Salts of S-(+)-ibuprofen formed via its reaction with the antifibrinolytic agents aminocaproic acid and tranexamic acid: synthesis and characterization

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SUPPLEMENTARY MATERIAL

CONTENTS:

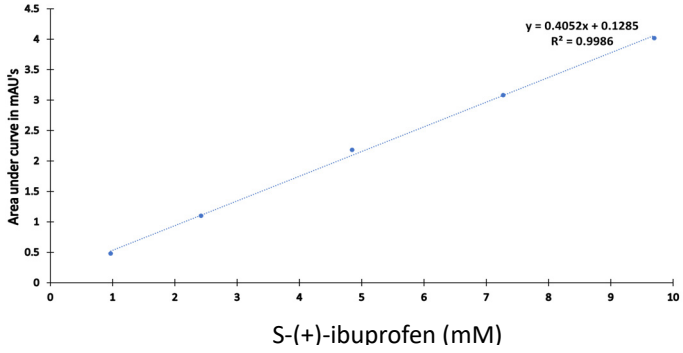

Figure S1: HPLC calibration curve.

Table S1: HPLC gradient elution program

Time (min)	Buffer (% v/v)	Methanol (%, v/v)
0.0	80	20
2.0	80	20
9.0	5	95
12	5	95
14	80	20
15	80	20

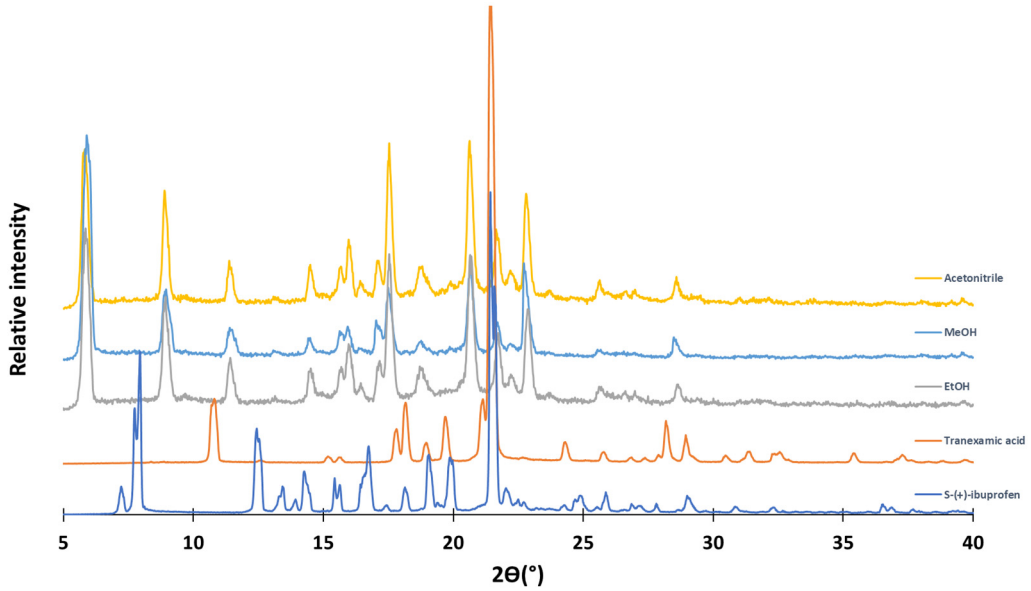

Figure S2: PXRD patterns of the starting components S-IBU and TXA, and those of the products obtained by liquid-assisted grinding.

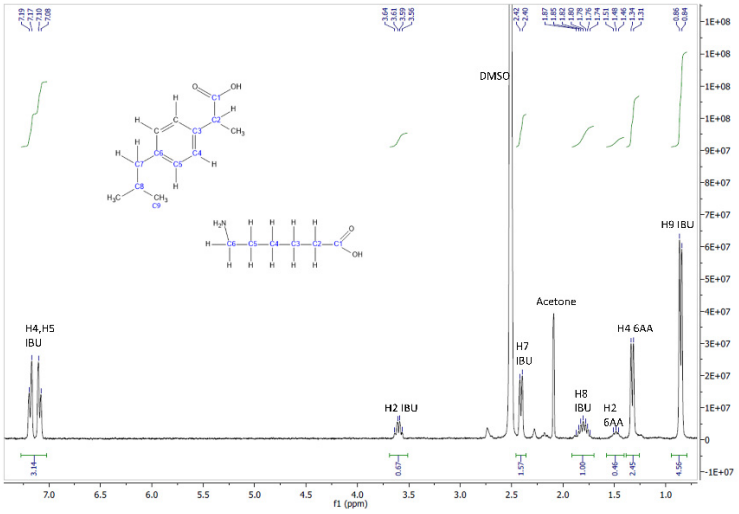

Figure S3: ^{1}H-NMR spectrum of $(S\text{-}IBU)^{-}(ACA)^{+}$

Table S2: Analysis of the ^{1}H-NMR spectrum of $(S\text{-}IBU)^{-}(ACA)^{+}$

Experimental details:
Bruker Ultrashield 300 (300 MHz) and interpreted on MestReNova [1].
1. Chemistry Software Solutions, Mestrelab Research, S.L. MestReNova, Version: 6.0.2-5475. (Copyright, 2009).

Assignment	δ (ppm)	Integration	Multiplicity	Proton representation (per molecule)	Stoichiometric ratio	Stoichiometric ratio (nearest integer)
4 x CH aromatic (IBU)	7.19-7.08	3.14	Doublets	4H	0.79	1
CH (2) (IBU)	3.64-3.56	0.67	Quartet	1H	0.67	1
CH2 (7) (IBU)	2.42-2.40	1.57	Doublet	2H	0.79	1
CH (8) (IBU)	1.87-1.74	1.00*	Multiplet	1H	1	1
CH2 (2) (6AA)	1.51-1.46	0.46	Multiplet	2H	0.23	-
CH2 (4) (6AA)	1.34-1.31	2.45	Doublet	2H	1.23	1
2 x CH3 (9) (IBU)	0.86-0.84	4.56	Doublet	6H	0.76	1

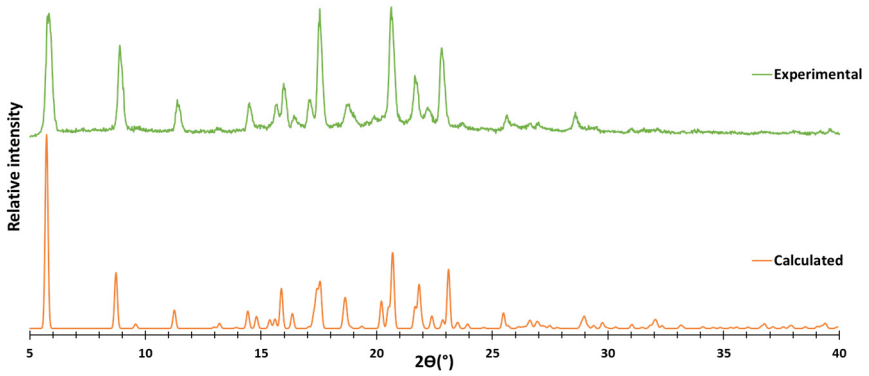

Figure S4: Experimental and calculated PXRD patterns for $(S\text{-}IBU)^{-}(TXA)^{+}$.

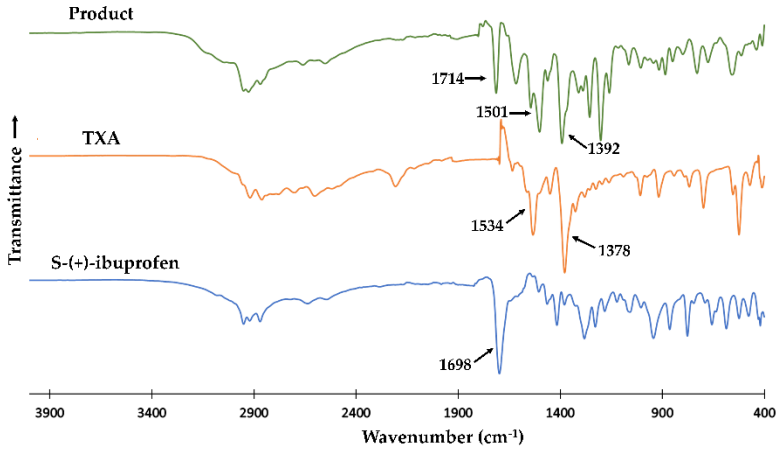

Figure S5: FTIR spectra of S-(+)-ibuprofen, TXA and their product.

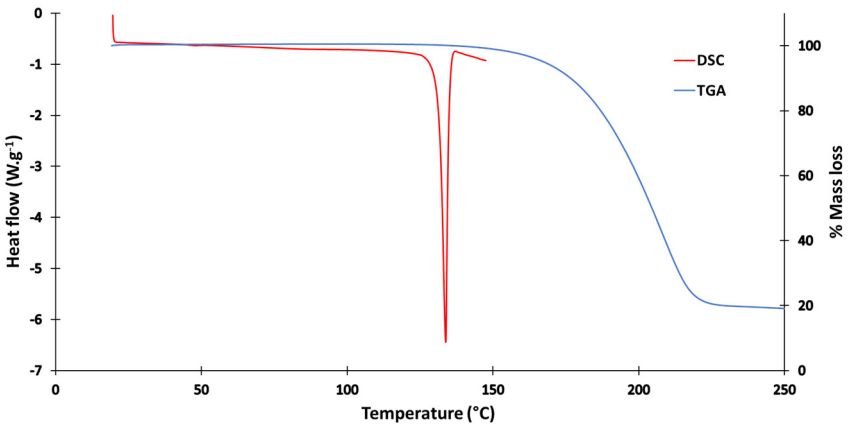

Figure S6: DSC and TGA curves for $(S\text{-}IBU)^{-}(ACA)^{+}$

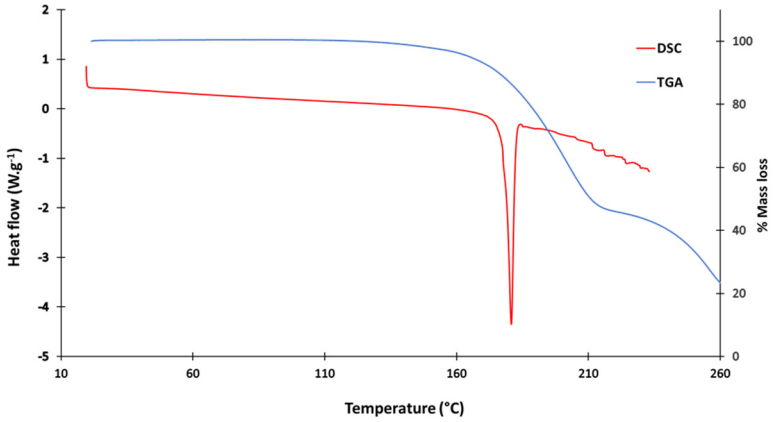

Figure S7: DSC and TGA curves for S-IBU)$^{-}$(TXA)$^{+}$

Table S3: Solubility data for four solid forms of S-(+)-ibuprofen

pH 6.5	**Molarity**	**Solubility mg/mL**	**Relative solubility**
S-(+)-ibuprofen	0.016	3.4	1.00
(S-IBU)$^{-}$(ACA)$^{+}$	0.016	3.4	1.00
(S-IBU)$^{-}$(TXA)$^{+}$	0.018	3.7	1.09
S-(+)-ibuprofen·benzamide	0.018	3.7	1.09
pH 2.0			
S-(+)-ibuprofen	0.001	0.21	1.00
(S-IBU)-(ACA)+	0.001	0.21	1.00
(S-IBU)-(TXA)+	0.001	0.21	1.00
S-(+)-ibuprofen·benzamide	0.001	0.21	1.00