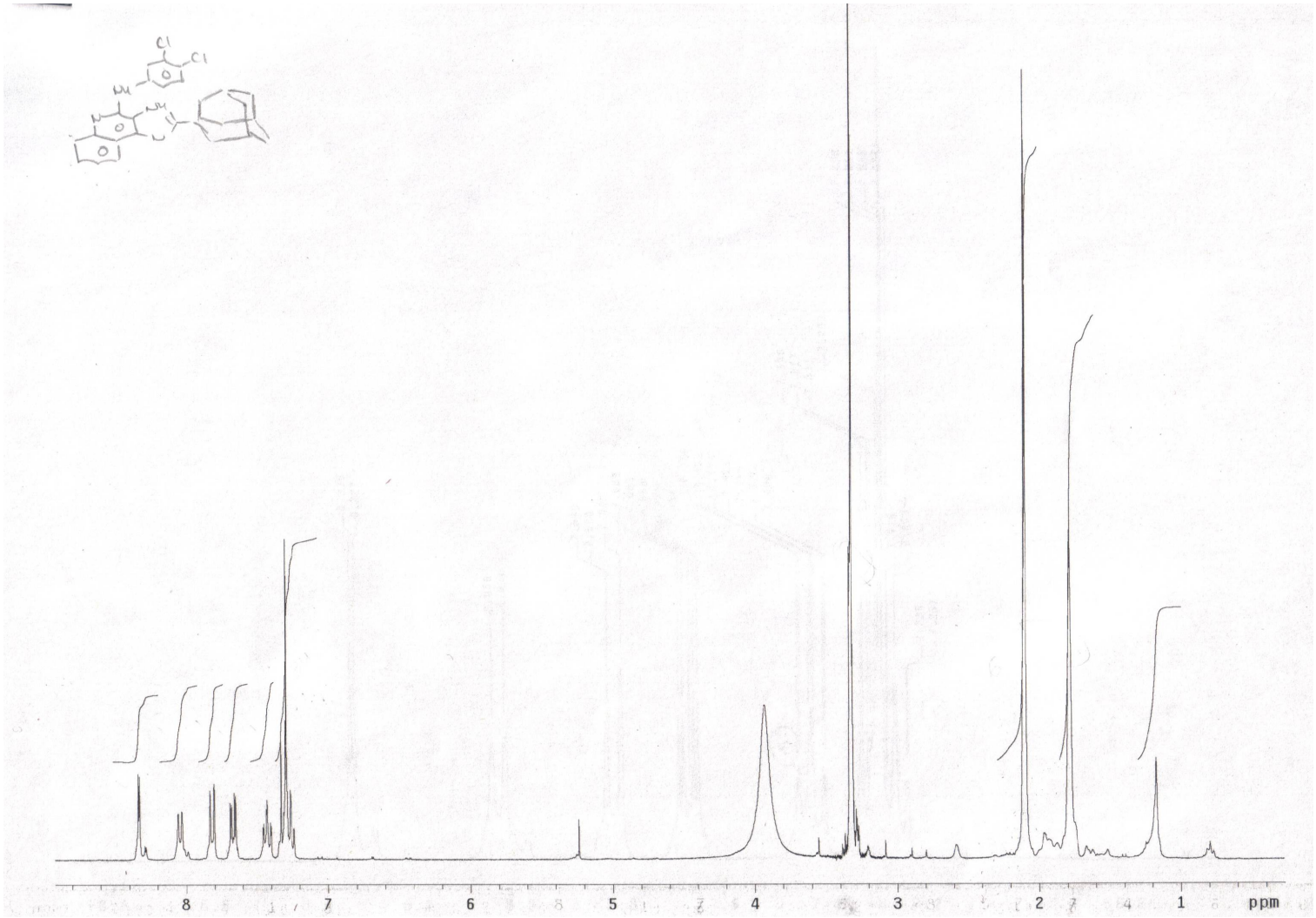

Figure S14. ^{1}H NMR spectra of compound **20** in $CD_3OD/CDCl_3$.

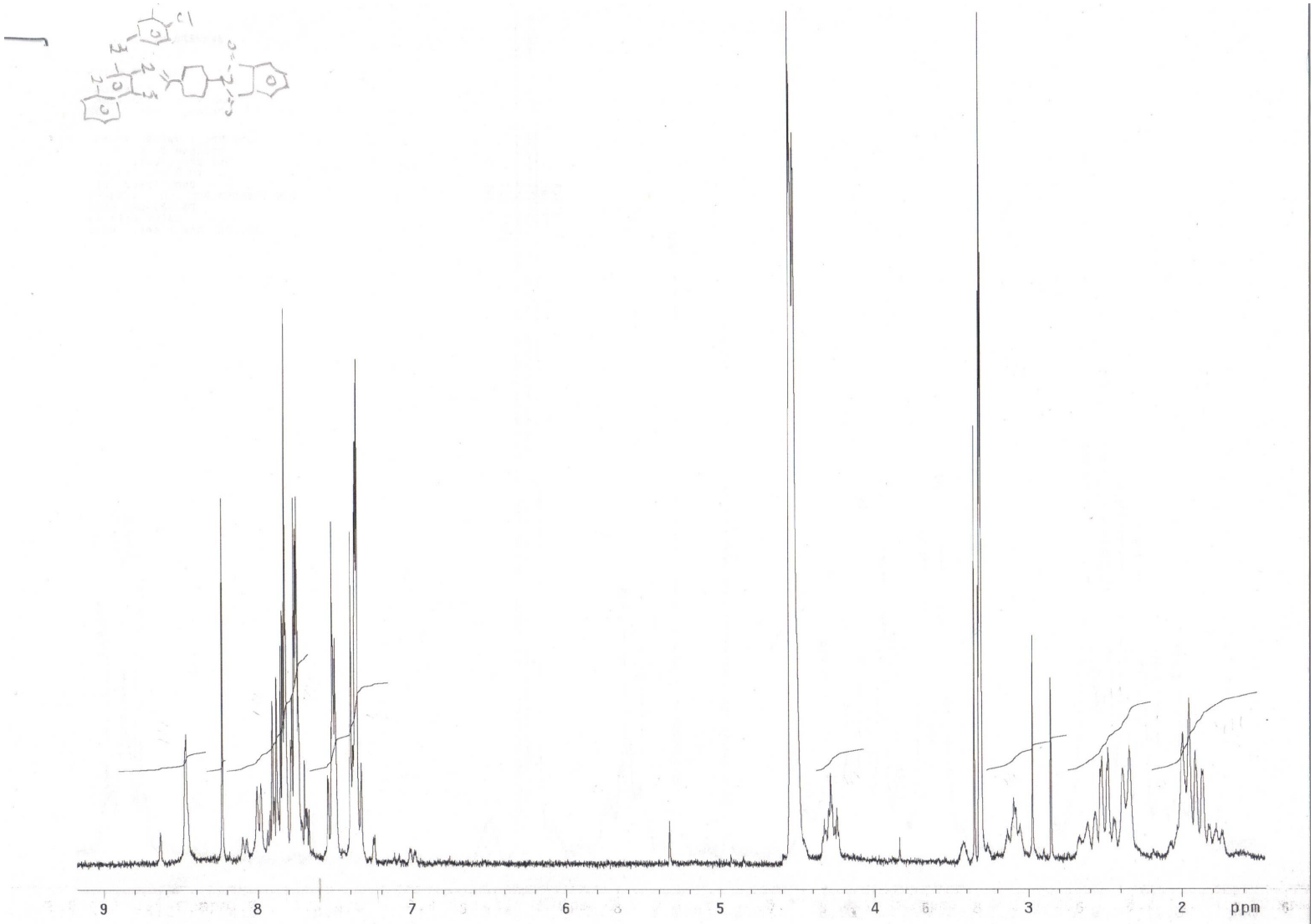

Figure S15. ^{1}H NMR spectra of compound **21** in $CD_3OD/CDCl_3$.

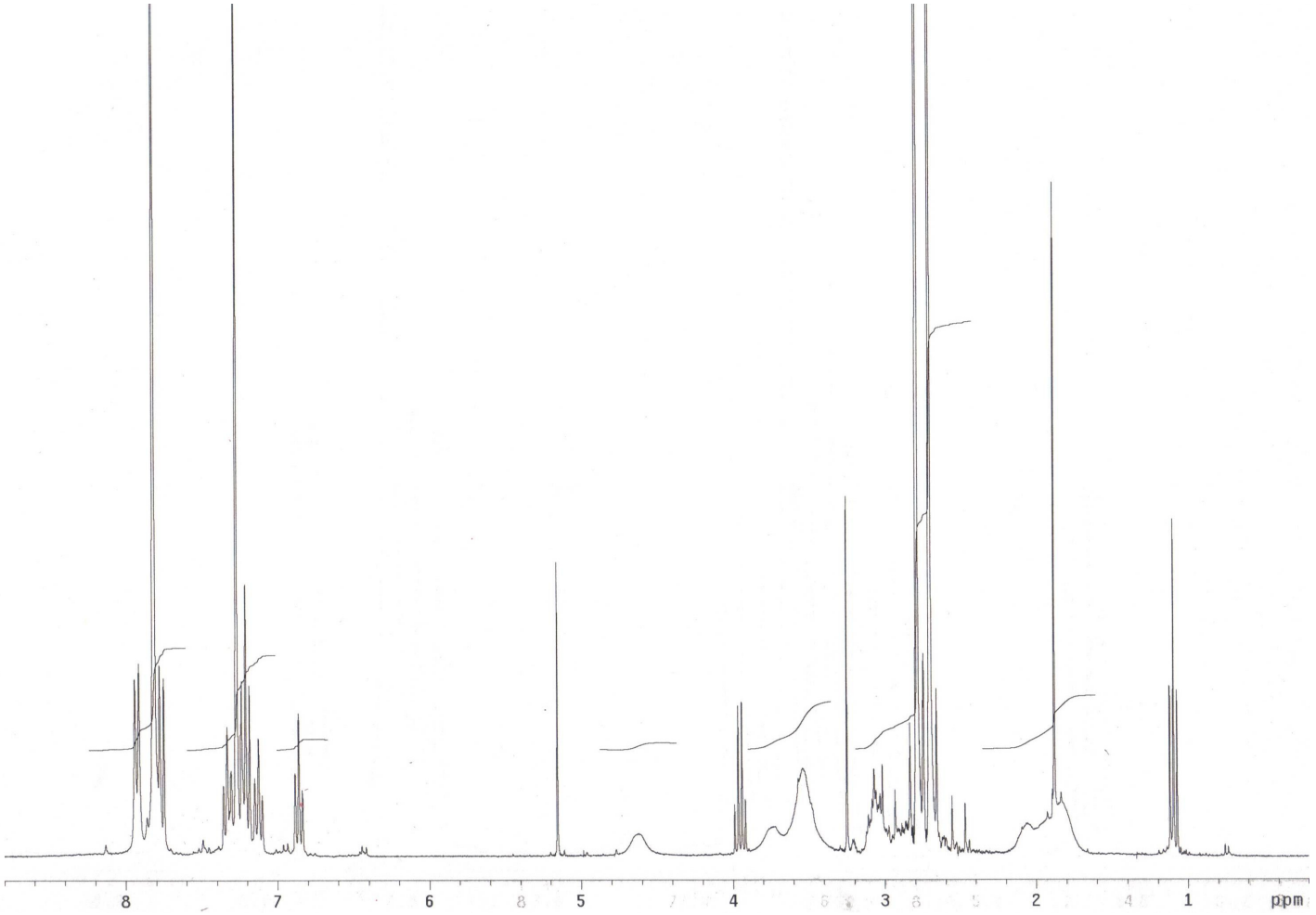

Figure S16. ^{1}H NMR spectra of compound **23** in $CD_3OD/CDCl_3$.

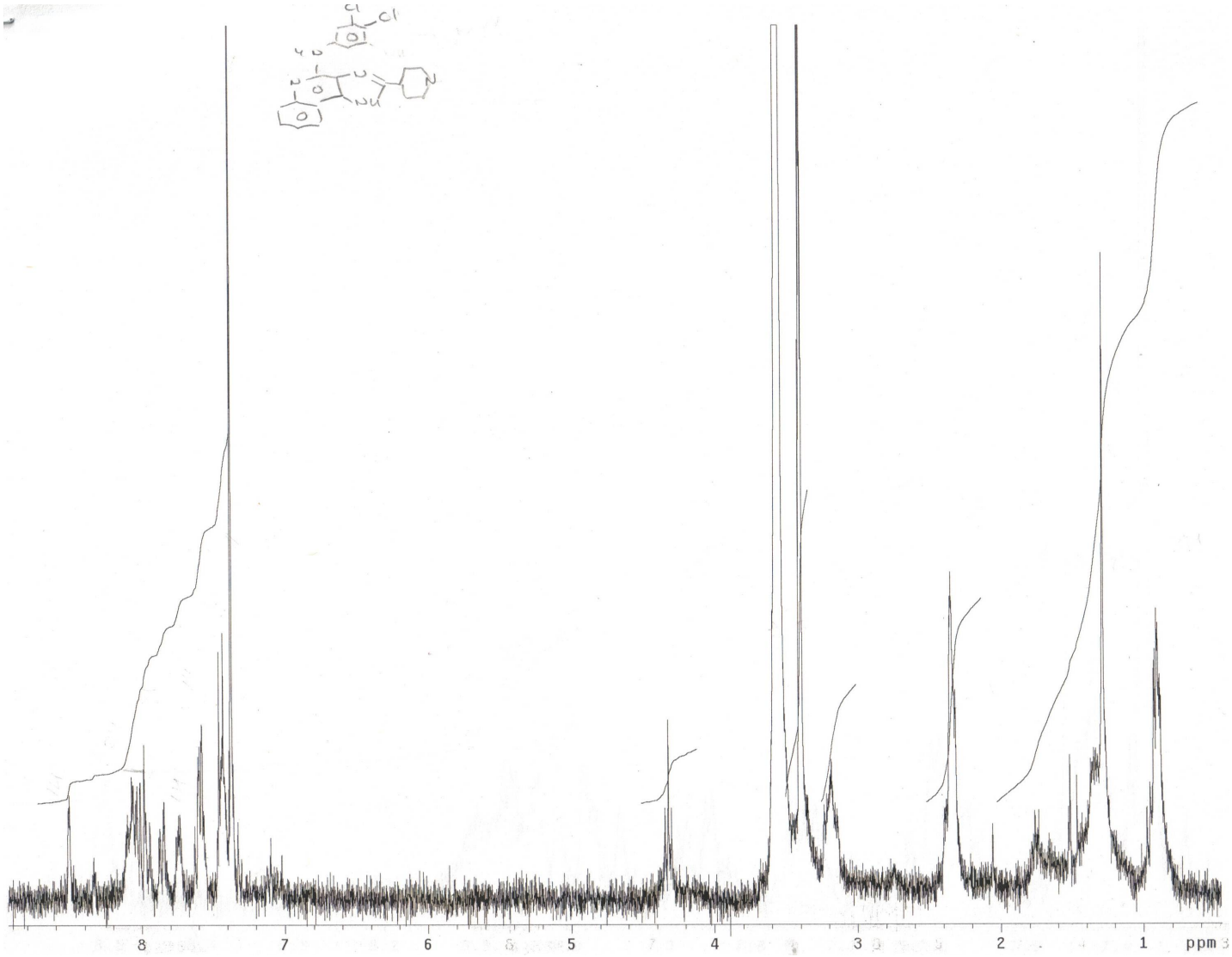

Figure S17. ^{1}H NMR spectra of compound **26** in $CD_3OD/CDCl_3$.