Electronic Supplementary Material (ESI) for RSC Advances.

Quantification of crystallinity during indomethacin crystalline trans-formation from α- to γ-polymorphic forms and of the thermody-namic contribution to dissolution in aqueous buffer and solutions of solubilizer

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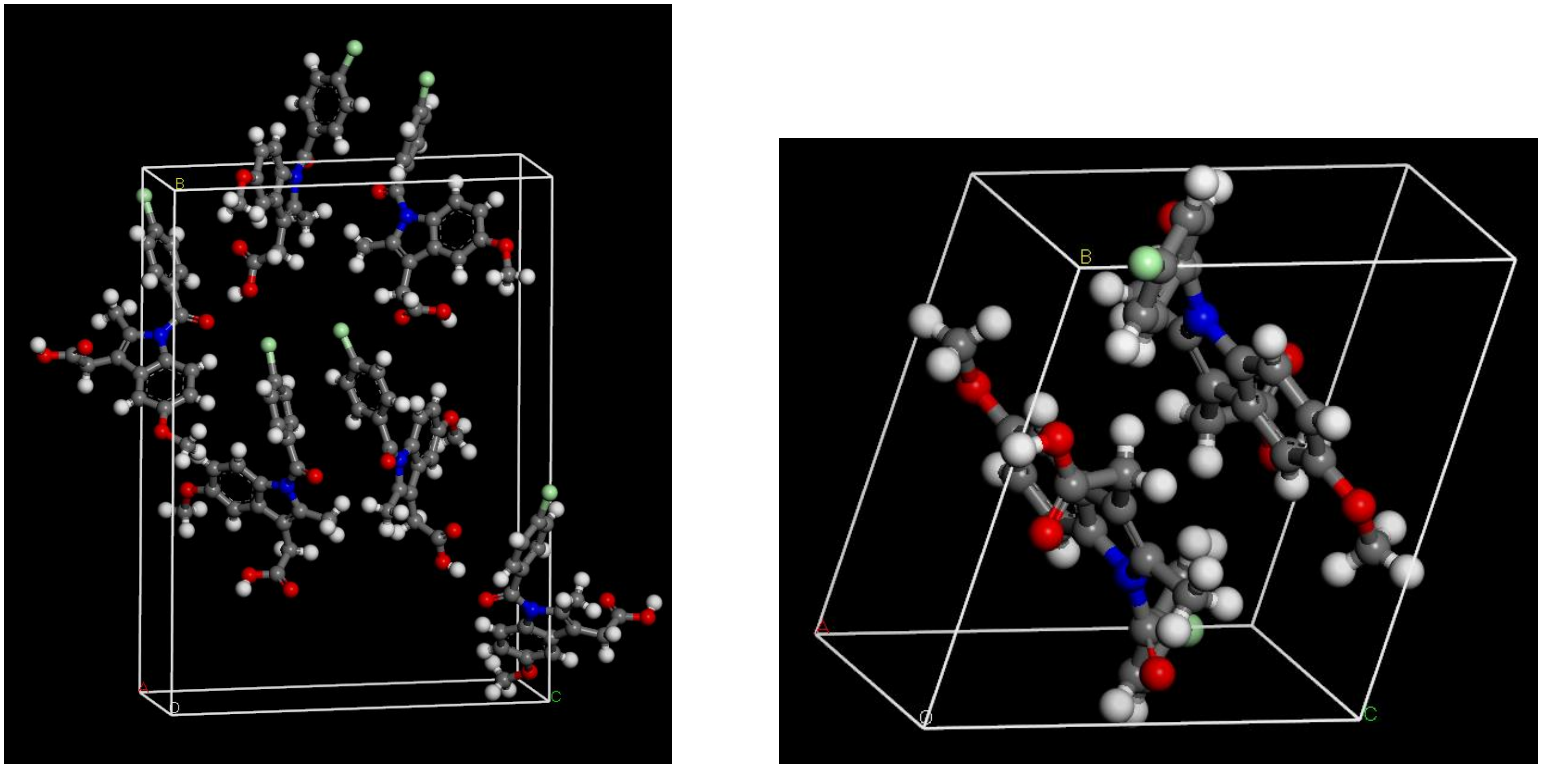
Supporting Information



Scheme S1. The three-dimensional structure of INM; α-form (left) and γ-form (right).

Table S1. Unique XRPD peak positions, C=O stretching modes, and melting point.

	XRPD	ATR-FTIR	DSC
solid-state form	unique peak position (2θ /°)	C=O stretch (cm^{-1})	T_m (K)
α form	6.92, 8.46, 14.54	1734, 1680, 1689, 1649	425.8 ± 0.4
γ form	11.64, 12.76, 16.74, 21.88	1713, 1690	433.4 ± 0.5

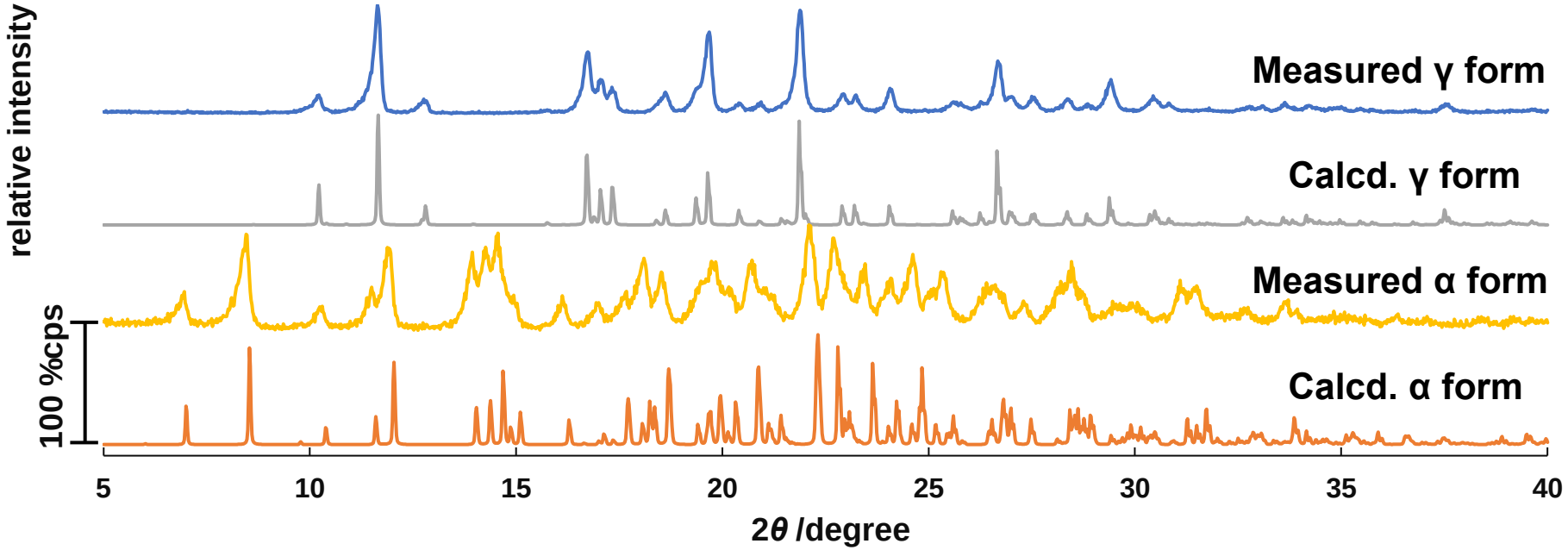
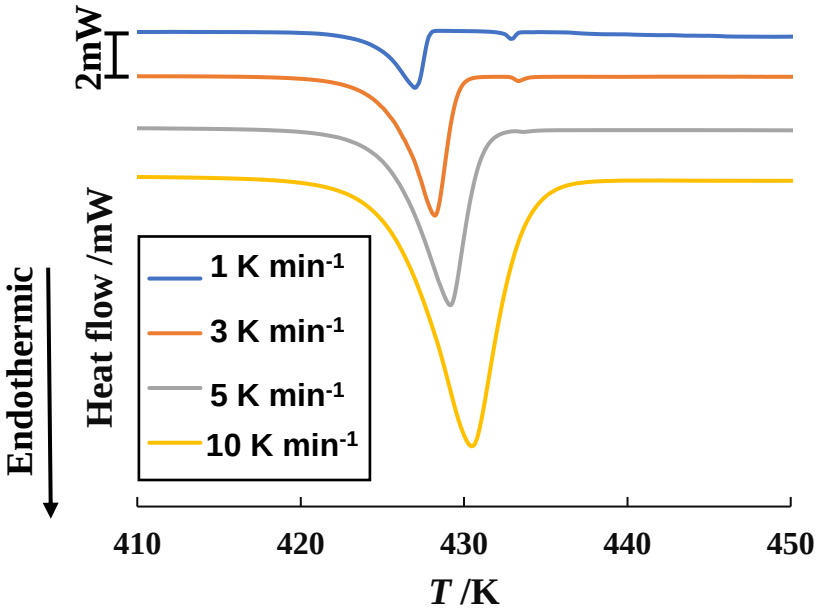


Figure S1. XRPD diffractograms and diffractograms calculated from the CCDC of α- and γ-forms.

(a)



(b)

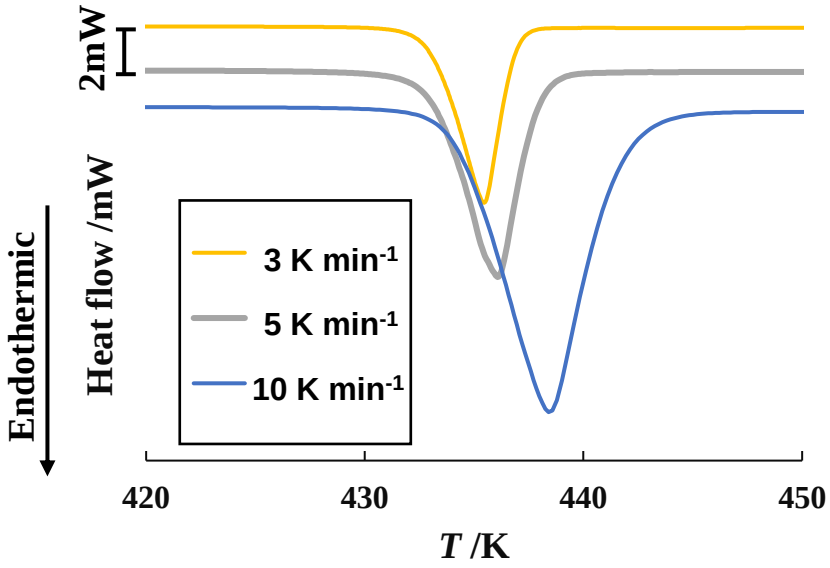


Figure S2. Differential scanning calorimetry (DSC) of INM crystals at various heating rates; α-form (a) and γ-form (b).

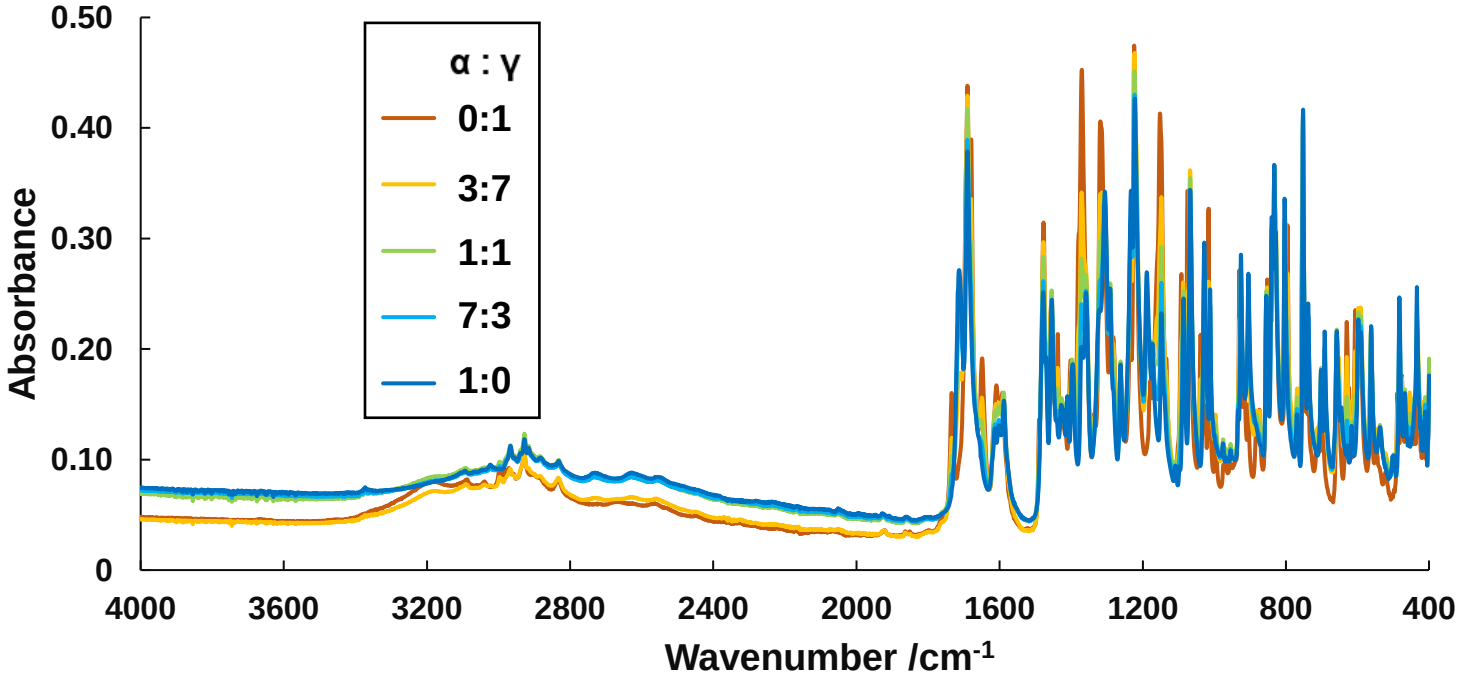


Figure S3. IR spectra of α- and γ-forms displayed in full range.

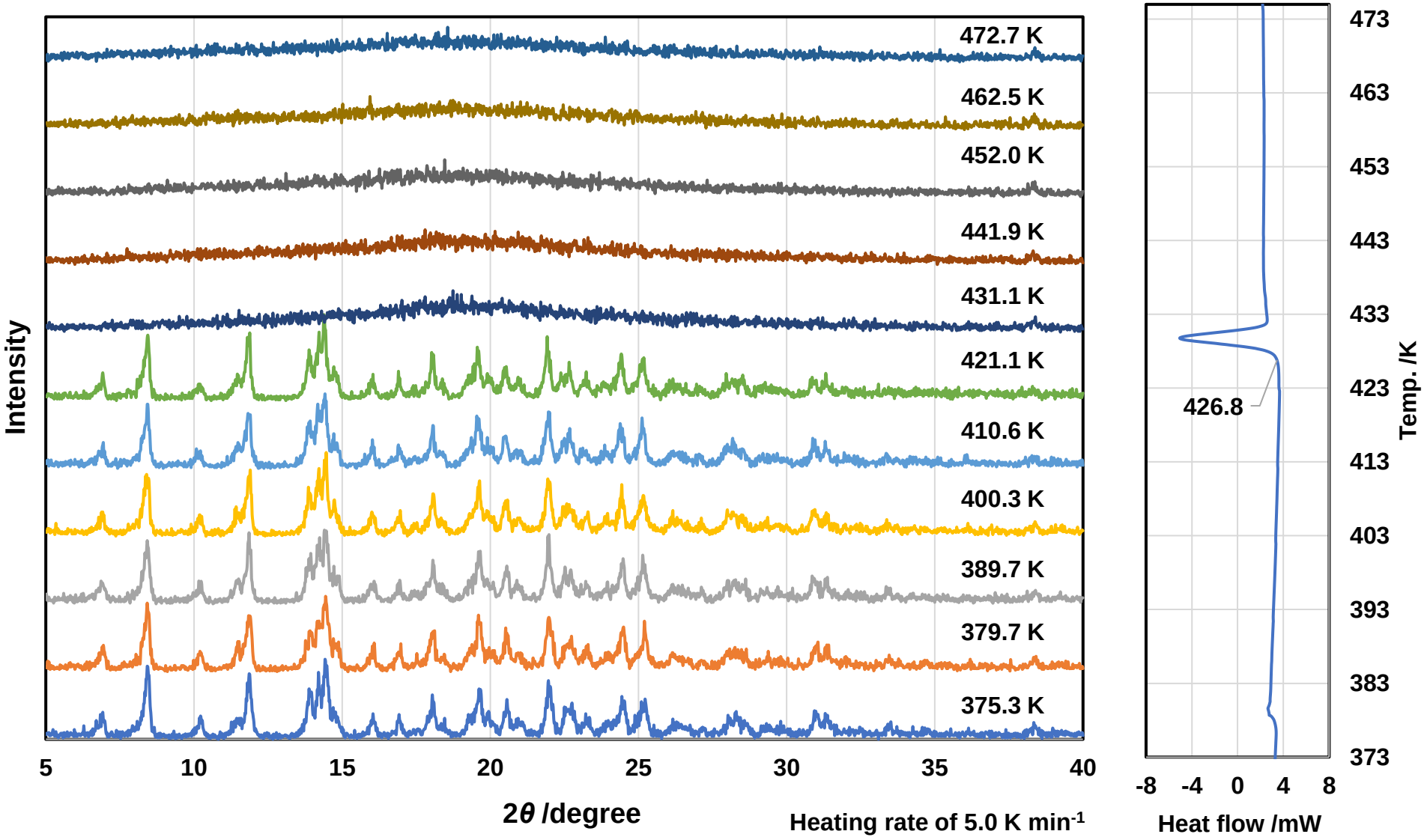


Figure S4 (a) The simultaneous DSC-XRD measurement of α-form of INM at heating rate of 5.0 K min^{-1}. XRD legend indicates starting temperature of measurement. An endothermic peak associated with α-form melting was observed from 426.8 K.

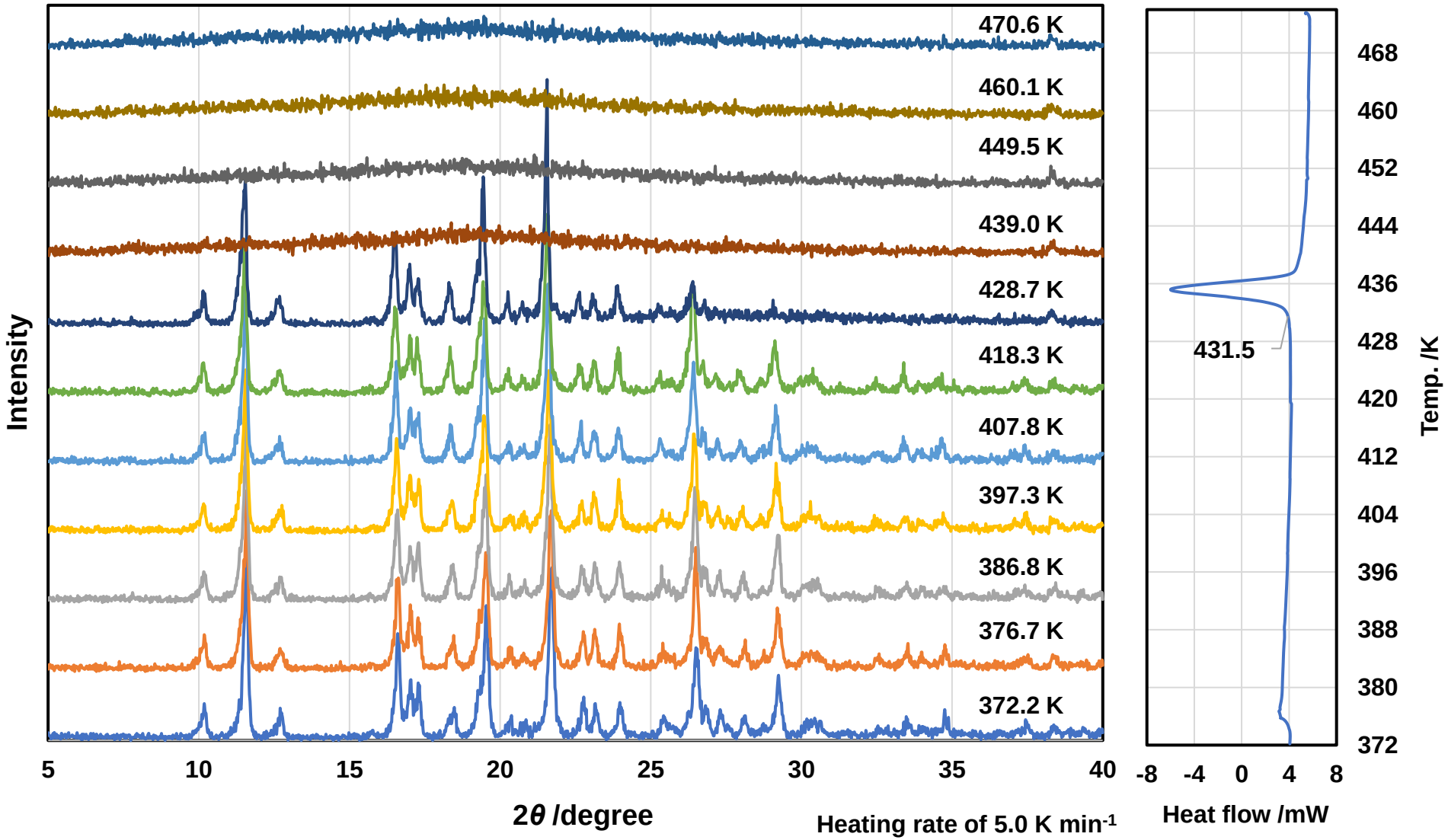


Figure S4 (b) The simultaneous DSC-XRD measurement of γ-form of INM at heating rate of 5.0 K min^{-1}. An endothermic peak associated with α-form melting was observed from 431.5 K.

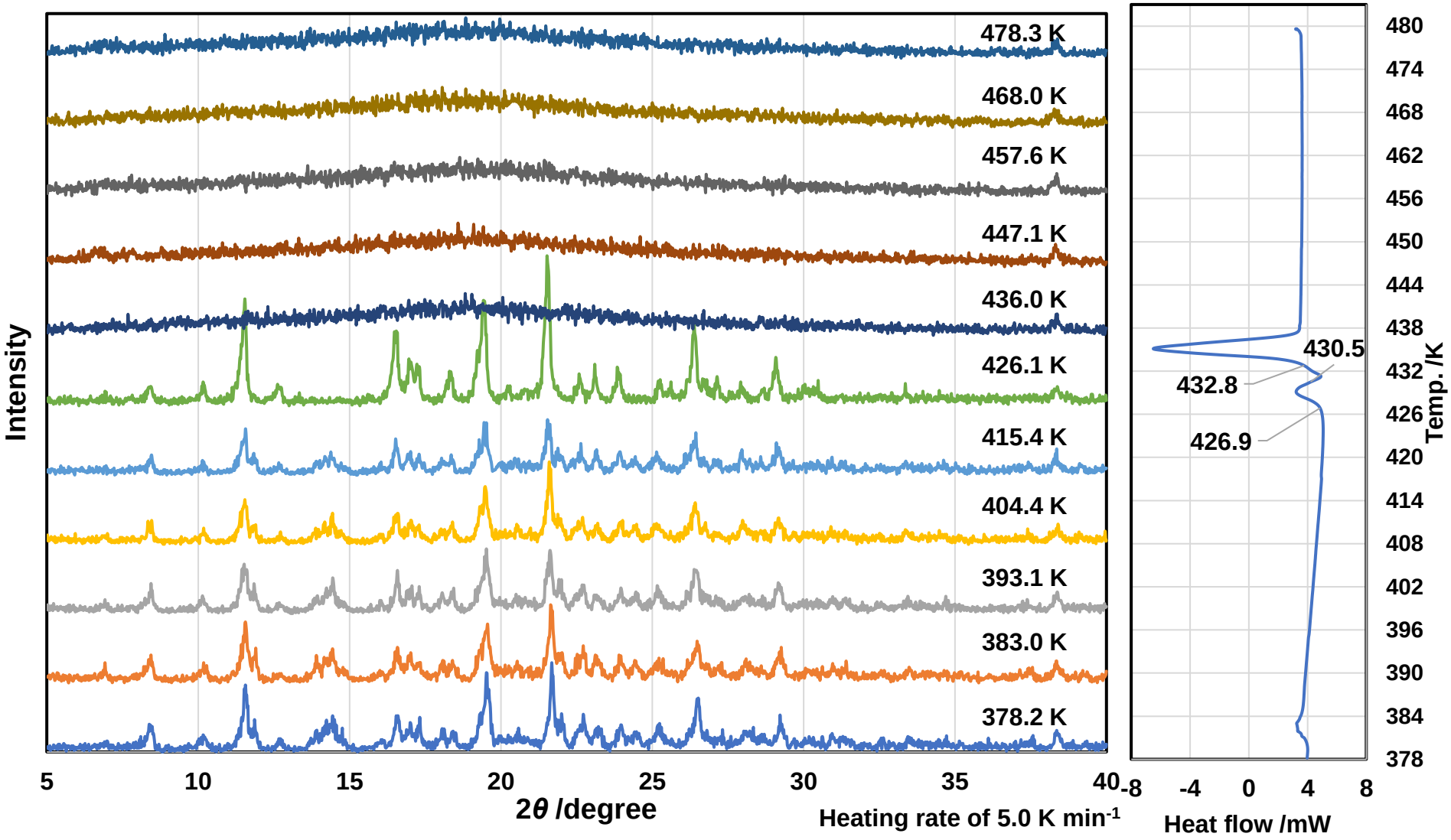


Figure S4 (c) The simultaneous DSC-XRD measurement of mixture of α-INM : γ-INM=1:1 at heating rate of 5.0 K min^{-1}. The fusion of the α-form is shown at 426.9 K. An exothermic peak was observed at 430.5 K. The fusion of the γ-form is shown at 432.8 K.

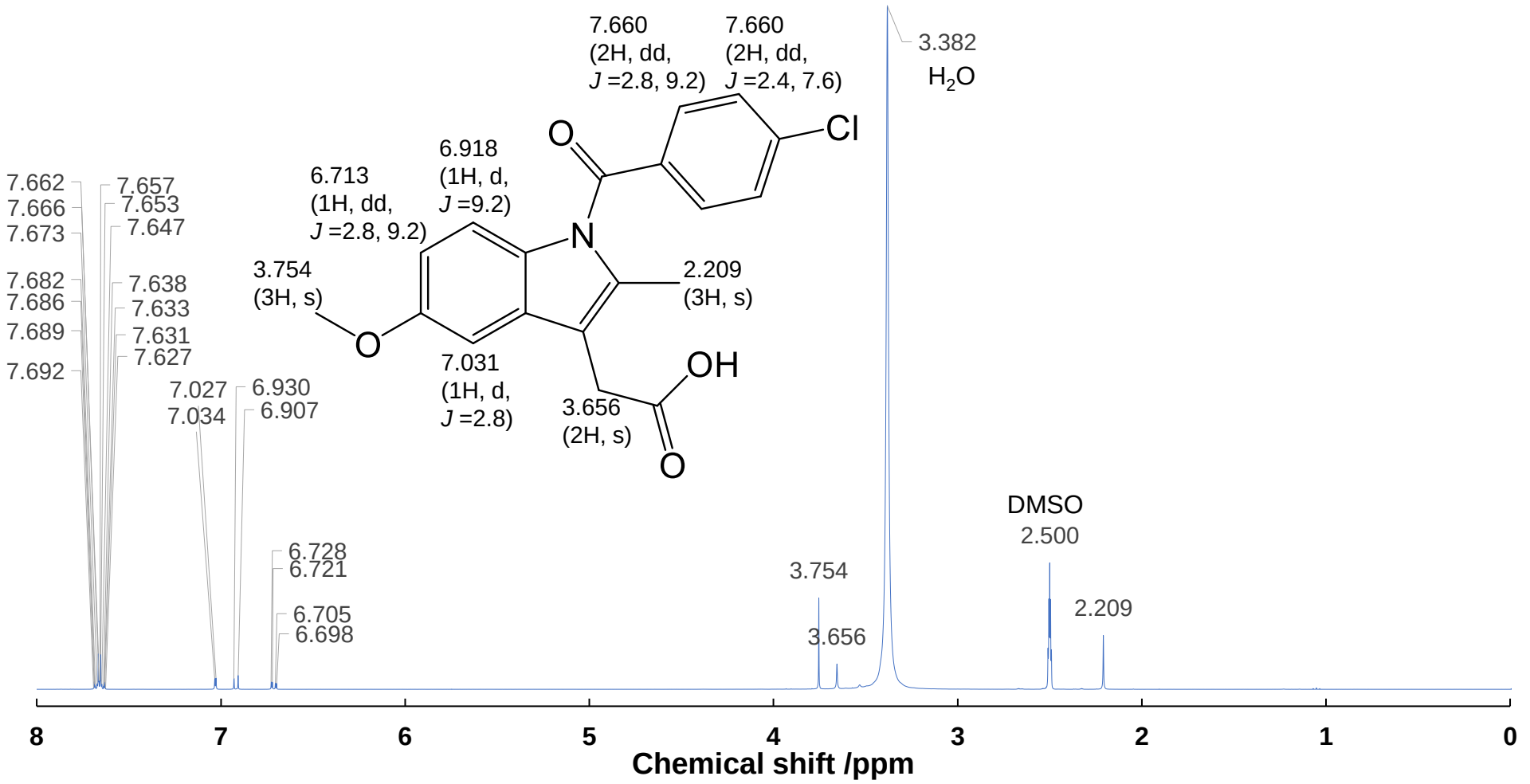


Figure S5(A) The ^{1}H-NMR (400 MHz , DMSO-d_6 at 2.500 ppm) spectrum of the precipitate after shaking α-form of INM in 25 mM KH_2PO_4/Na_2HPO_4 buffer (pH 6.8). Chemical shifts are listed at the assigned positions in the chemical structural formulas. The number of protons, coupling, and spin-spin coupling constants are shown in parentheses.

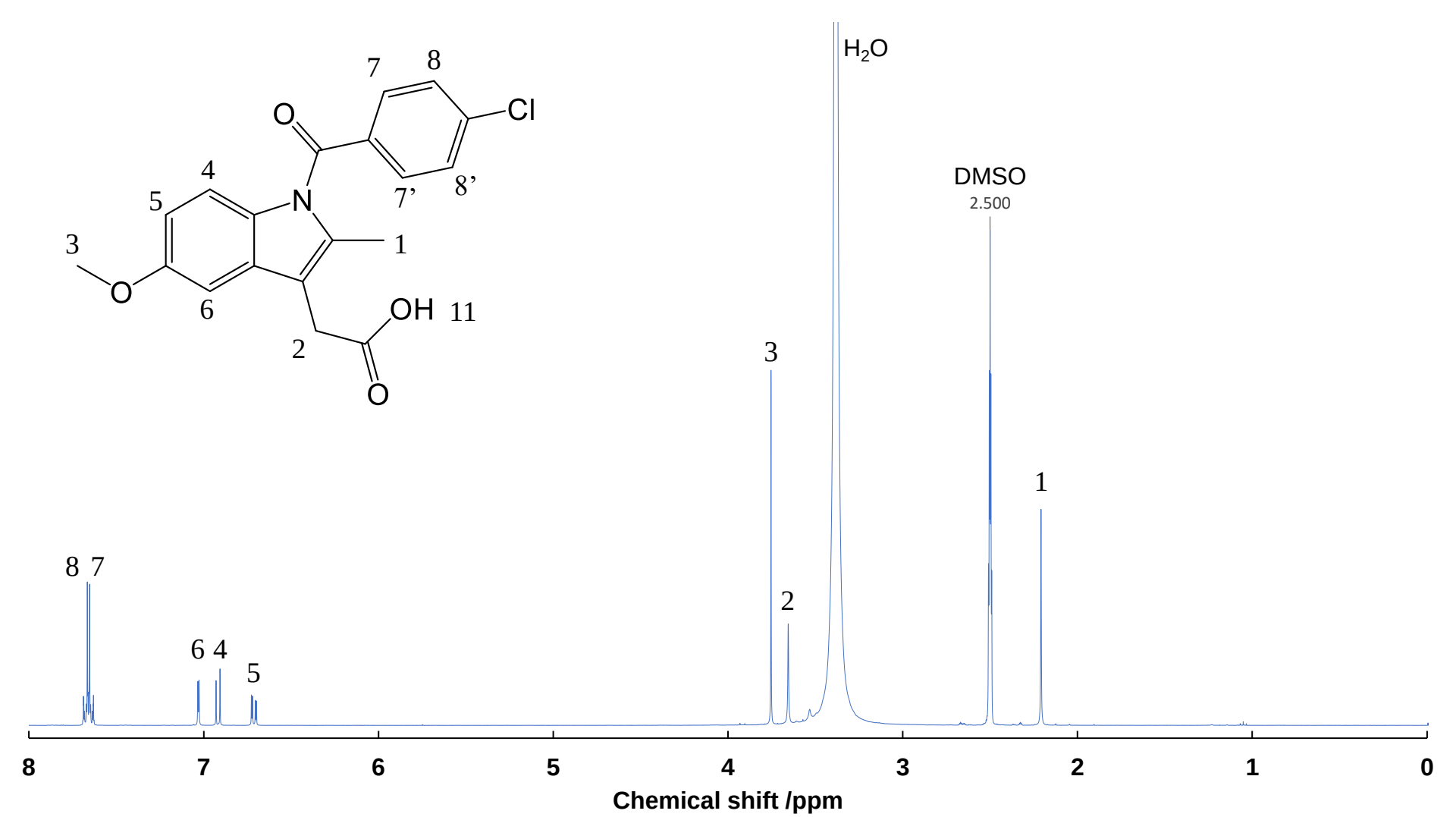


Figure S5(B) The 400 MHz ^{1}H-NMR spectrum of the precipitate after shaking α-form of INM in 25 mM KH_2PO_4/Na_2HPO_4 buffer (pH 6.8) in the presence of 10 mM LDC for 120 min. Only the indomethacin signal was observed and no LDC signal was assigned.

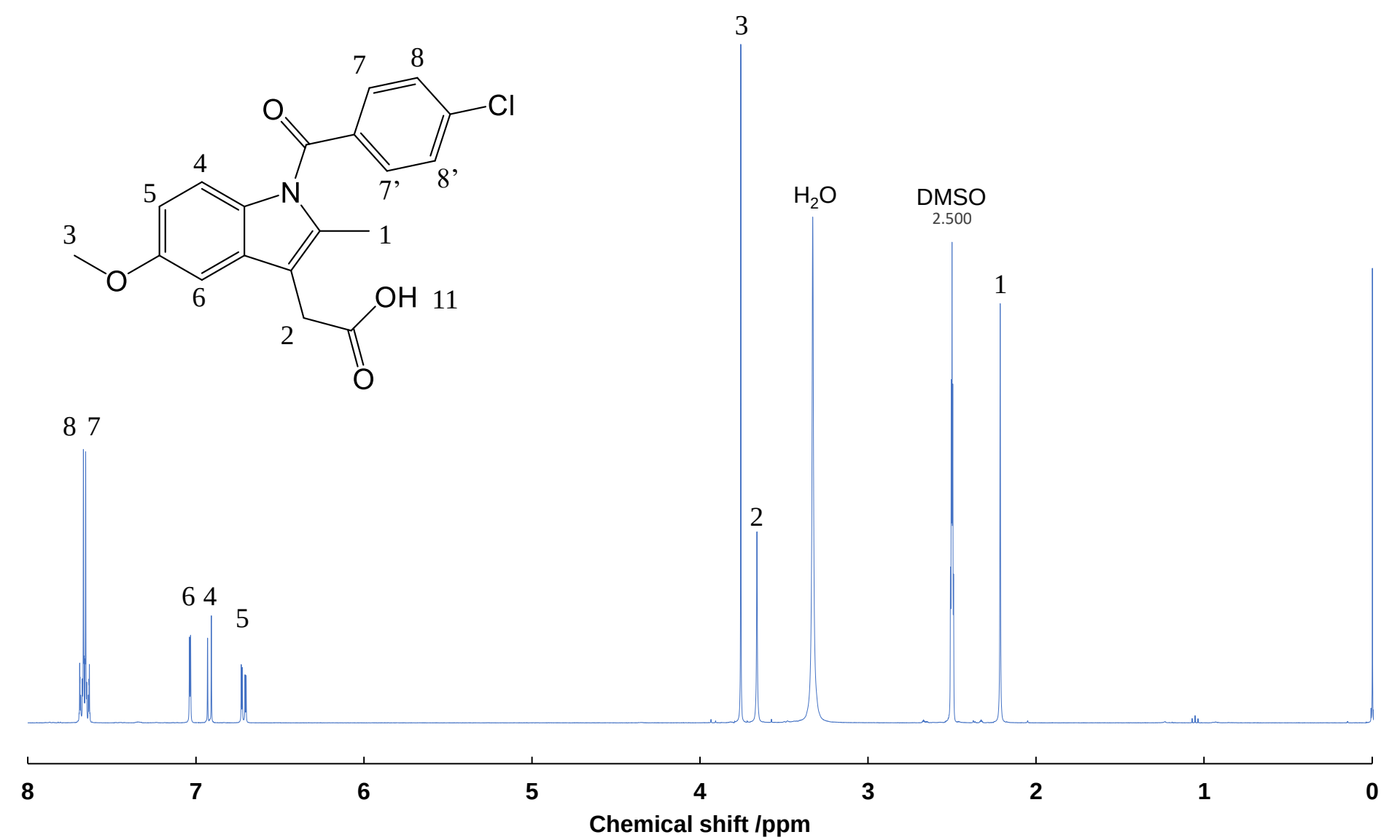


Figure S5(C) The 400 MHz ^{1}H-NMR spectrum of the precipitate after shaking α-form of INM in 25 mM KH_2PO_4/Na_2HPO_4 buffer (pH 6.8) in the presence of 10 mM CNS for 120 min. Only the indomethacin signal was observed and no CNS signal was assigned.

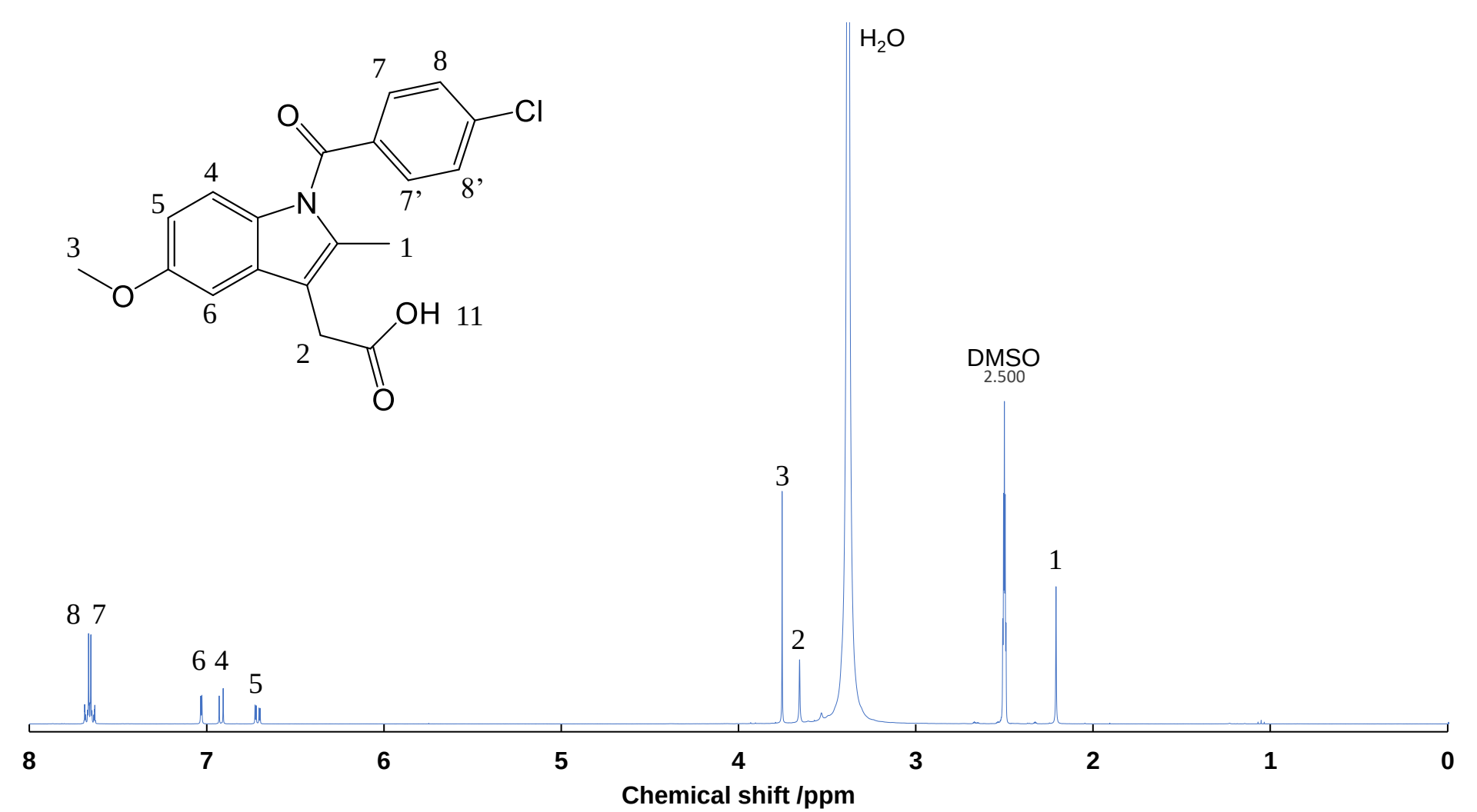


Figure S5(D) The 400 MHz ^{1}H-NMR spectrum of the precipitate after shaking α-form of INM in 25 mM KH_2PO_4/Na_2HPO_4 buffer (pH 6.8) in the presence of 10 mM APM for 120 min. Only the indomethacin signal was observed and no APM signal was assigned.

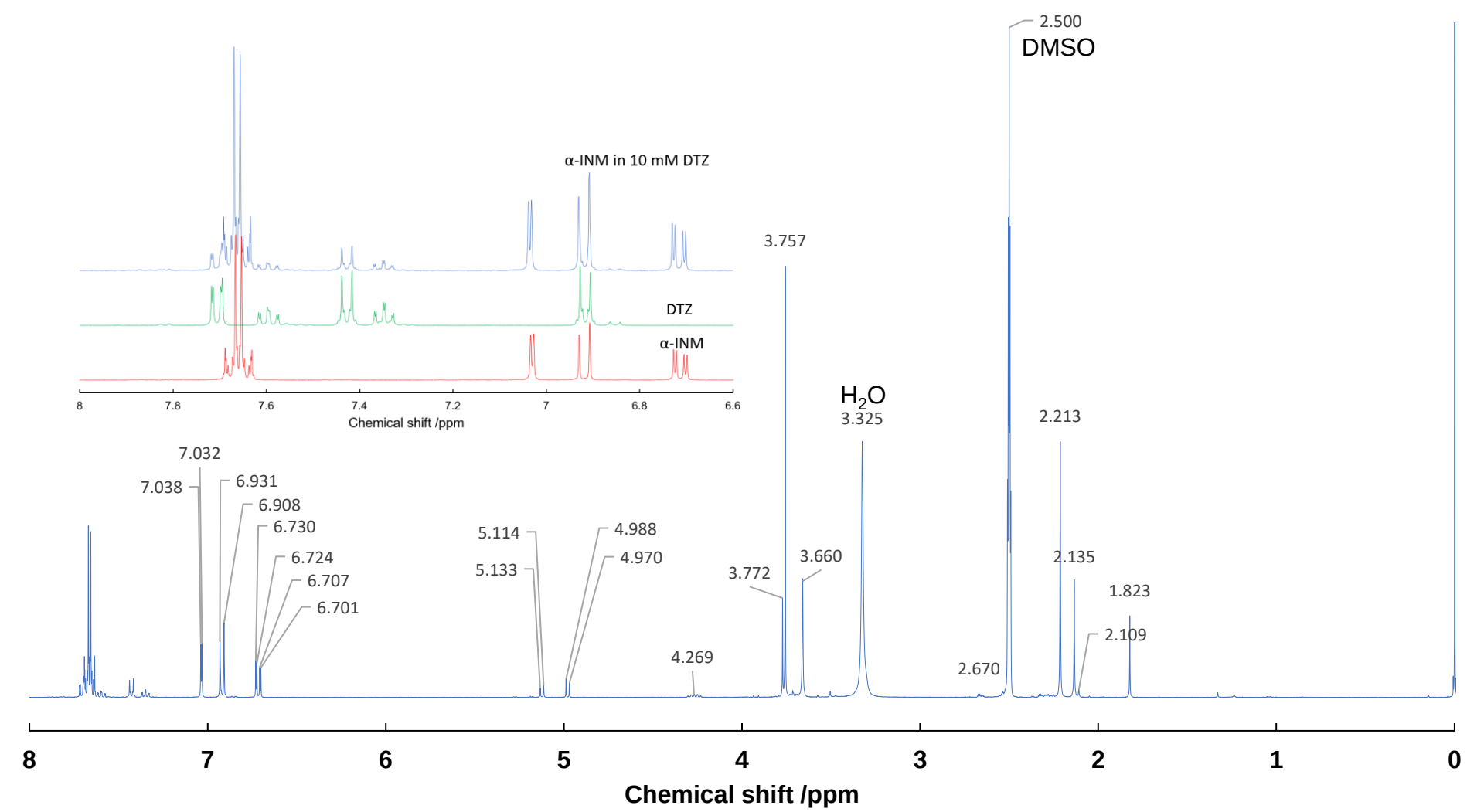


Figure S5(E) The 400 MHz ^{1}H-NMR spectrum of the precipitate after shaking α-form of INM in 25 mM KH_2PO_4/Na_2HPO_4 buffer (pH 6.8) in the presence of 10 mM DTZ for 120 min. Judging from the integral value of protons, it was confirmed that DTZ : INM was present in the precipitate at a ratio of 1:7.5, but no change in signal was observed. These findings suggest that the possibility of salt formation or co-crystallization between indomethacin and the solubilizers is low, indicating that indomethacin remains unaffected.

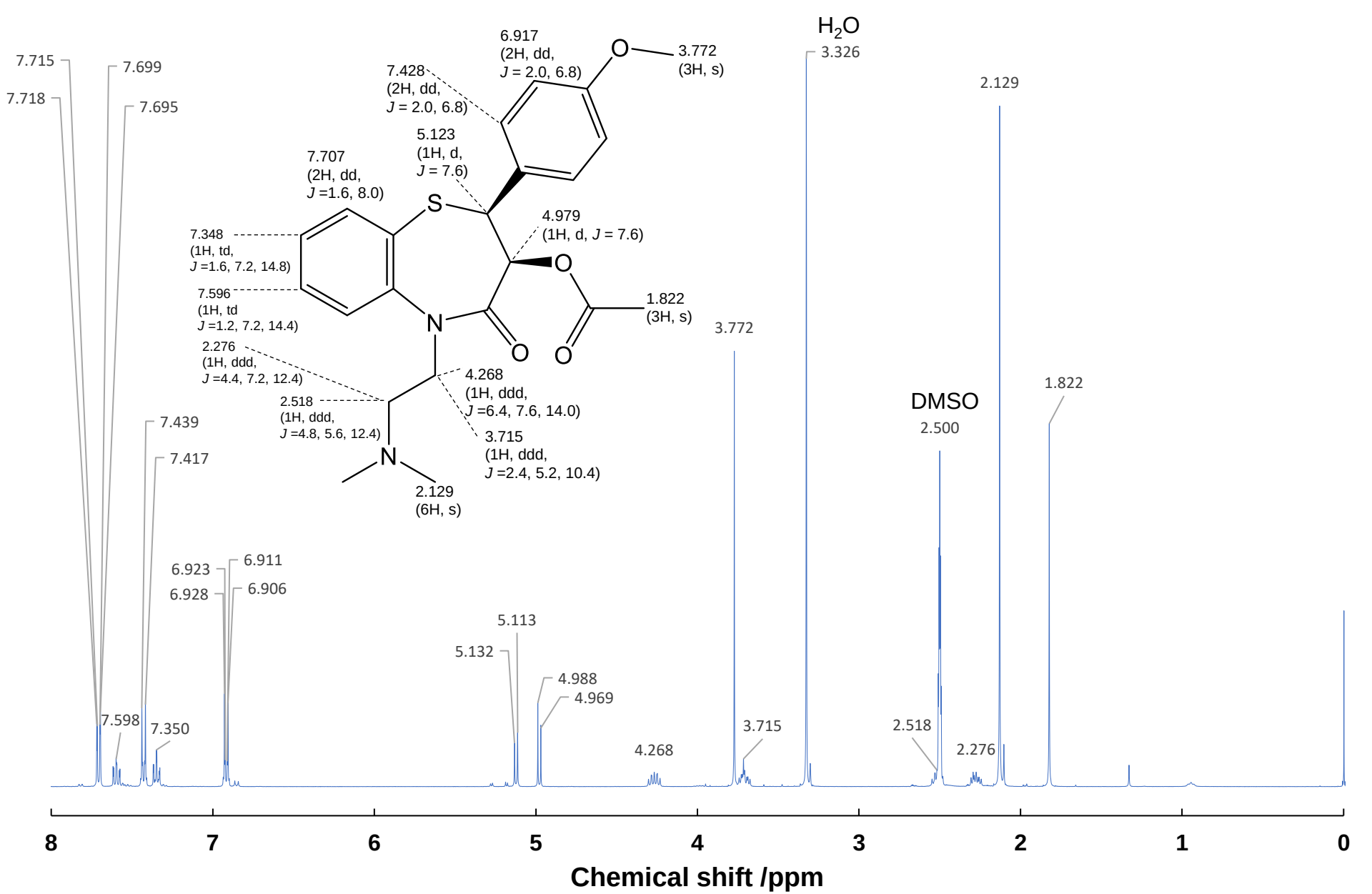


Figure S5(F-1) The 400 MHz ^{1}H-NMR spectrum of DTZ in DMSO-d_6 (at 2.500 ppm). Chemical shifts are listed at the assigned positions in the chemical structural formulas. The number of protons, coupling, and spin-spin coupling constants are shown in parentheses.

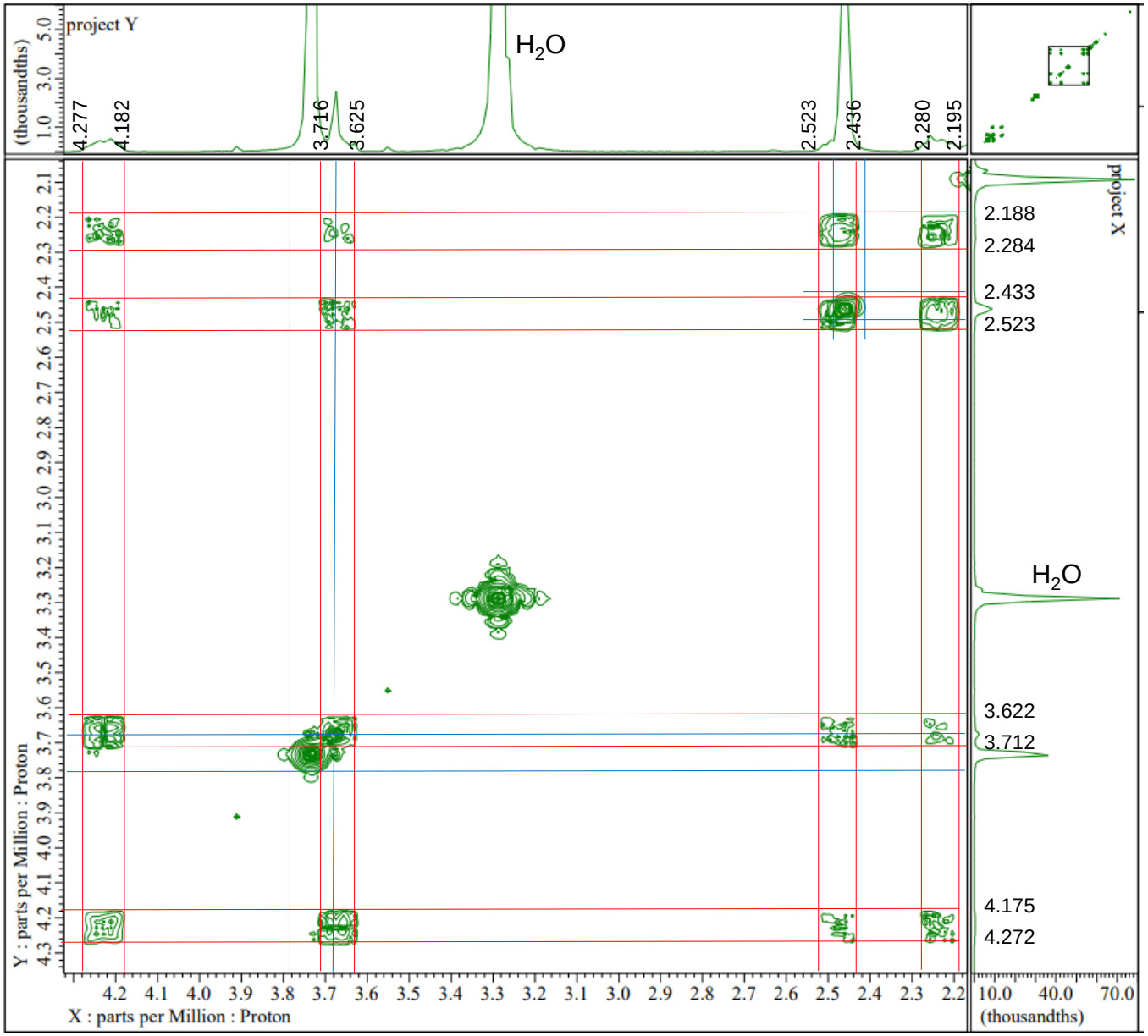


Figure S5(F-2) The 400 MHz ^{1}H-^{1}H COSY spectrum of DTZ in DMSO-d_6. It was shown that 3.715 and 4.268, 2.518 and 2.276 are geminal couplings.