

Electronic Supplementary Information

The effect of hydrogen bonding propensity and enantiomeric composition on the dynamics of supercooled ketoprofen - dielectric, rheological and NMR studies

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I. Synthesis of ketoprofen methyl ester:

In a round-bottomed flask á 250 mL, equipped with a condenser and a calcium chloride (CaCl₂) guard tube, 7 g of racemic ketoprofen, 50 mL of absolute methanol and 1 mL of concentrated sulfuric acid were placed and warmed under reflux until boiling. The mixture was refluxed for 10 hours and left over night at the room temperature. Reaction was monitored by thin-layer-chromatography (TLC) on the precoated Silica gel F254 plates using chloroform-methanol (9:1) as a mobile phase. The excess of methanol was evaporated on the rotary evaporator so that the mixture was concentrated to half volume. The residue was poured into 180 mL of distilled water, the flask was washed with water and both two portions of water were combined. The water was extracted four times with n-hexane (4x35 mL). Combined hexane layers were washed 3 times with saturated sodium bicarbonate solution, 3 times with 30 mL portions of water and dried over anhydrous magnesium sulfate for 3 hours. The hexane was evaporated by using rotary evaporator to afford a colorless oily product (4.9 g). The TLC analysis confirmed purity of the product, R_f = 0.82. Schematic reaction scheme is given in Fig. S1.

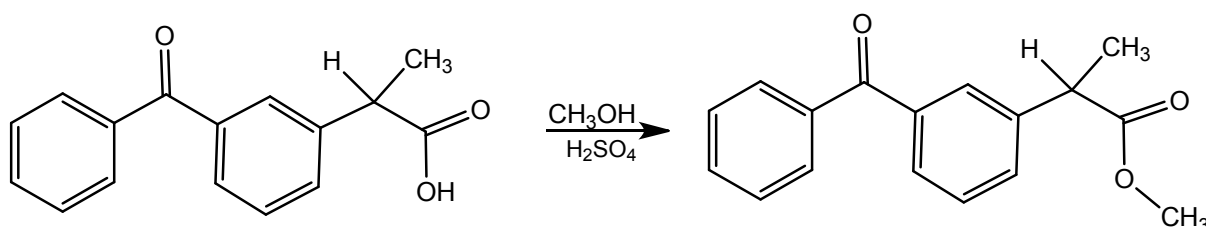


Fig. S1. Reaction scheme of obtaining racemic ketoprofen methyl ester.

II. Chemical purity verification (NMR studies)

The NMR spectra were recorded at 298 K on an Agilent DD2 800 spectrometer operating at resonance frequencies of 799.903 and 201.146 MHz for ^1H and ^{13}C , respectively. Chemical shifts are reported in ppm relative to residual solvent peak (CDCl_3 , $\delta_{\text{H}} = 7.26$ ppm, $\delta_{\text{C}} = 77.16$ ppm) as an internal standard. Data are presented as follows: chemical shift, multiplicity (s = singlet, d = doublet, ddd = doublet of doublet of doublets, t = triplet, q = quartet, m = multiplet and/or multiple resonances), coupling constants (Hz), integration, and assignment. The ^1H NMR spectrum of ketoprofen methyl ester showed no changes upon heating the compound to 80 °C for ca 15 minutes and cooling it back to room temperature. Synthesized methyl ester of ketoprofen is also chemically stable upon storage at room temperature (no changes in NMR spectra were observed with time). The ^1H and ^{13}C NMR spectra are presented in Fig. S2 and S3, respectively.

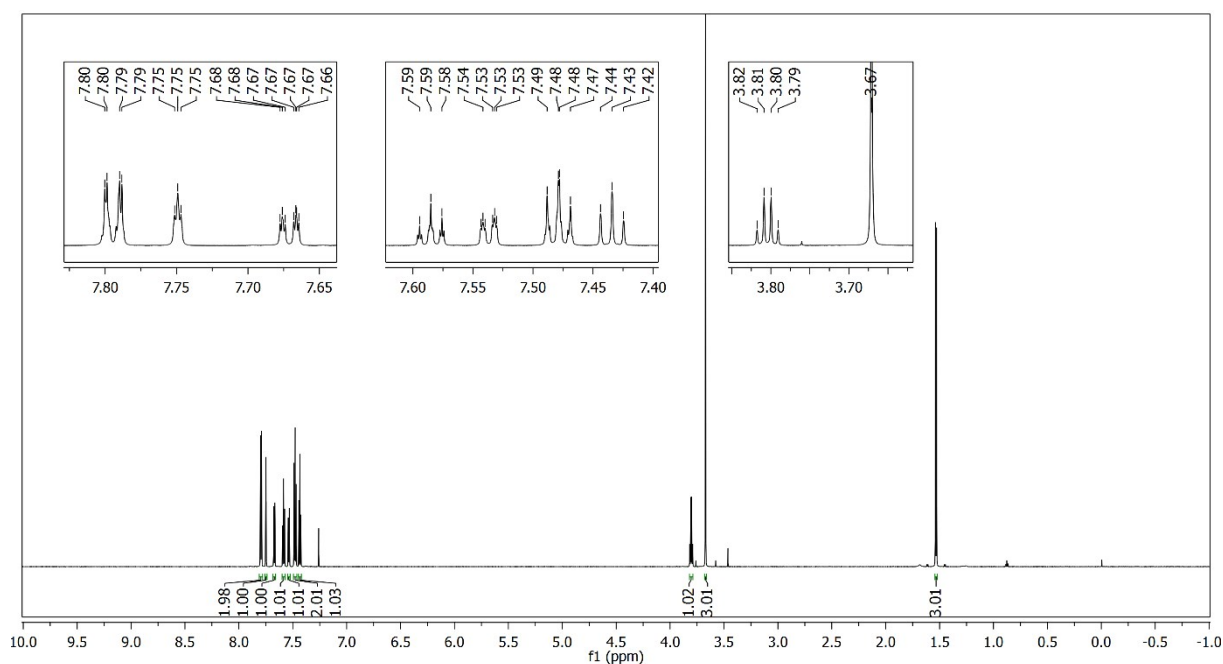


Fig. S2. ^1H NMR spectrum of ketoprofen methyl ester (800 MHz, CDCl_3 , 298 K).

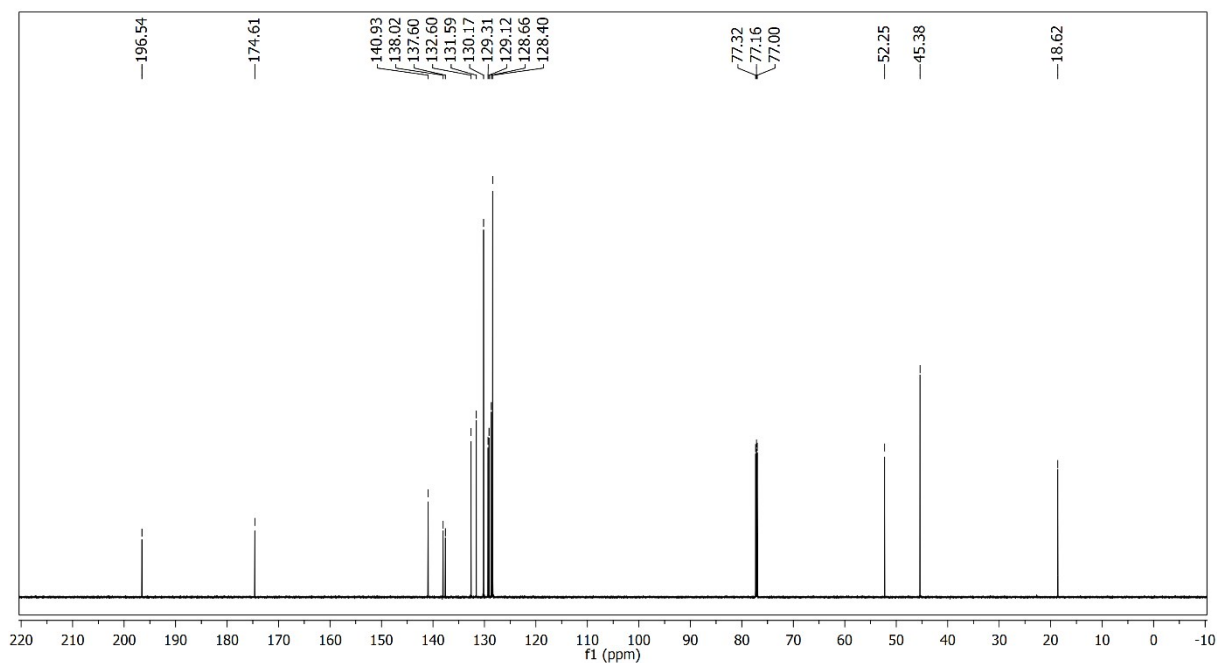


Fig. S3. ^{13}C NMR spectrum of ketoprofen methyl ester (800 MHz, CDCl_3 , 298 K).

NMR data:

^1H NMR (800 MHz, CDCl_3): δ_{H} 1.53 (d, $J = 7.2$ Hz, 3H, CH_3), 3.68 (s, 3H, OCH_3), 3.80 (q, $J = 7.2$ Hz, 1H, CH), 7.43 (t, $J = 7.7$ Hz, 1H, Ar), 7.46-7.50 (m, 2H, Ar), 7.52-7.55 (m, 1H, Ar), 7.57-7.60 (m, 1H, Ar), 7.67 (ddd, $J = 7.6$ Hz, $J = 1.7$ Hz, $J = 1.1$ Hz, 1H, Ar), 7.75 (t, $J = 1.8$ Hz, 1H, Ar), 7.78-7.80 (m, 2H, Ar). ^{13}C NMR (201 MHz, CDCl_3): δ_{C} 18.62 (CH_3), 45.38 (CH), 52.25 (OCH_3), 128.40 (Ar), 128.66 (Ar), 129.12 (Ar), 129.31 (Ar), 130.17 (Ar), 131.59 (Ar), 132.60 (Ar), 137.60 (Ar), 138.02 (Ar), 140.93 (Ar), 174.61 (ester C=O), 196.54 (ketone C=O).

III. Additional results of high pressure studies

In figure S4 we present structural relaxation time for RS-ketoprofen, S-ketoprofen and methyl ester of RS-ketoprofen plotted as a function of temperature and pressure. As can be seen, when isobaric and isothermal dielectric data are analysed together they form a two dimensional surface that can be described with the use of the Avramov model [47]

$$\tau_{\alpha} = \tau_{\infty} \left(\varepsilon \frac{T_g(p_0)}{T} \right)^{\alpha} \left(1 + \frac{p}{\Pi} \right)^{\beta} \quad (\text{eq. S1})$$

where $\varepsilon = \log \tau_g / \log \tau_{\infty}$. In the above equation we assumed that the volume expansion coefficient α changes with pressure according to the following expression,

$$\alpha(p) = \alpha_0 \left[1 - \frac{C}{C_{p_0}} \ln \left(1 + \frac{p}{\Pi} \right) \right] \quad (\text{eq. S2})$$

From the global fitting analysis, we have obtained the following set of parameters: $\log \tau_{\infty} = -11.64$ s, $T_g(p_0) = 228.3$ K, $\alpha_0 = 5.44$, $C/C_{p_0} = 0.13$, $\Pi = 330.13$ MPa, $\beta = 1.38$, $\log \tau_g = 1.94$ for Me-RS-ketoprofen, $\log \tau_{\infty} = -12.00$ s, $T_g(p_0) = 266.5$ K, $\alpha_0 = 5.36$, $C/C_{p_0} = 0.08$, $\Pi = 357.83$ MPa, $\beta = 1.47$, $\log \tau_g = 1.98$ for RS-ketoprofen, and $\log \tau_{\infty} = -11.71$ s, $T_g(p_0) = 265.6$ K, $\alpha_0 = 5.36$, $C/C_{p_0} = 0.09$, $\Pi = 412.34$ MPa, $\beta = 1.63$, $\log \tau_g = 2.03$ for S-ketoprofen. Using obtained parameters, we have plotted the fitted curves for isobaric and isothermal dependences separately, as seen in fig. S5. It is clearly visible that the pressure and temperature dependences of the relaxation times for studied samples can be satisfactorily described by the Avramov model. Therefore, parameterized in this way $\tau_{\alpha}(T,p)$ dependences were used to calculate the activation volume for investigated materials, as demonstrated in the main paper (fig. 6c).

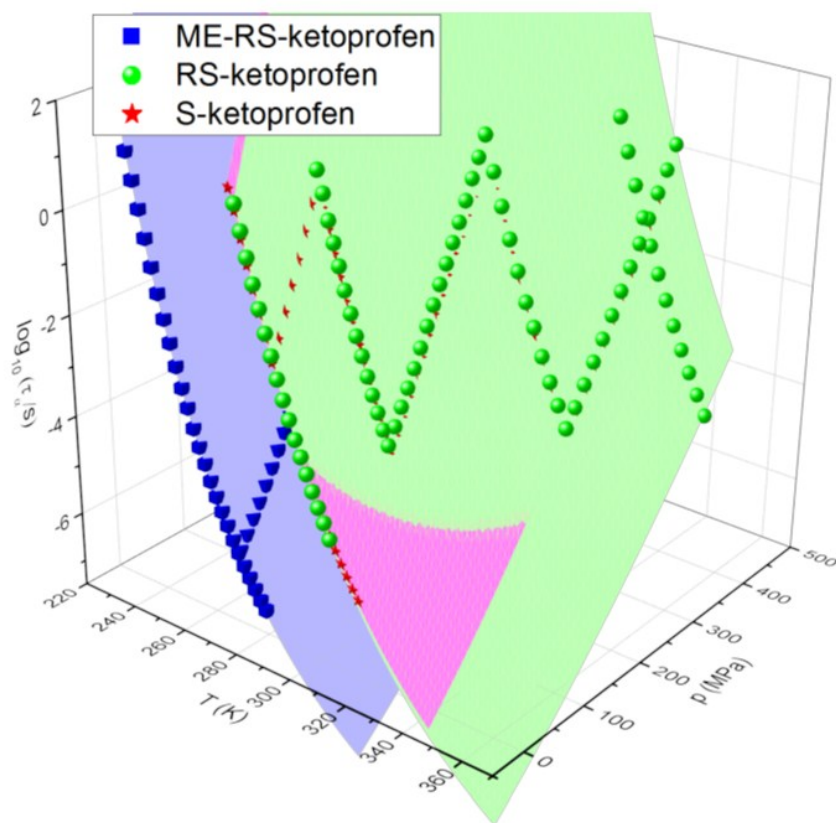


Fig. S4. Structural relaxation time plotted versus pressure and temperature presented in the T - P plane for Me-RS-ketoprofen, RS-ketoprofen and S-ketoprofen. The wire surface was described by using the modified version of the Avramov model.

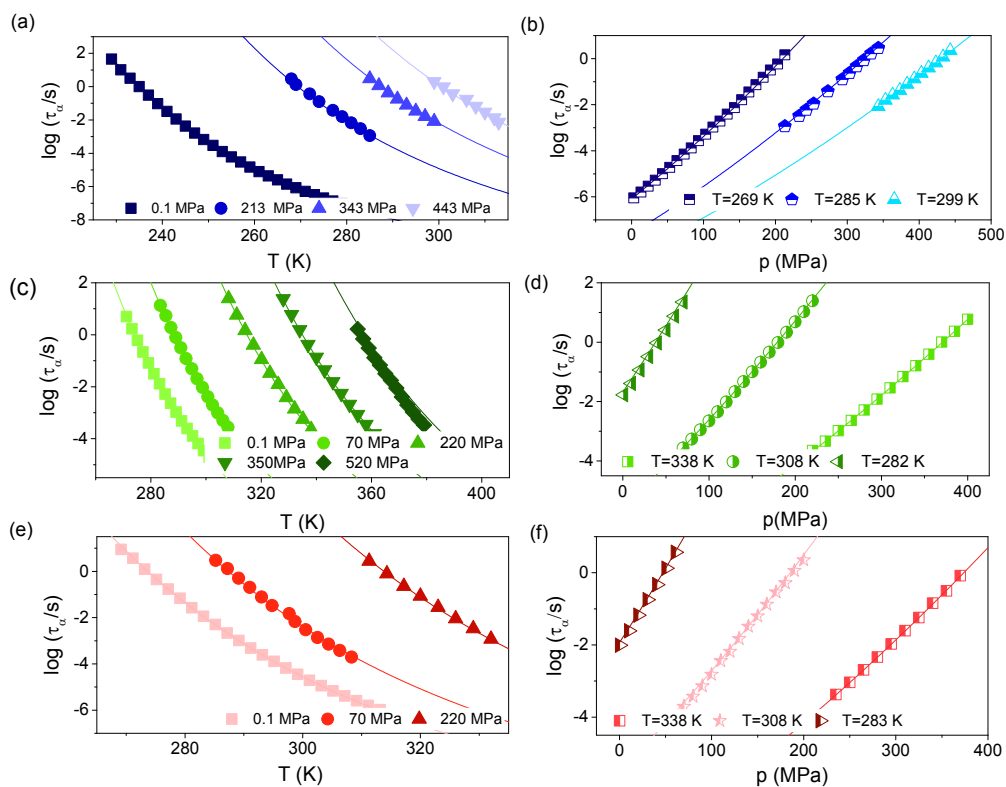


Fig. S5. Temperature and pressure dependences of the structural relaxation time for ME-RS-ketoprofen (a,b), RS-ketoprofen (c,d) and S-ketoprofen (e,f). Solid lines are fits of the data to the Avramov model.