Supplementary Data

Semisynthesis, cytotoxicity, antiviral activity, and drug interaction liability of 7-*O*-methylated analogues of flavonolignans from milk thistle

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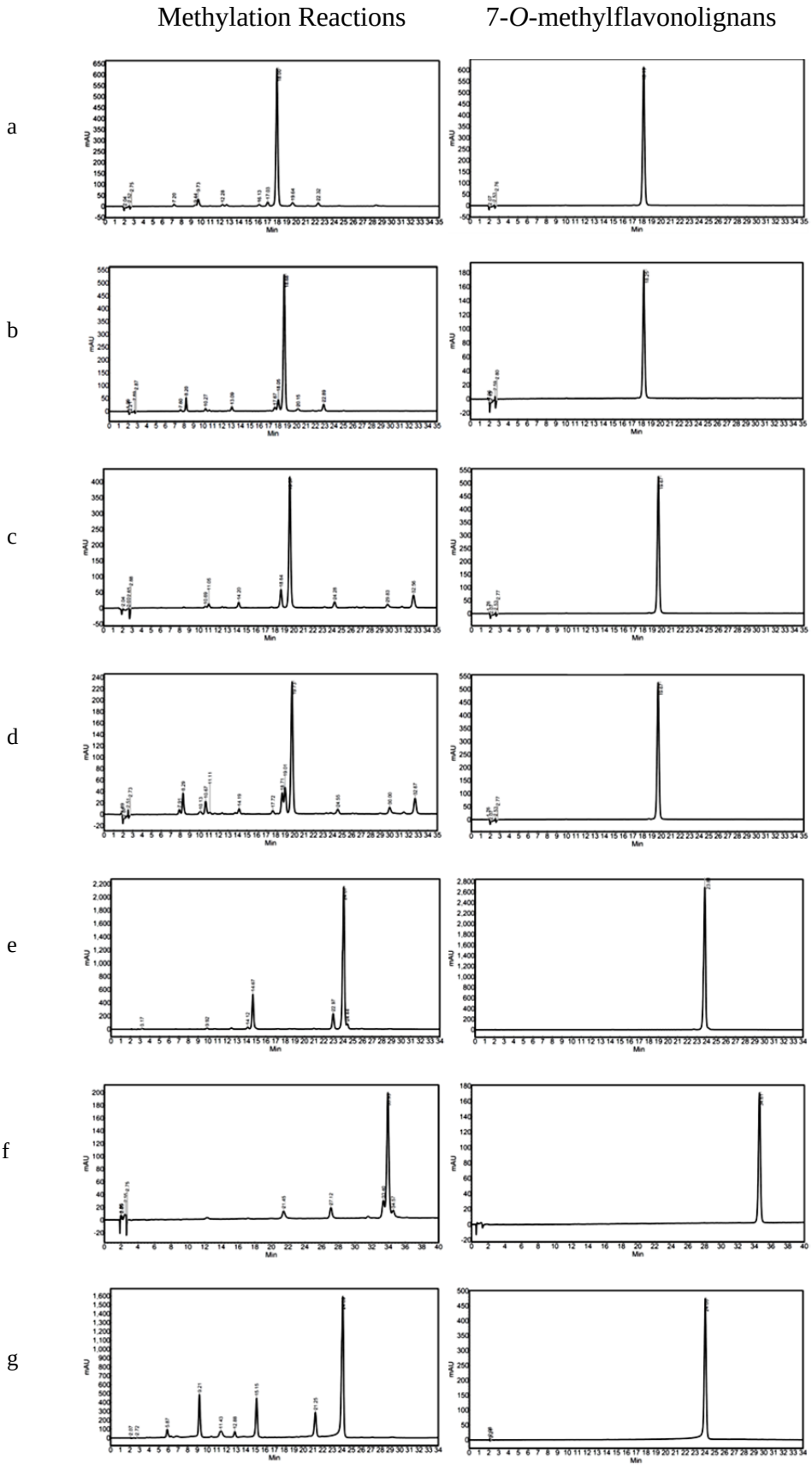
Figure S1. HPLC chromatograms of crude reaction mixtures (left column) and purified 7-*O*-methylflavonolignans (right column) at 288 nm



Starting materials were (a) silybin A; (b) silybin B; (c) isosilybin A; (d) isosilybin B; (e) silychristin; (f) isosilychristin; (g) silydianin

Figure S2. ^{1}H NMR spectra (500 MHz, 30 °C) of silybin A (**1**) and 7-*O*-methylsilybin A (**2**) in DMSO-d_6

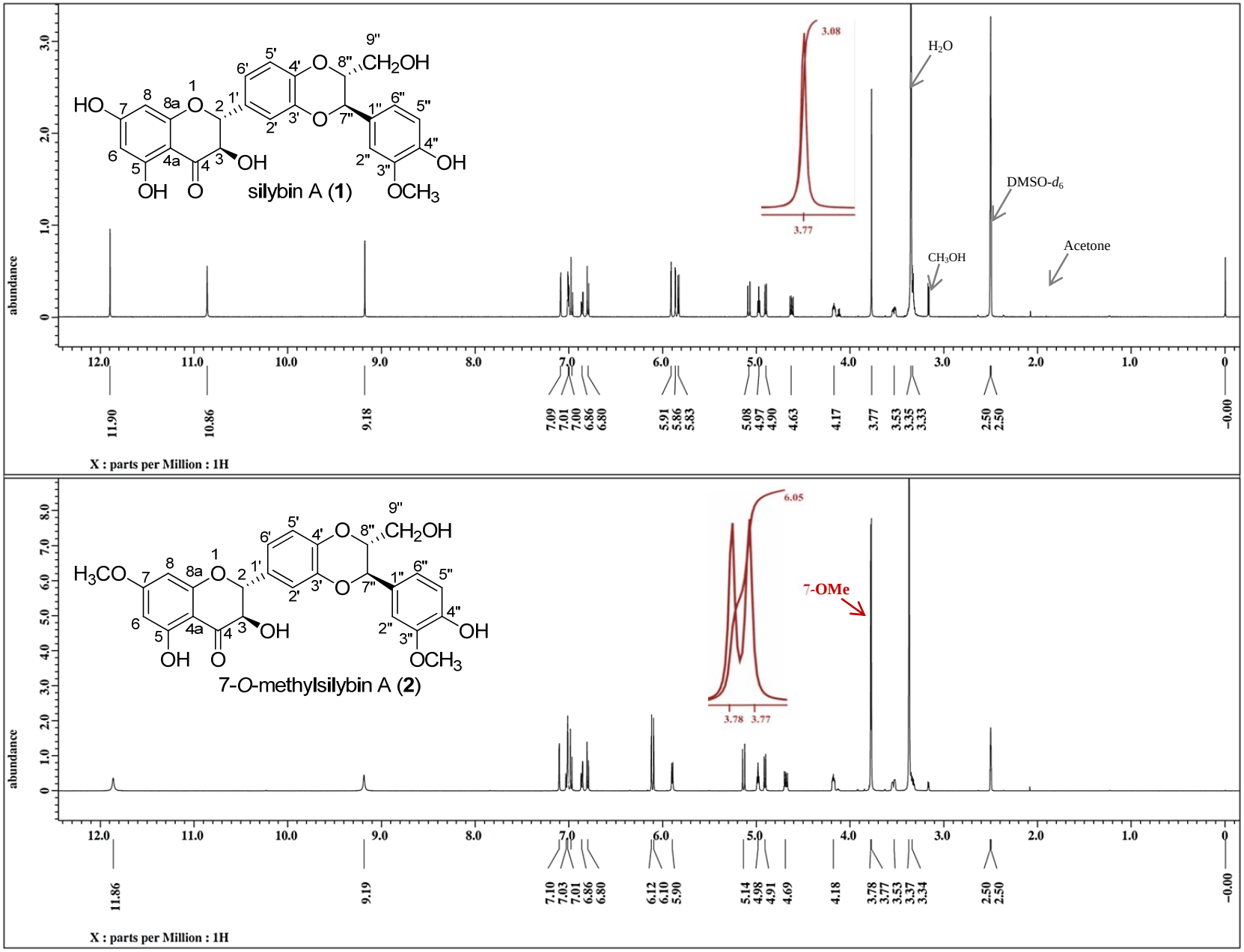


Figure S3. ^{13}C NMR spectra (125 MHz, 30 °C) of silybin A (**1**) and 7-*O*-methylsilybin A (**2**) in DMSO-d_6

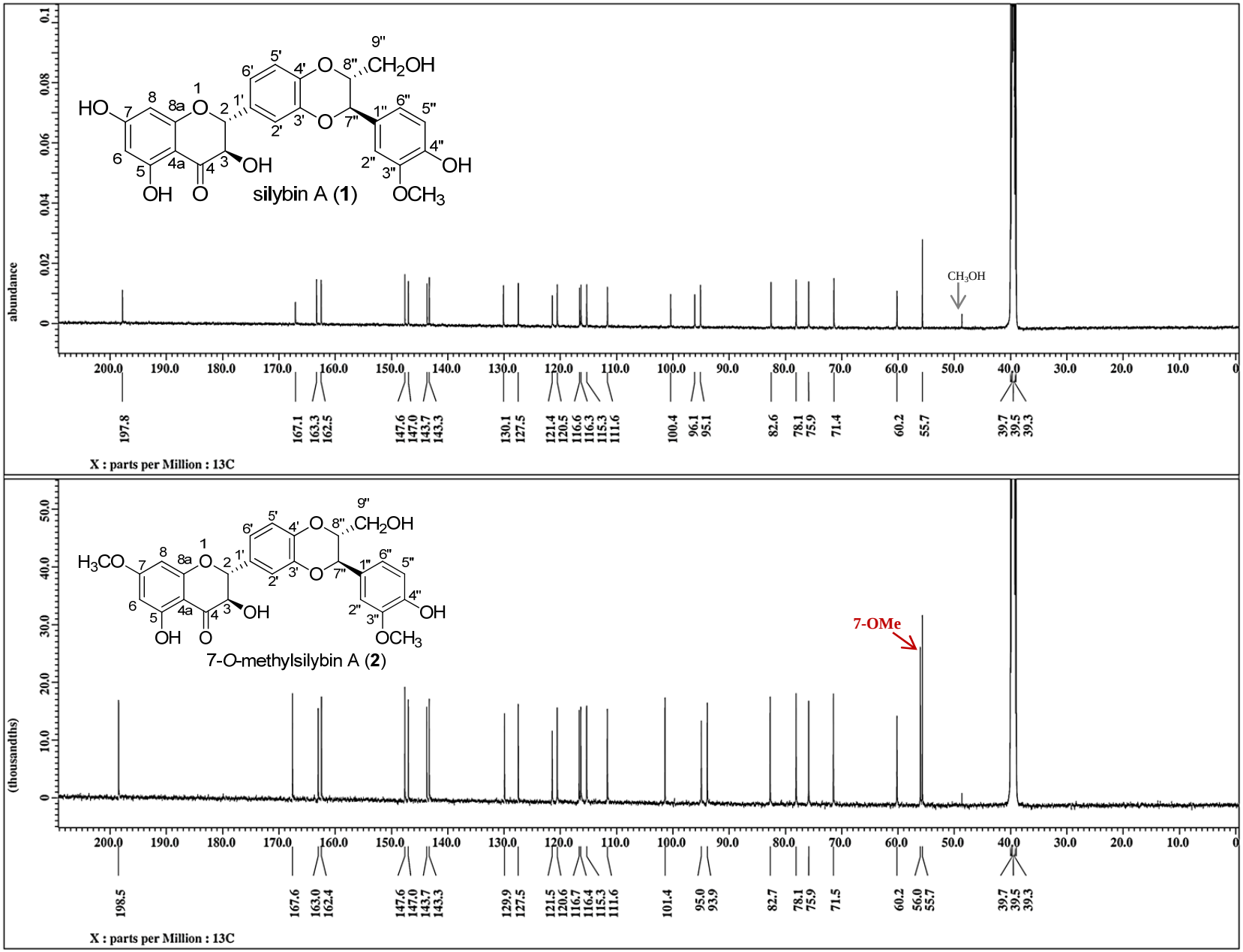


Figure S4. HMBC NMR spectrum (DMSO-d_6, 30°C) of 7-*O*-methylsilybin A (**2**) showing the key correlation between the methoxy protons and C-7

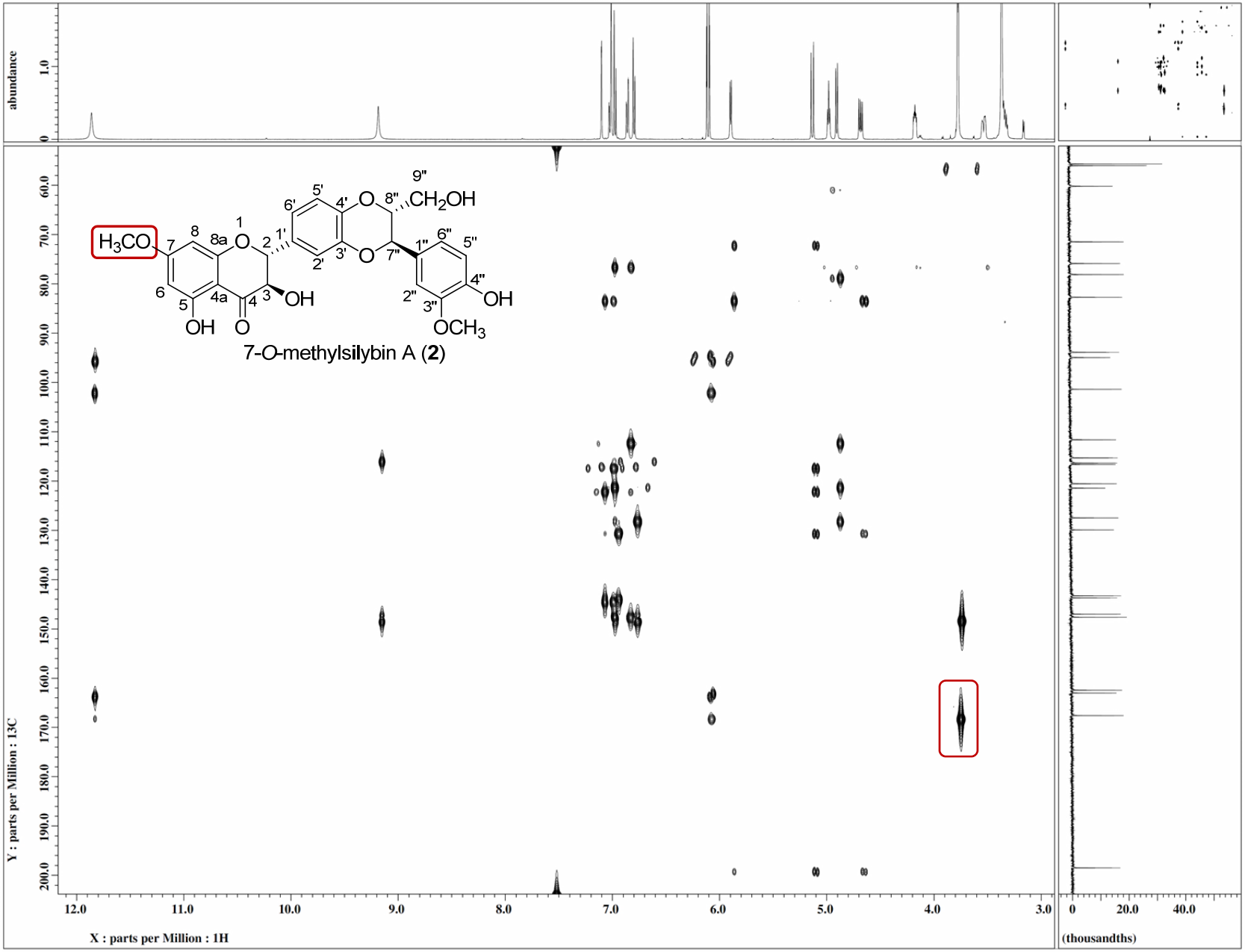


Figure S5. ^{1}H NMR spectra (500 MHz, 30 °C) of silybin B (**3**) and 7-*O*-methylsilybin B (**4**) in DMSO-d_6

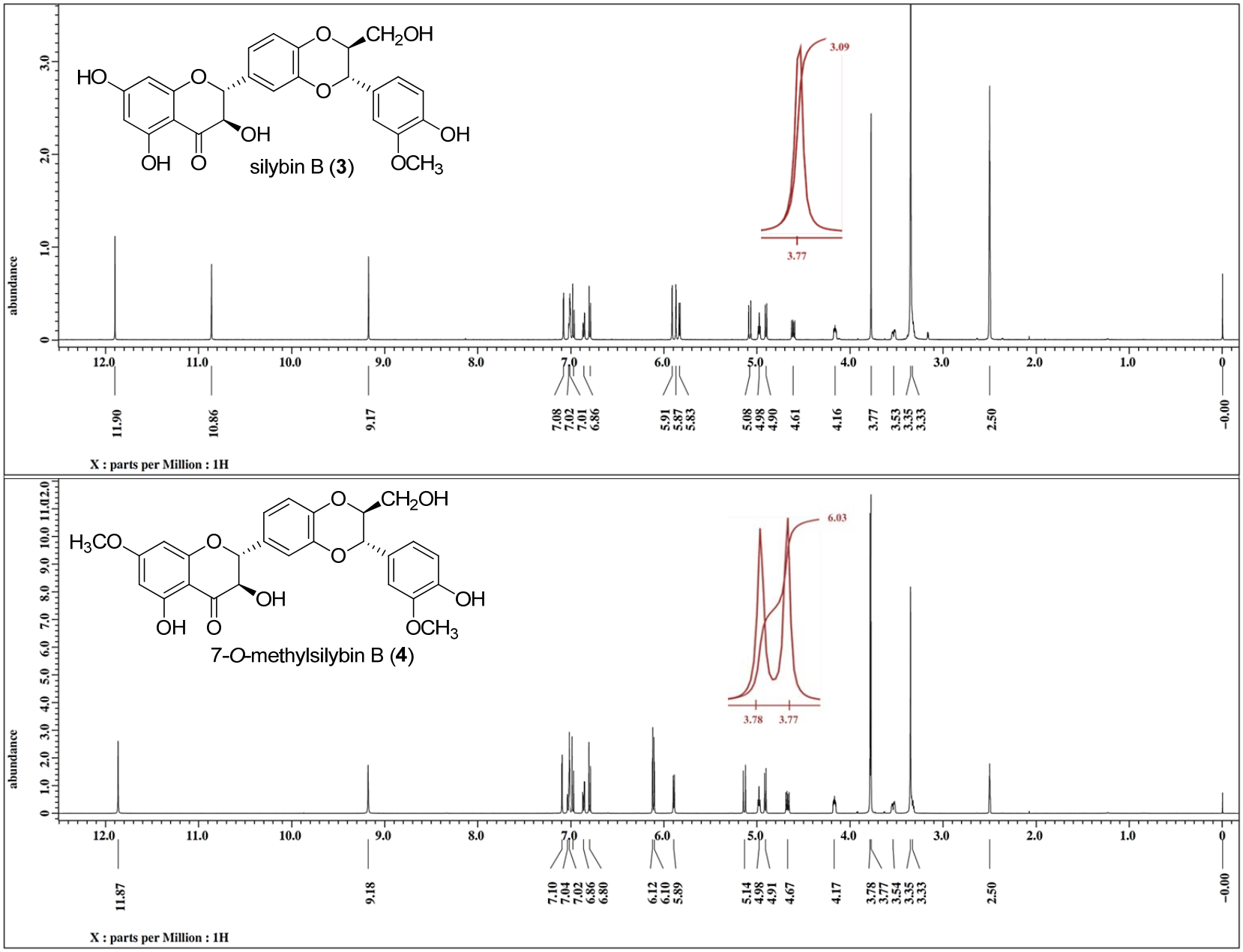


Figure S6. ^{13}C NMR spectra (125 MHz, 30°C) of silybin B (**3**) and 7-*O*-methylsilybin B (**4**) in DMSO-d_6

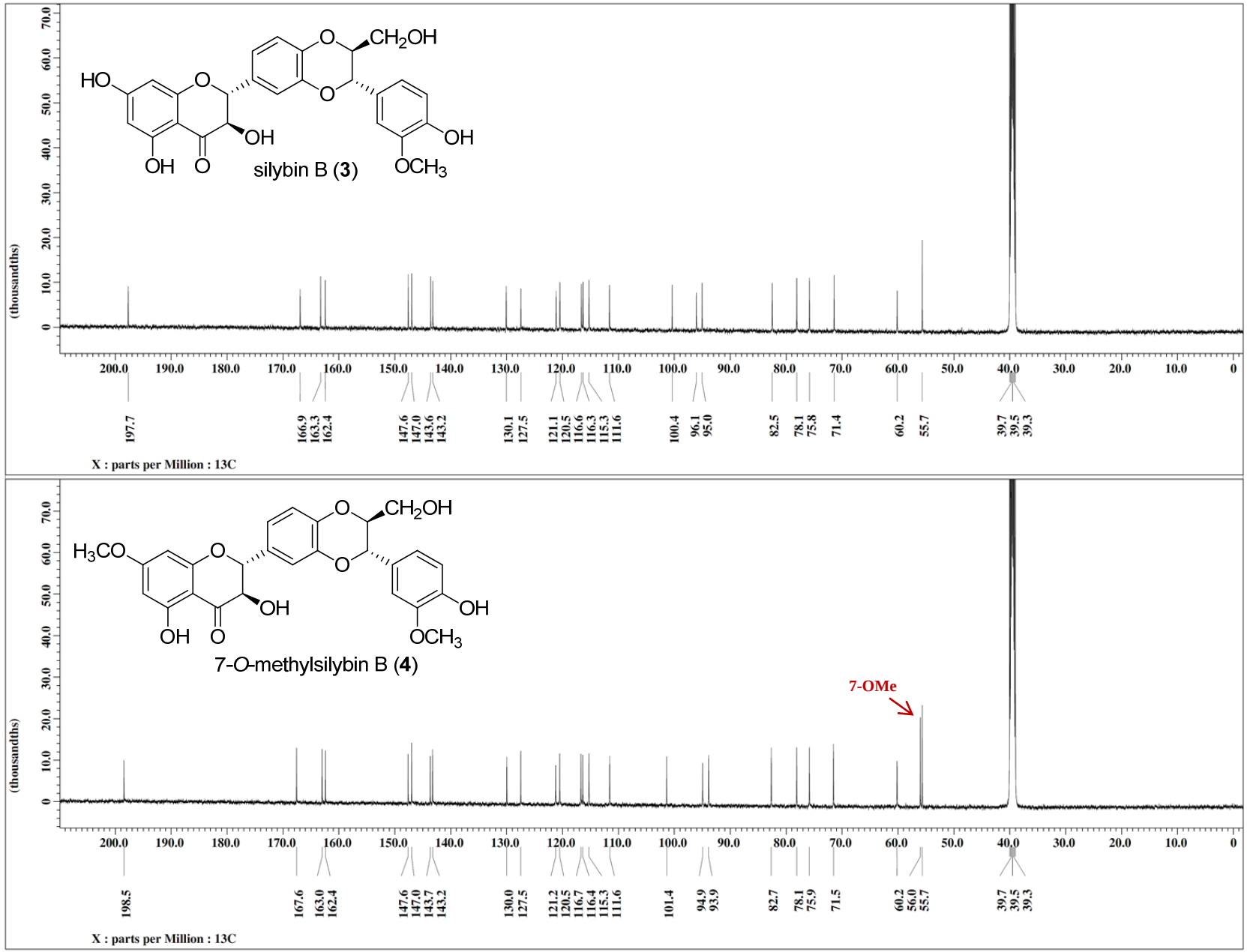


Figure S7. HMBC NMR spectrum (DMSO-d_6, 30 °C) of 7-*O*-methylsilybin B (**4**) showing the key correlation between the methoxy protons and C-7

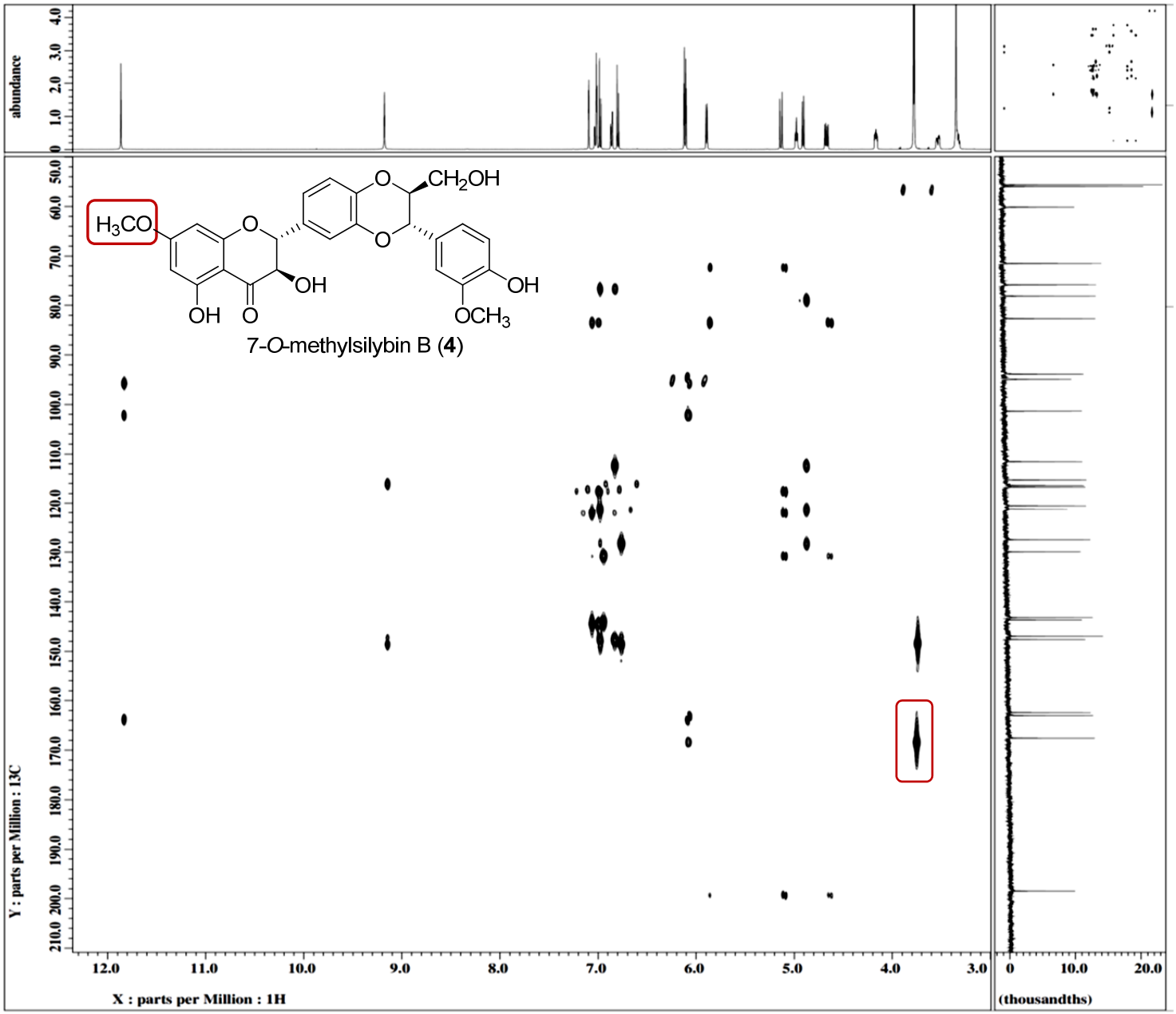


Figure S8. ^{1}H NMR spectra (500 MHz, 30 °C) of isosilybin A (**5**) and 7-*O*-methylisosilybin A (**6**) in DMSO-d_6

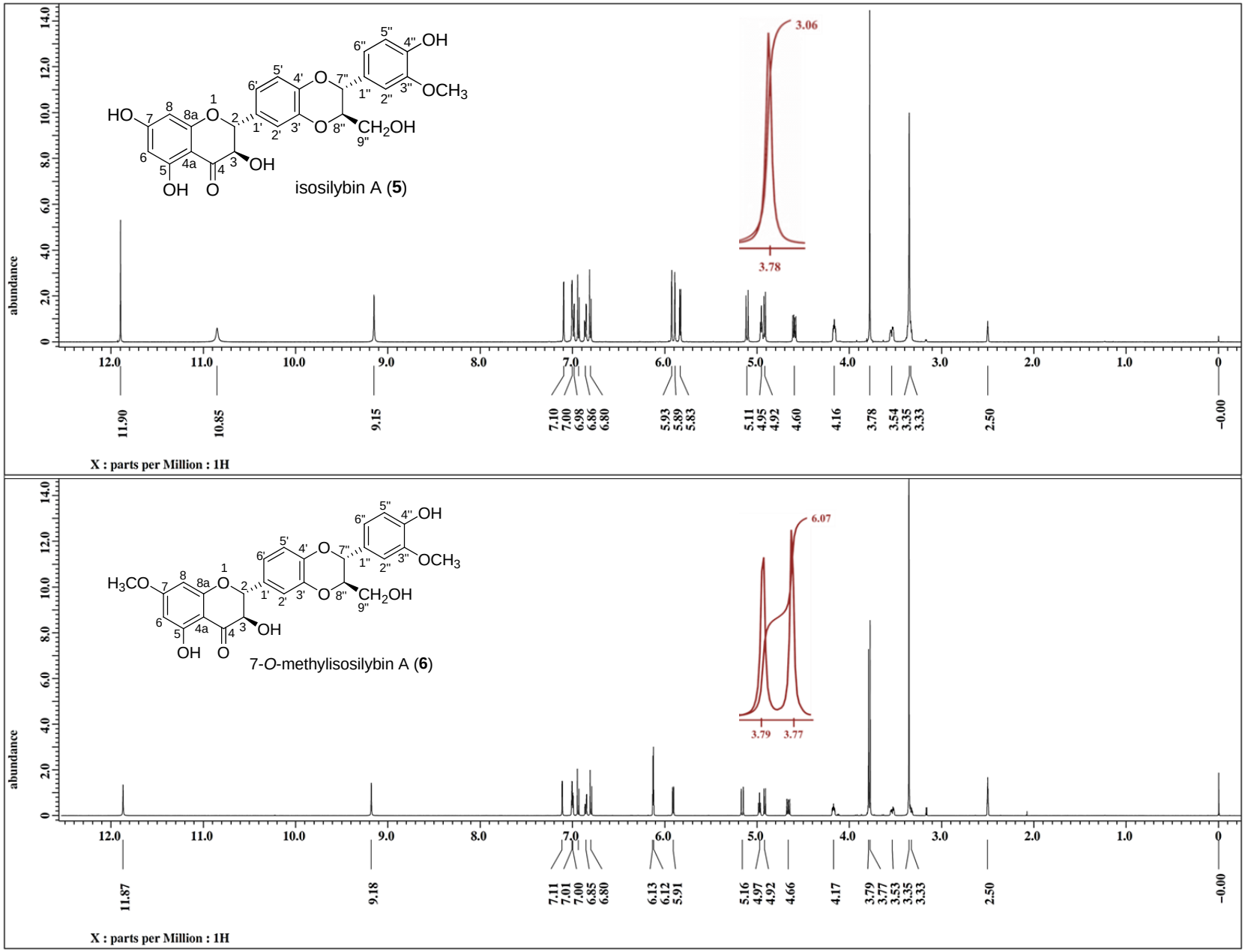


Figure S9. ^{13}C NMR spectra (125 MHz, 30°C) of isosilybin A (**5**) and 7-*O*-methylisosilybin A (**6**) in DMSO-d_6

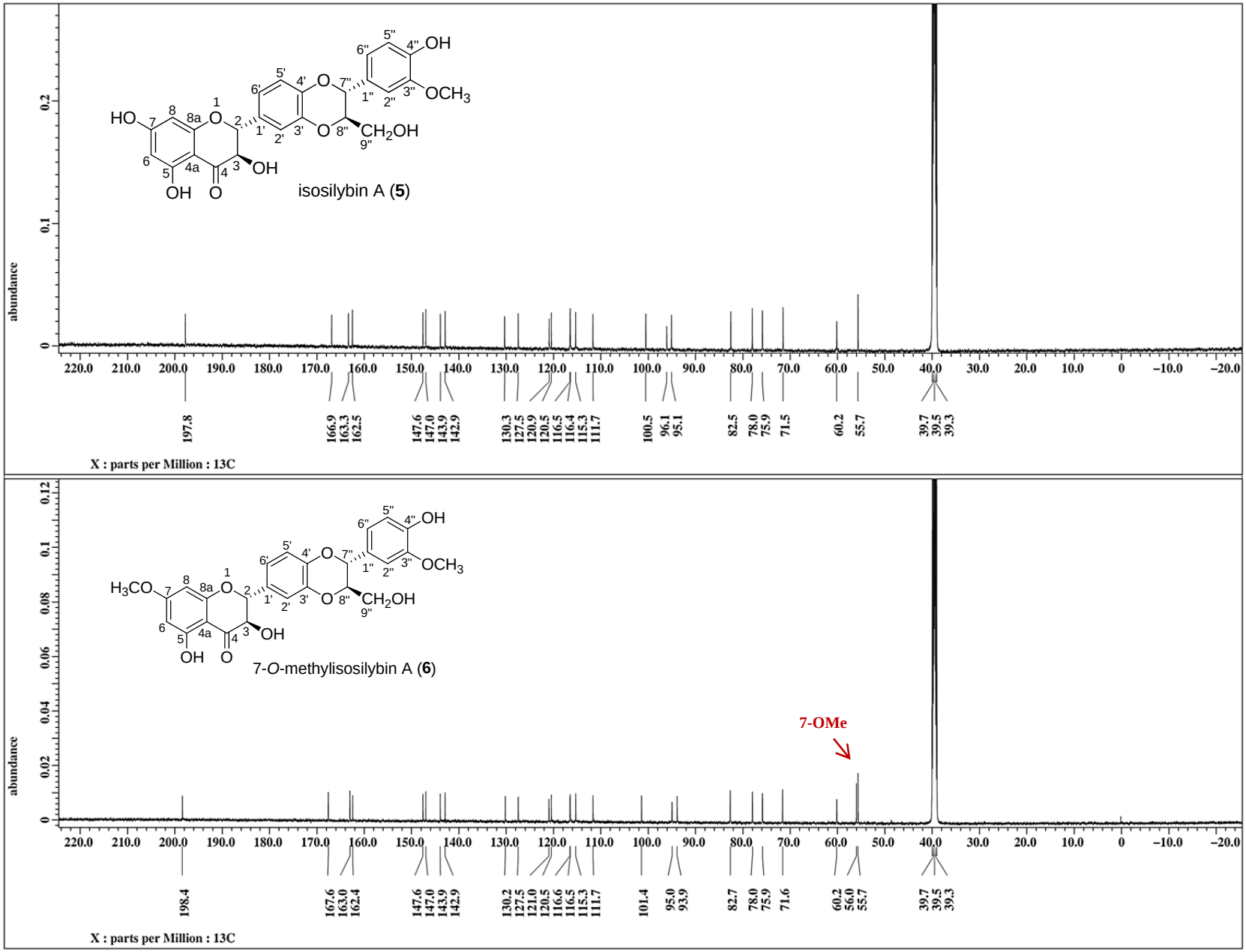


Figure S10. HMBC NMR spectrum (DMSO-d_6, 30 °C) of 7-*O*-methylisosilybin A (**6**) showing the key correlation between the methoxy protons and C-7

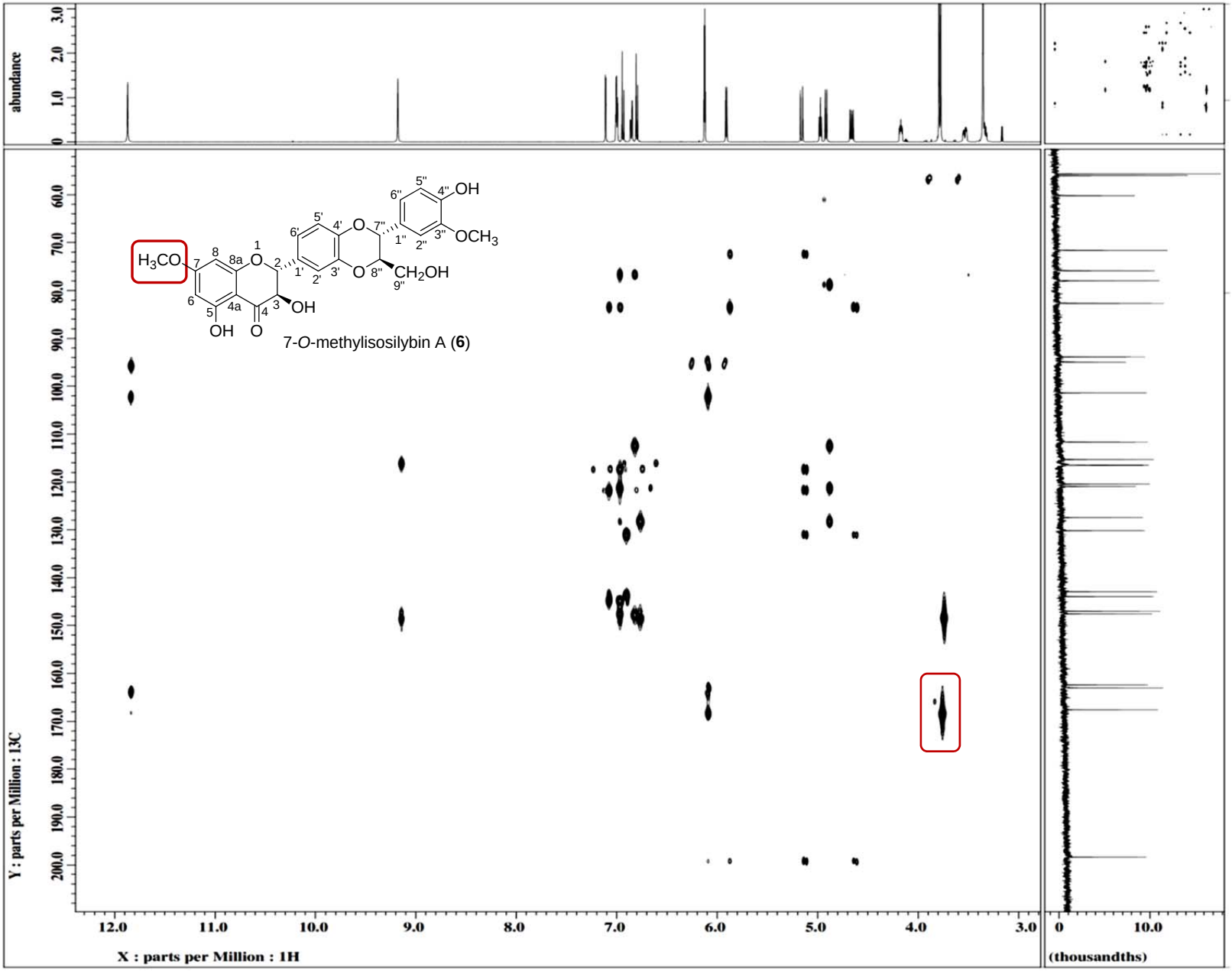


Figure S11. [1]H NMR spectra (500 MHz, 30 °C) of isosilybin B (**7**) and 7-*O*-methylisosilybin B (**8**) in DMSO-d_6

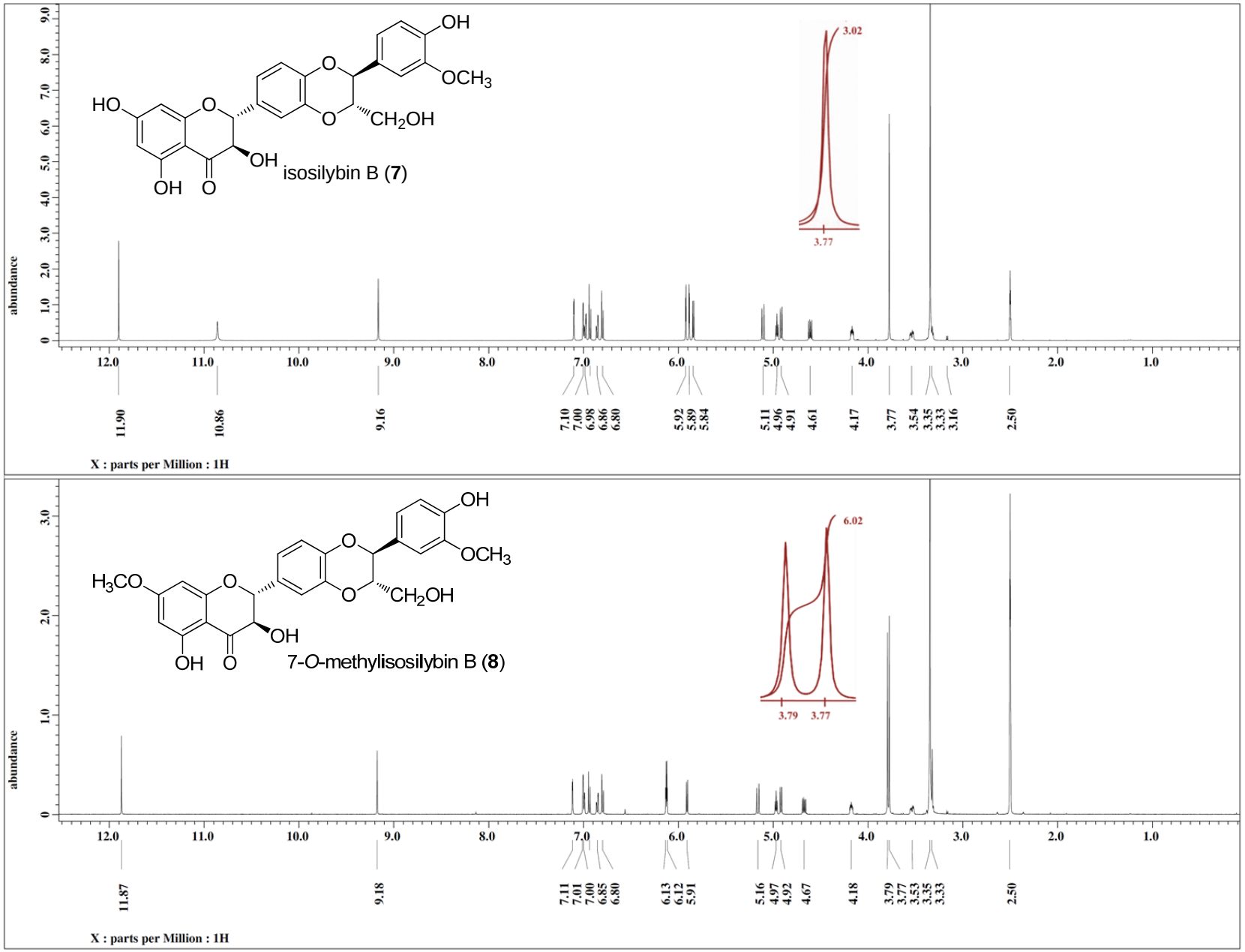


Figure S12. ^{13}C NMR spectra (125 MHz, 30 °C) of isosilybin B (**7**) and 7-*O*-methylisosilybin B (**8**) in DMSO-d_6

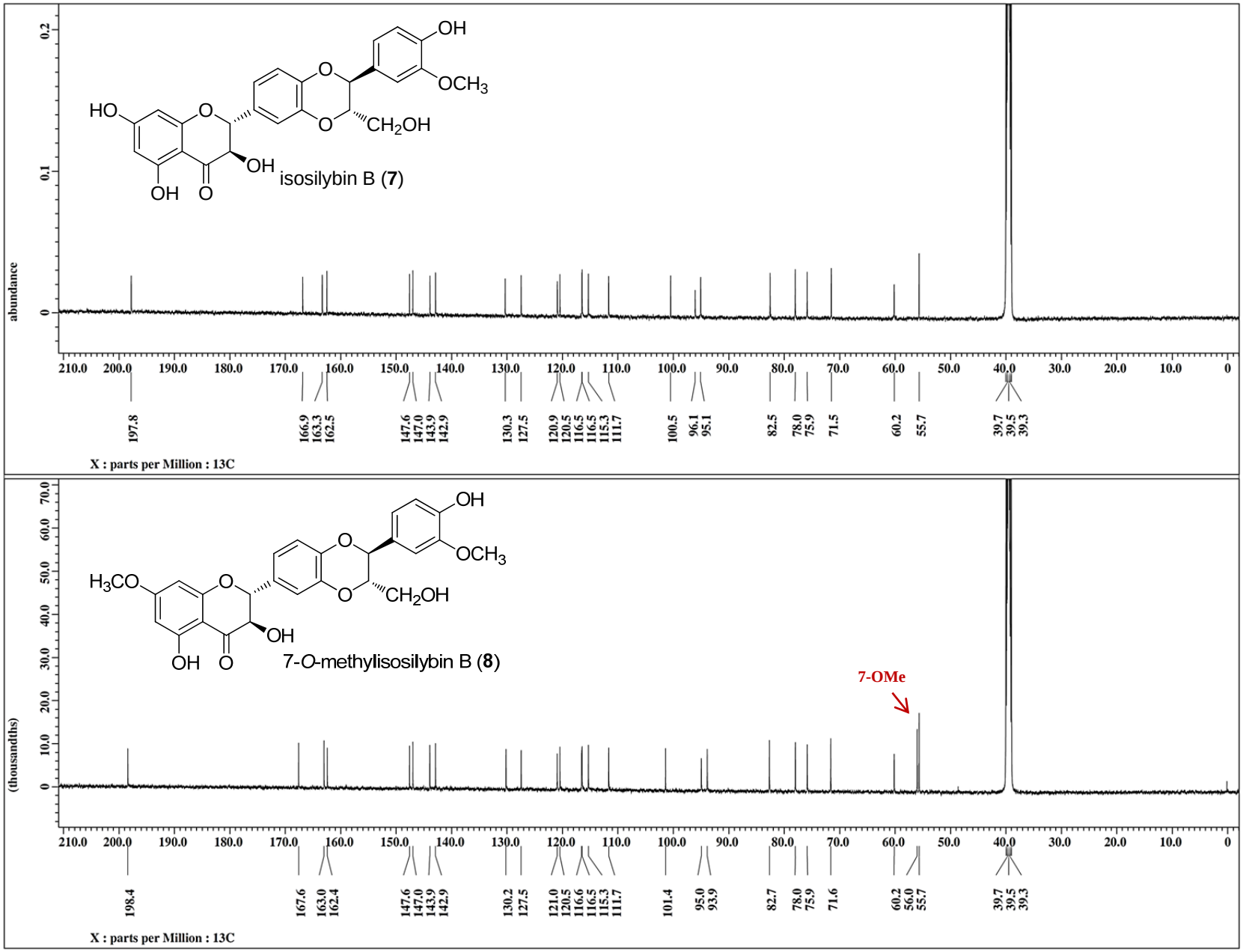


Figure S13. HMBC NMR spectrum (DMSO-d_6, 30 °C) of 7-*O*-methylisosilybin B (**8**) showing the key correlation between the methoxy protons and C-7

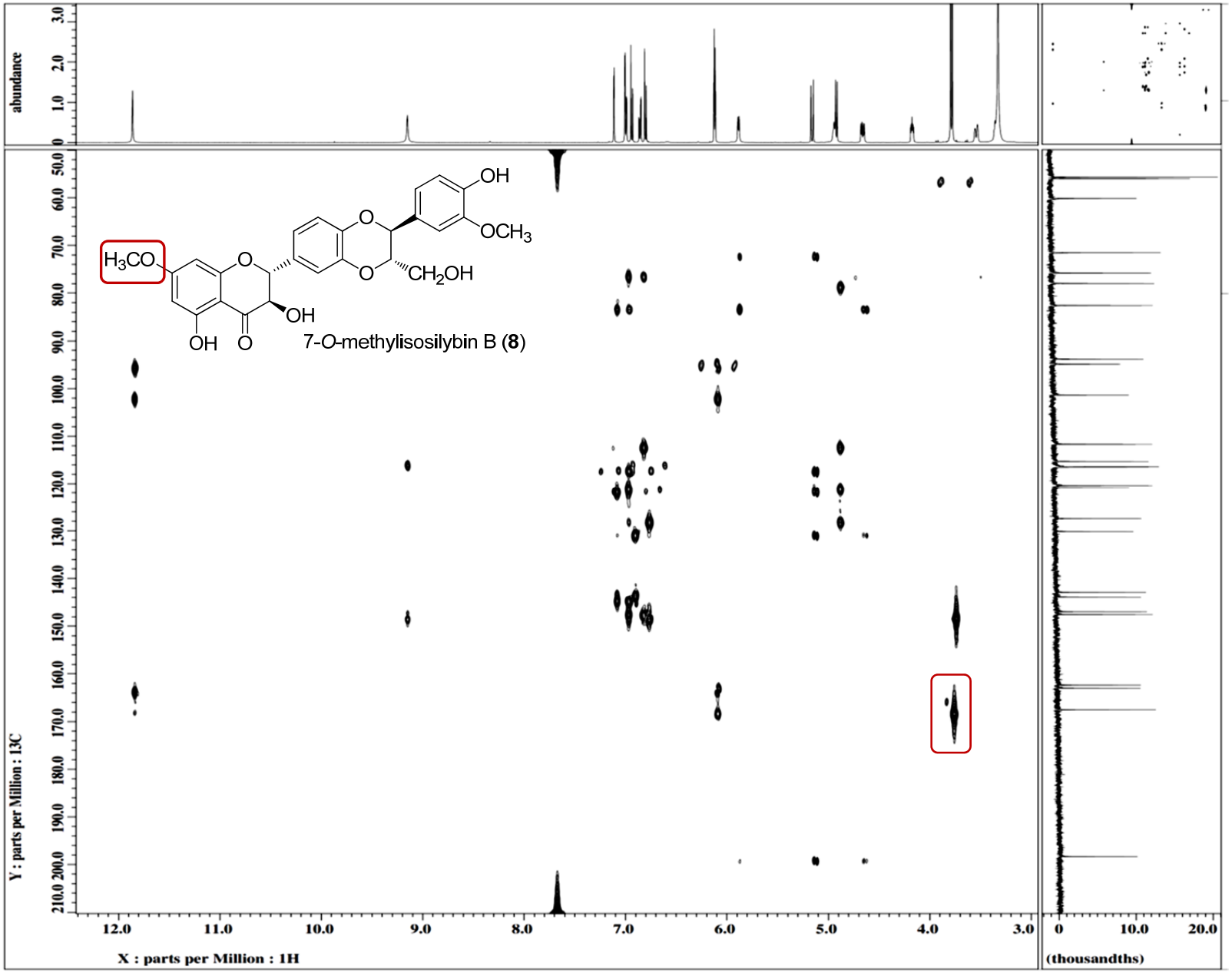


Figure S14. [1]H NMR spectra (500 MHz, 30 °C) of silychristin (**9**) and 7-*O*-methylsilychristin (**10**) in DMSO-d_6

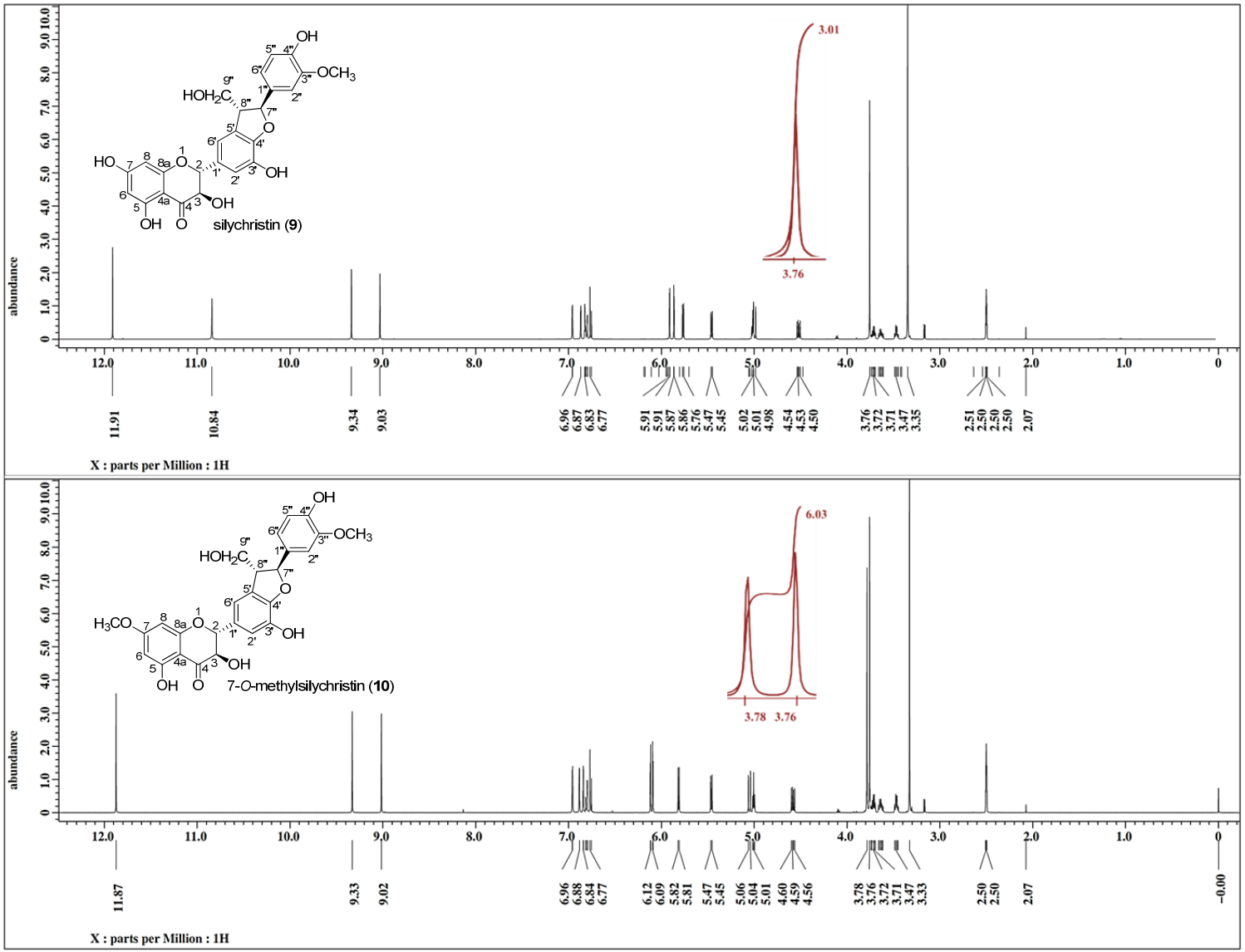


Figure S15. ^{13}C NMR spectra (125 MHz, 30 °C) of silychristin (**9**) and 7-*O*-methylsilychristin (**10**) in DMSO-d_6

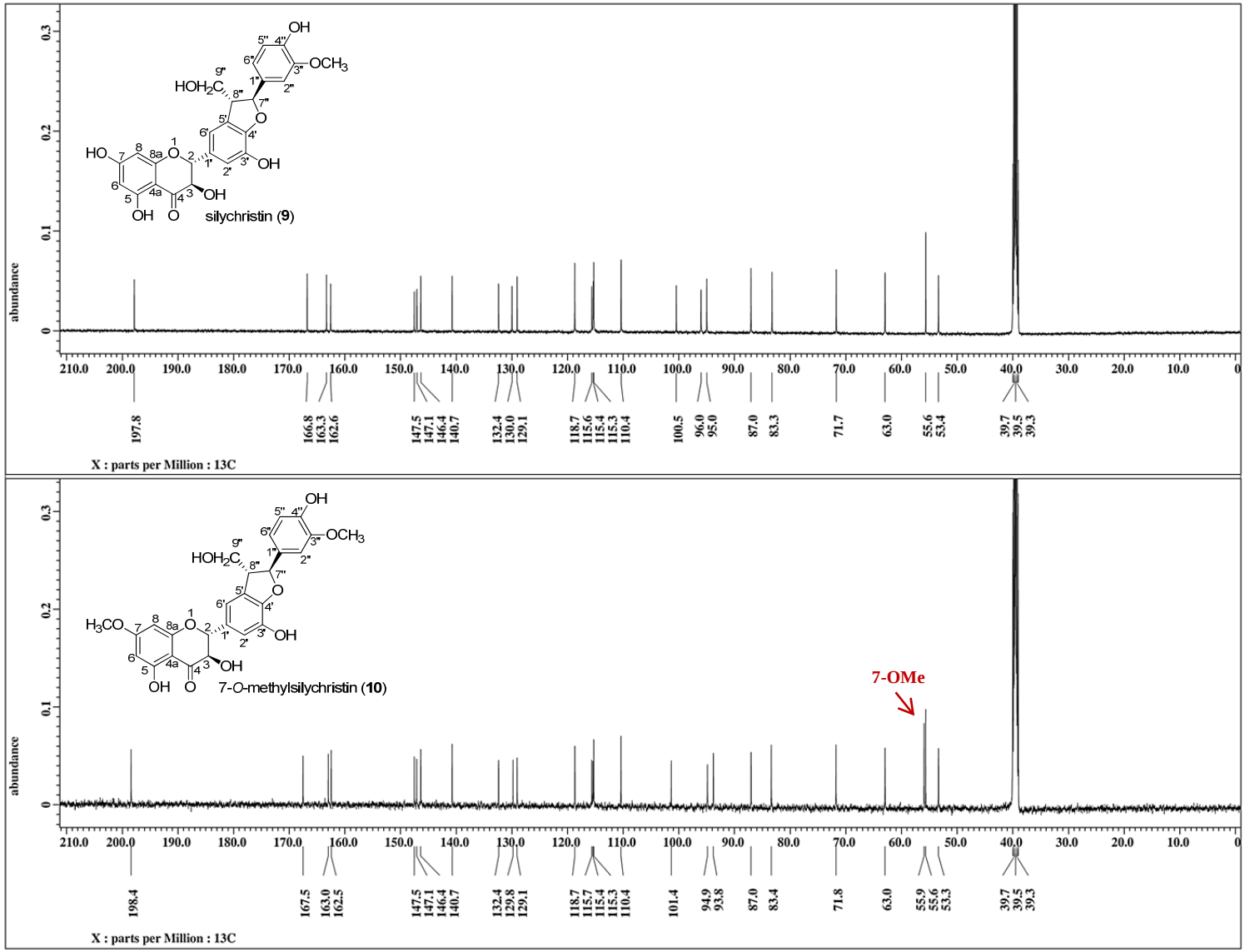


Figure S16. HMBC NMR spectrum (DMSO-d_6, 30 °C) of 7-*O*-methylsilychristin (**10**) showing the key correlation between the methoxy protons and C-7

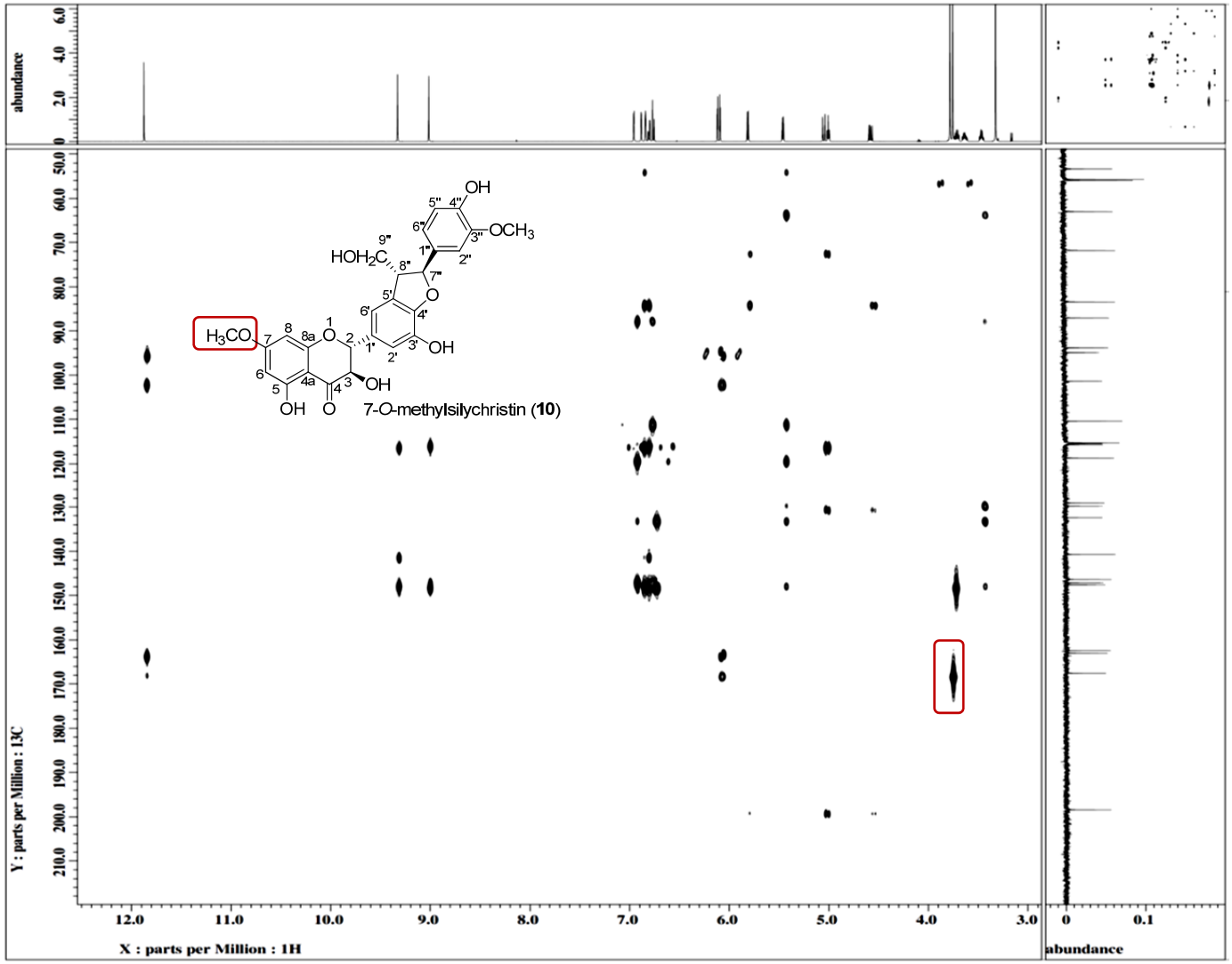


Figure S17. ^{1}H NMR spectra (500 MHz, 30 °C) of isosilychristin (**11**) and 7-*O*-methylisosilychristin (**12**) in DMSO-d_6

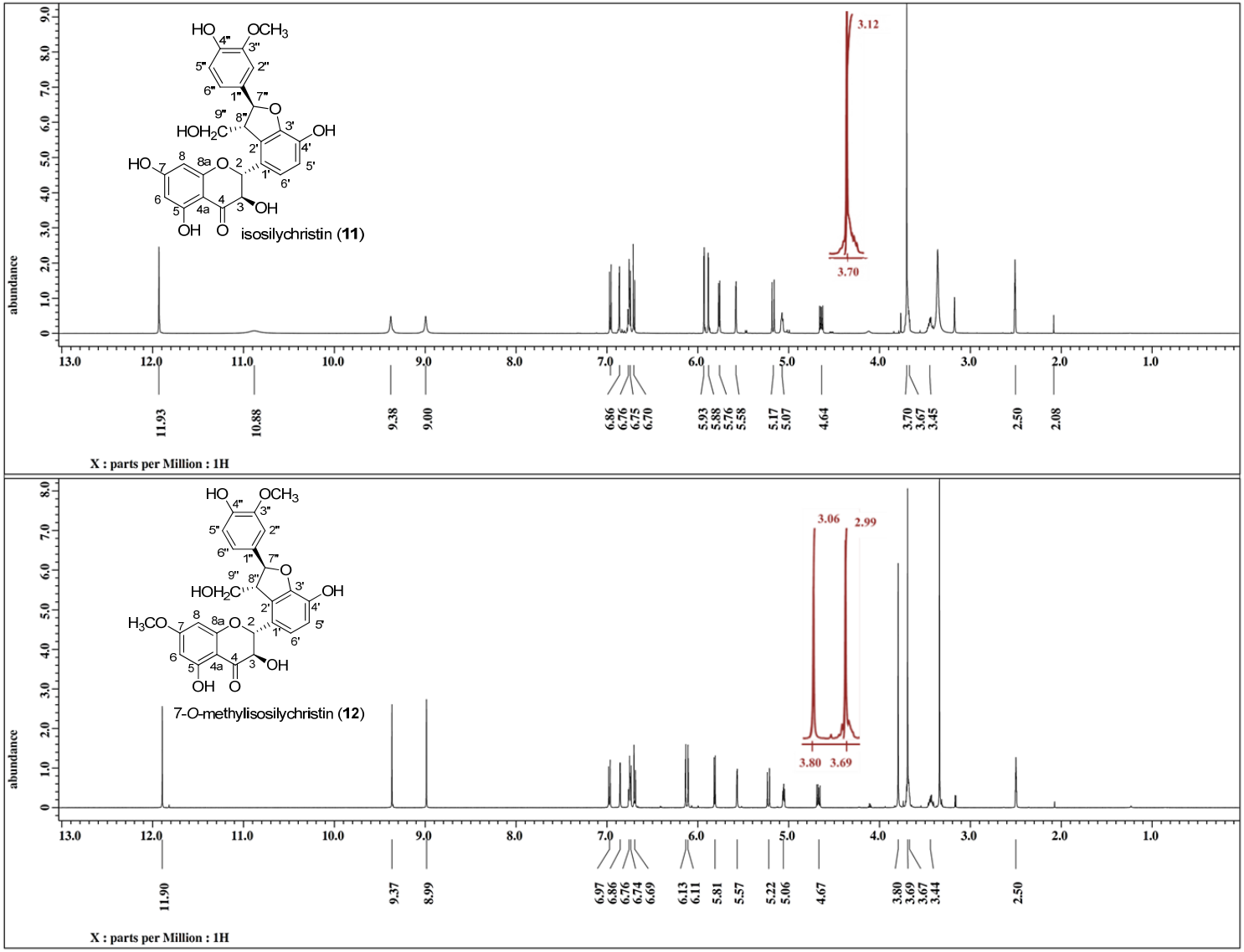


Figure S18. ^{13}C NMR spectra (125 MHz, 30°C) of isosilychristin (**11**) and 7-*O*-methylisosilychristin (**12**) in DMSO-d_6

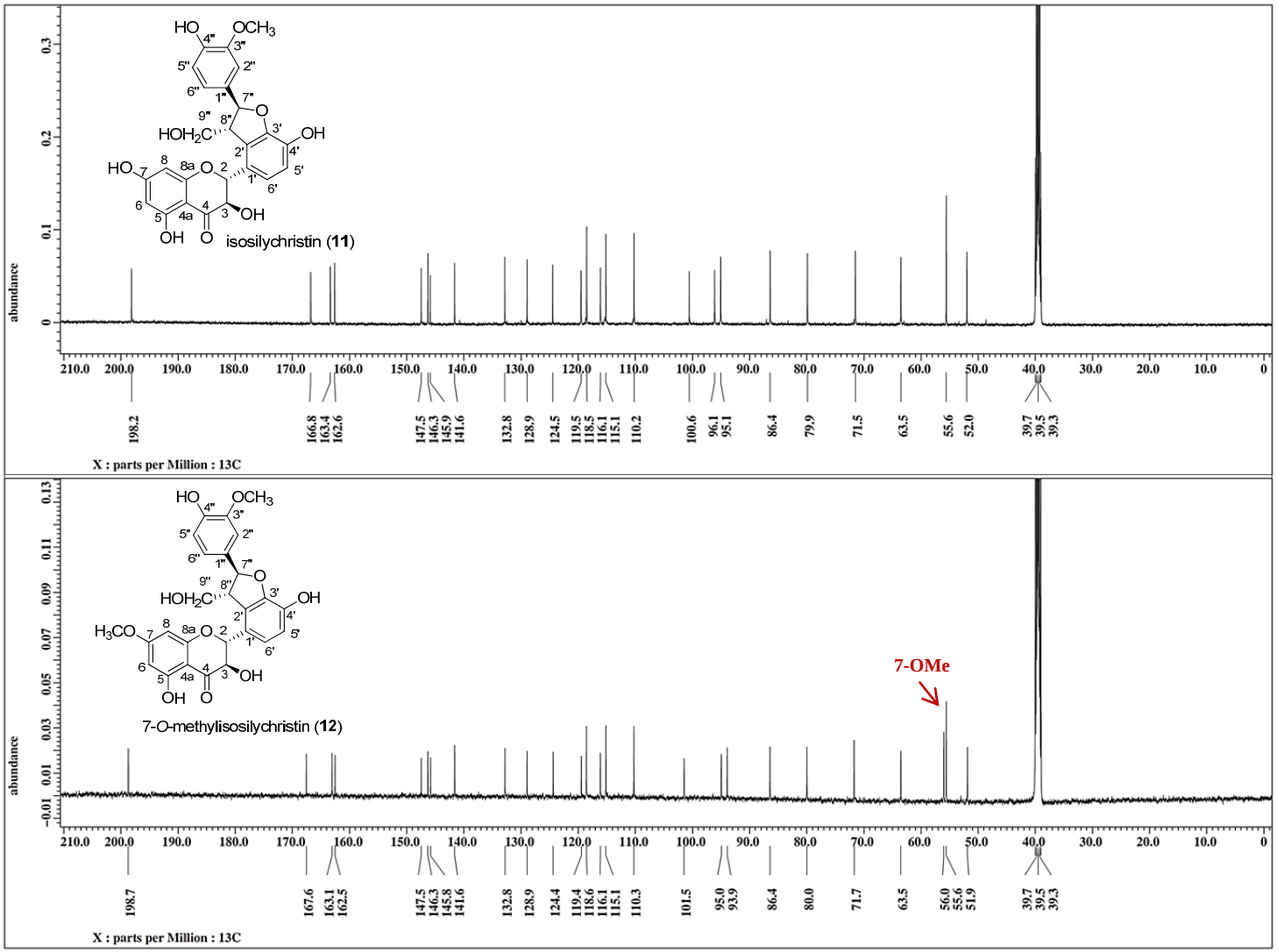


Figure S19. HMBC NMR spectrum (DMSO-d_6, 30 °C) of 7-*O*-methylisosilychristin (**12**) showing the key correlation between the methoxy protons and C-7

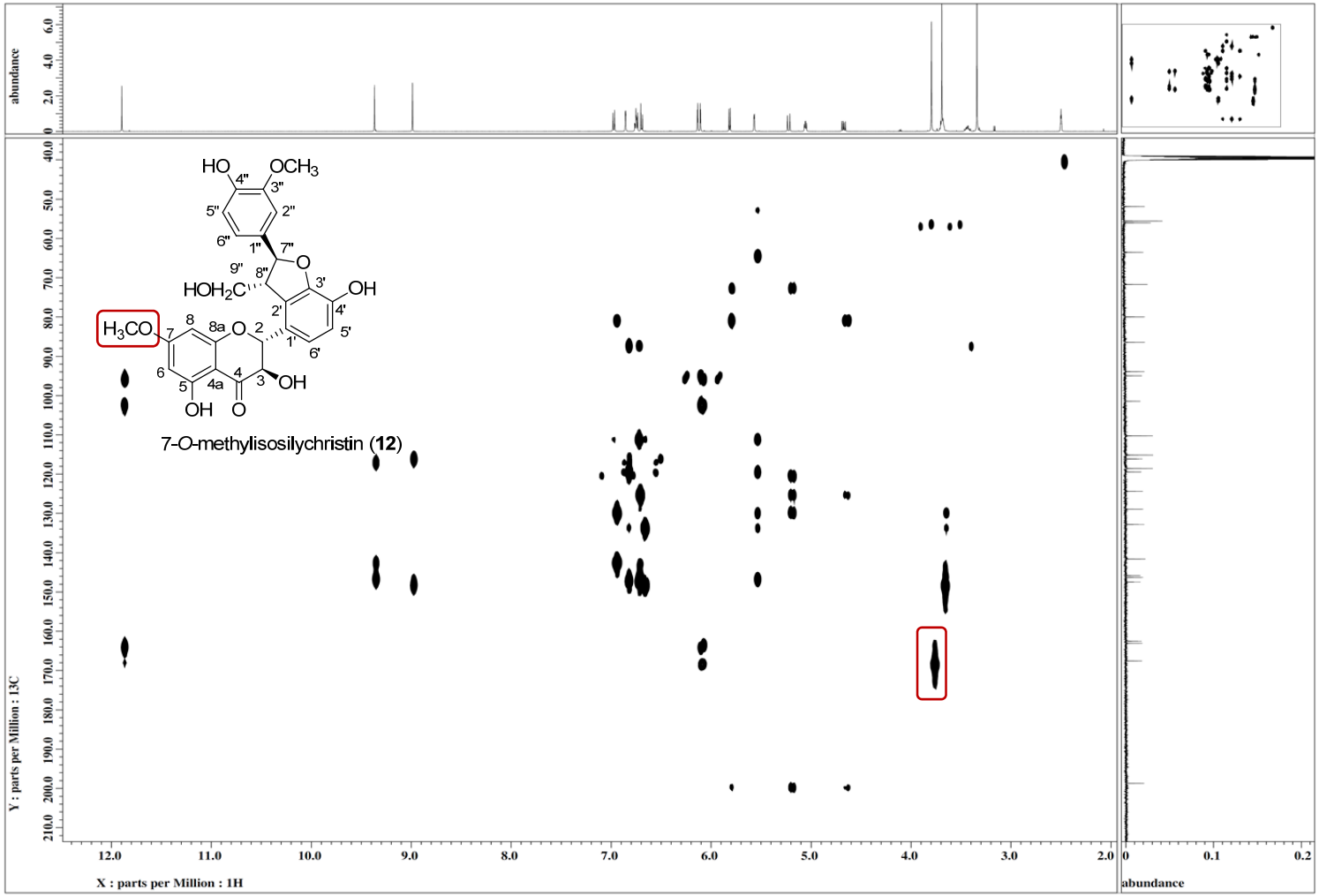


Figure S20. ^{1}H NMR spectra (500 MHz, 30 °C) of silydianin (**13**) and 7-*O*-methylsilydianin (**14**) in DMSO-d_6

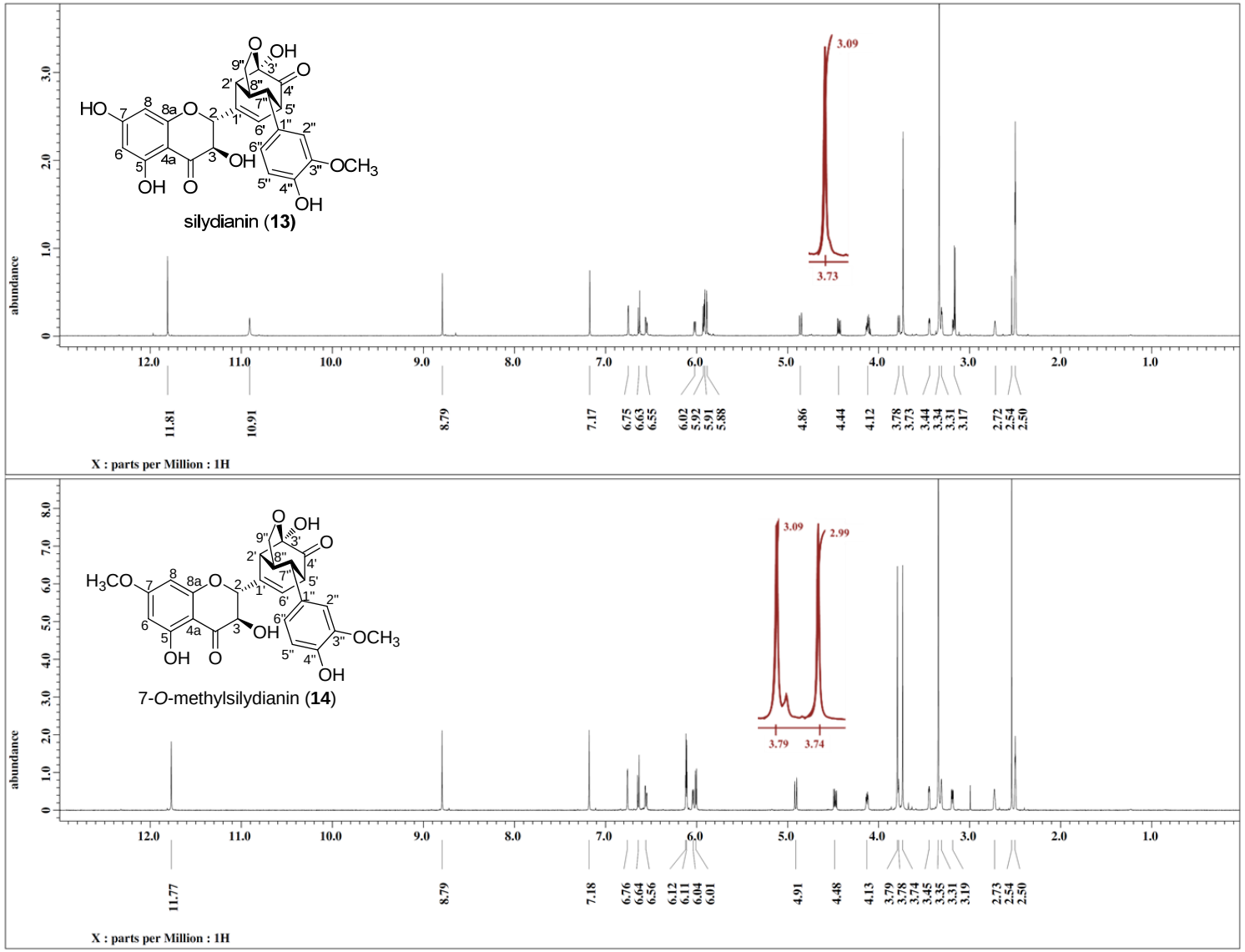


Figure S21. ^{13}C NMR spectra (125 MHz, 30 °C) of silydianin (**13**) and 7-*O*-methylsilydianin (**14**) in DMSO-d_6

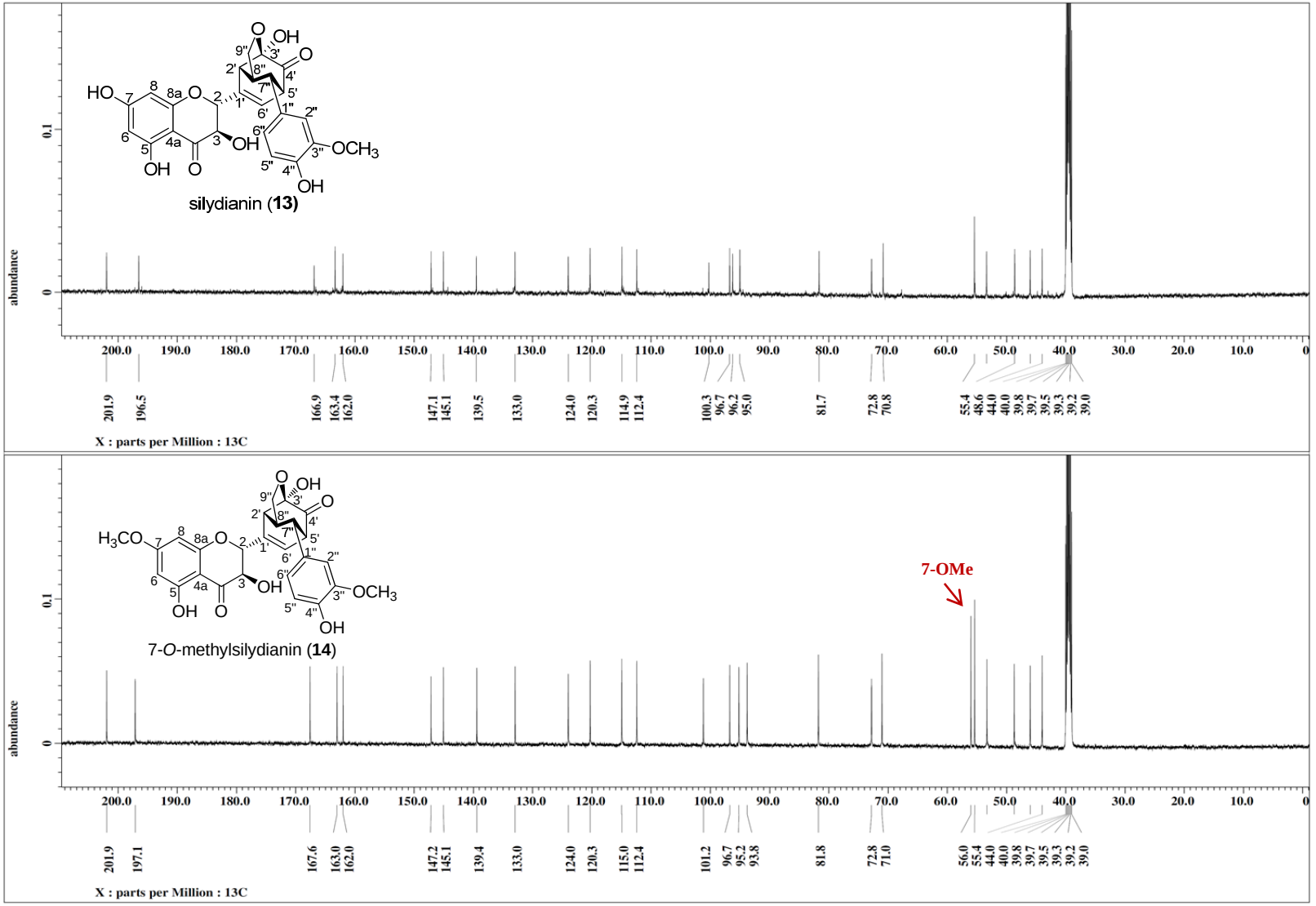


Figure S22. HMBC NMR spectrum (DMSO-d_6, 30 °C) of 7-*O*-methylsilydianin (**14**) showing the key correlation between the methoxy protons and C-7

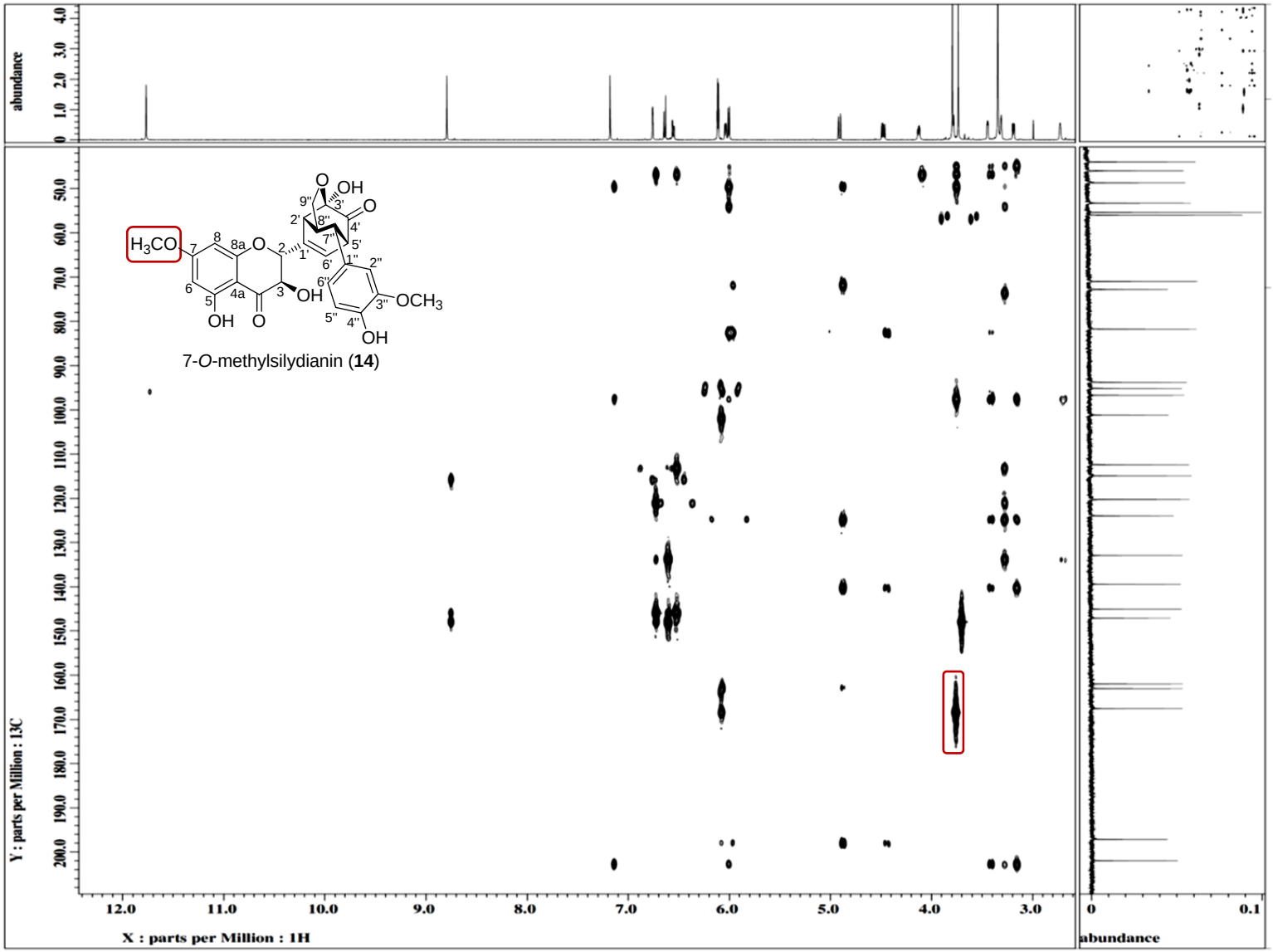
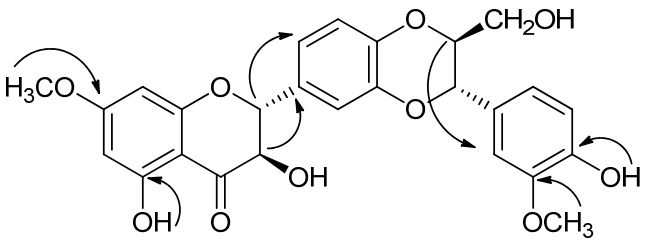
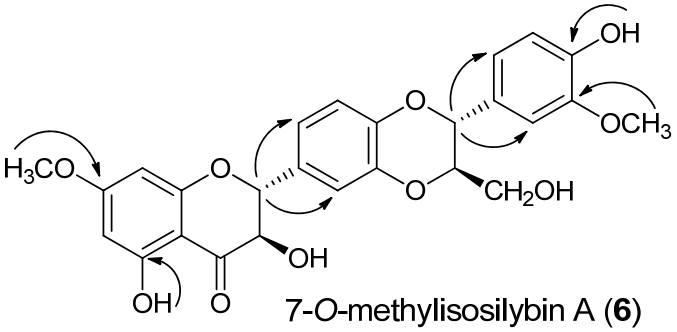


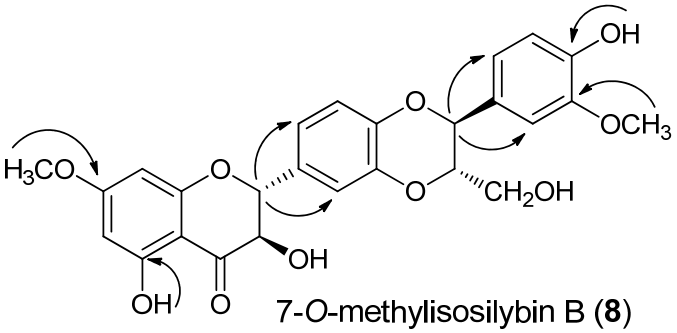
Figure S23. Key HMBC correlations of 7-*O*-methylflavonolignans



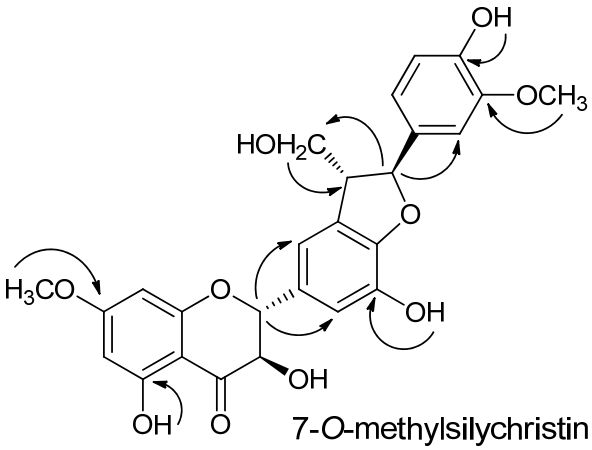
7-*O*-methylsilybin B (**4**)



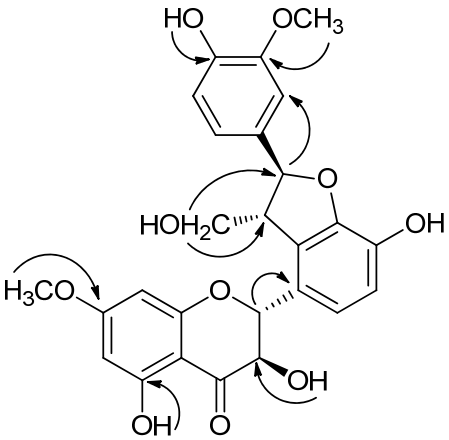
7-*O*-methylisosilybin A (**6**)



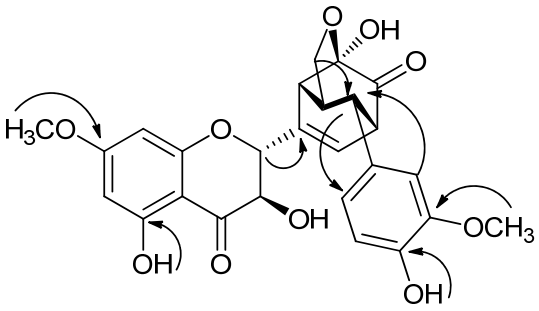
7-*O*-methylisosilybin B (**8**)



7-*O*-methylsilychristin (**10**)



7-*O*-methylisosilychristin (**12**)



7-*O*-methylsilydianin (**14**)