

Electronic supplementary information (ESI) file of the paper

**Rationalization of liquid assisted grinding intercalation yields of
organic molecules into layered double hydroxides by multivariate
analysis**

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Sample ID	Yield	Mol. Weight	Refractivity	Min.Proj. Size	ASA pH 13.3	LogP pH 13.3	Avg. Mol. Pol.	Volume	Max Proj Area	ASA pH7.4	LogD pH7	An. Char.	Ring Num.	LogD pH5	Rot. bonds	Min Proj Area	Max Proj Size	PKA	PSA	LogP	LogD pH9	LogD pH13.3
C	0.00	325.32	97.81	17.48	552.29	-3.45	33.86	275.30	100.1	537.86	-0.94	3	3	0.69	5	46.08	6.05	3.76	118.07	1.40	-2.00	-4.49
FLUO_c	0.00	332.30	103.41	11.81	459.93	-0.21	33.22	267.67	89.28	457.59	-0.79	2	4	1.59	1	55.83	7.72	8.72	81.65	3.88	3.30	-0.52
VG1-C8	0.00	680.87	224.86	24.61	1026.83	3.34	81.53	687.87	176.4	1026.83	4.81	2	5	6.97	18	119.4	15.64	3.53	126.64	8.46	1.95	1.54
INDO_c	0.05	357.79	94.81	16.88	551.49	0.39	36.62	298.13	97.58	551.49	0.5	1	3	2.31	4	49.87	6.69	3.80	71.36	3.53	0.01	0.00
COUM_c	0.05	190.15	47.62	11.04	316.34	-1.77	17.56	152.29	61.25	316.34	-1.99	1	2	-0.49	1	26.39	4.01	3.14	66.43	1.37	-2.16	-2.16
VG1-C10	0.10	736.98	243.26	27.09	1276.66	5.12	89.51	755.67	193.4	1276.66	6.59	2	5	8.75	22	131.5	20.17	3.53	126.64	10.24	3.73	3.32
PFBS	0.18	300.10	32.31	10.89	361.50	0.25	14.26	164.03	52.6	361.50	0.25	1	0	0.25	4	28.44	6.71	-3.31	65.58	2.63	0.25	0.25
6-A-4-H-2	0.42	208.23	59.81	12.2	381.32	-3.33	22.58	183.70	68.56	378.59	-1.35	2	2	-0.57	1	31.41	5.63	-2.07	114.66	1.42	-1.91	-3.48
COUM	0.50	190.15	47.62	11.04	316.34	-1.77	17.56	152.29	61.25	316.34	-1.99	1	2	-0.49	1	26.39	4.01	3.14	66.43	1.37	-2.16	-2.16
2-NSA	0.56	208.23	53.13	11.48	364.49	-0.23	20.28	163.86	63.11	364.49	-0.23	1	2	-0.23	1	27.8	5.65	-1.81	65.58	2.14	-0.23	-0.23
KET	0.56	254.28	72.52	13.1	443.28	0.47	26.93	231.79	75.23	443.28	0.64	1	2	2.47	4	40.83	8.14	3.88	57.20	3.61	0.09	0.08
A	0.66	350.43	106.62	18.22	628.52	-0.90	37.42	328.23	97.06	624.82	-0.68	2	2	0.76	9	55.39	10.69	3.68	95.12	1.77	-0.77	-1.68
VG1-C2_c	0.80	512.55	169.8	19.04	764.72	-2.15	56.38	485.61	138.4	764.72	-0.69	2	5	1.48	6	73.55	9.79	3.52	126.64	2.97	-3.56	-3.95
KET_c	0.85	254.28	72.52	13.1	443.28	0.47	26.93	231.79	75.23	443.28	0.64	1	2	2.47	4	40.83	8.14	3.88	57.20	3.61	0.09	0.08
B	0.87	216.24	62.54	14.13	416.82	-1.08	22.81	201.16	70.51	416.82	-0.68	1	1	0.76	3	28.06	5.74	2.67	67.16	0.78	-1.47	-1.47
FLUR_c	0.88	244.26	67.29	13.63	430.31	0.80	25.26	216.72	72.76	430.31	1.41	1	2	3.26	3	35.43	5.9	4.42	40.13	3.94	0.45	0.41
TIAP	0.98	260.31	69.19	13.58	457.07	0.52	26.93	223.54	77.64	457.07	0.8	1	2	2.65	4	37.43	6.8	4.03	85.44	3.66	0.14	0.13
IBU	0.98	206.29	60.73	13.08	426.09	0.70	23.81	210.07	64.35	426.09	1.71	1	1	3.46	4	36.38	6.99	4.85	40.13	3.84	0.41	0.31
FLUR	0.98	244.26	67.29	13.63	430.31	0.80	25.26	216.72	72.76	430.31	1.41	1	2	3.26	3	35.43	5.9	4.42	40.13	3.94	0.45	0.41
SDS	1.00	265.39	67.81	21.58	618.92	2.04	31.16	260.61	92.51	618.92	2.04	1	0	2.04	12	26.73	7.19	-1.45	74.81	4.42	2.04	2.04
IBU_c	1.00	206.29	60.73	13.08	426.09	0.70	23.81	210.07	64.35	426.09	1.71	1	1	3.46	4	36.38	6.99	4.85	40.13	3.84	0.41	0.31
TIAP_c	1.00	260.31	69.19	13.58	457.07	0.52	26.93	223.54	77.64	457.07	0.8	1	2	2.65	4	37.43	6.8	4.03	85.44	3.66	0.14	0.13

Figure SI1: Complete dataset. In red the variables excluded from the analysis after the variable screening data mining procedure (the suffix “_c” means “prepared in capillary”, as detailed in the experimental section).

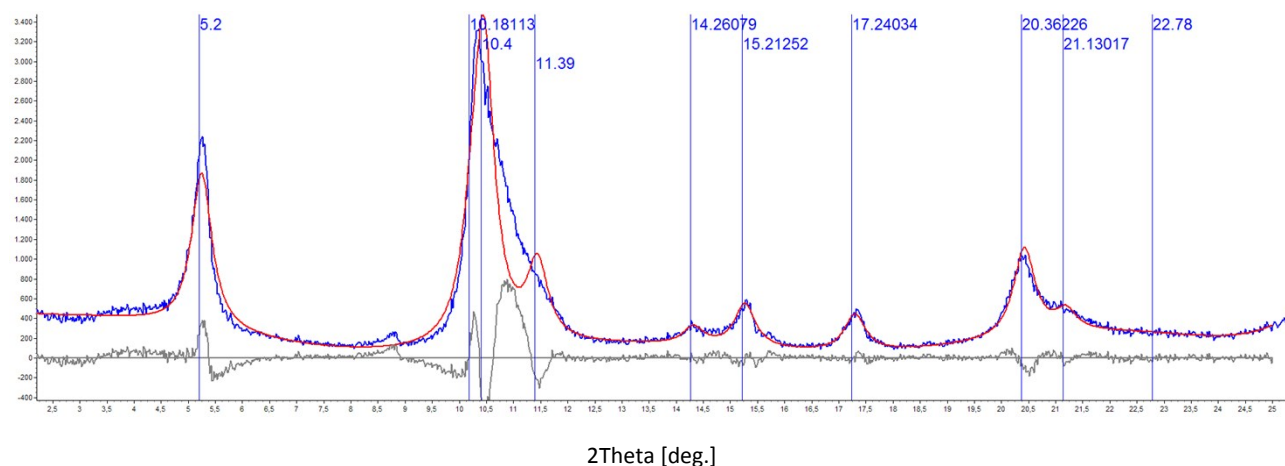


Figure SI2: XRPD pattern (in blue) and Single peak fit (in red) of LDH_COUM obtained by LAG intercalation. The peaks at 5.2° (001), 10.4° (002), 14.26° (003) and 21.13° (004) are those of the intercalated LDH_COUM phase. At 11.39° (003) and 22.78° (006) fall two peaks that are most probably due to CO₃ contamination and the formation of a LDH_CO₃ phase. The peaks at 10.18°, and 20.36° are the (003) and (006) peak of the starting LDH_NO₃ respectively. The remaining peaks are due to not intercalated Coumarin. Since the peaks of the desired product and of impurities and starting material are superimposed (between 10° and 11° 2Theta) it is difficult to have a precise estimate of the yield. Anyway, performing the fit restraining the peak positions and CS_L (Crystallite Size) to achieve the best fit of the non-superimposed peaks the yield resulted to be, quite confidently, about 50%.

In Figure SI2 the peak falling at about 10.4° is more intense than the (001) peak of LDH_COUM since it is formed by three superimposed peaks, namely the (002) peak of the LDH_COUM phase, the (003) peak of LDH_NO₃ and the partially superimposed (003) peak of the LDH_CO₃ phase. The intercalation of complex organic molecules inside LDH layers instead of simple inorganic anions (such as nitrate, chloride, or carbonate) causes a lowering of the symmetry from *R*-3*m* to *P*-1. For this reason we indexed the lamellar peaks of the organic intercalated LDHs as (001), (002), (003) etc. while the lamellar peaks of LDH_CO₃ and LDH_NO₃ are indexed as (003), (006), (009) etc.

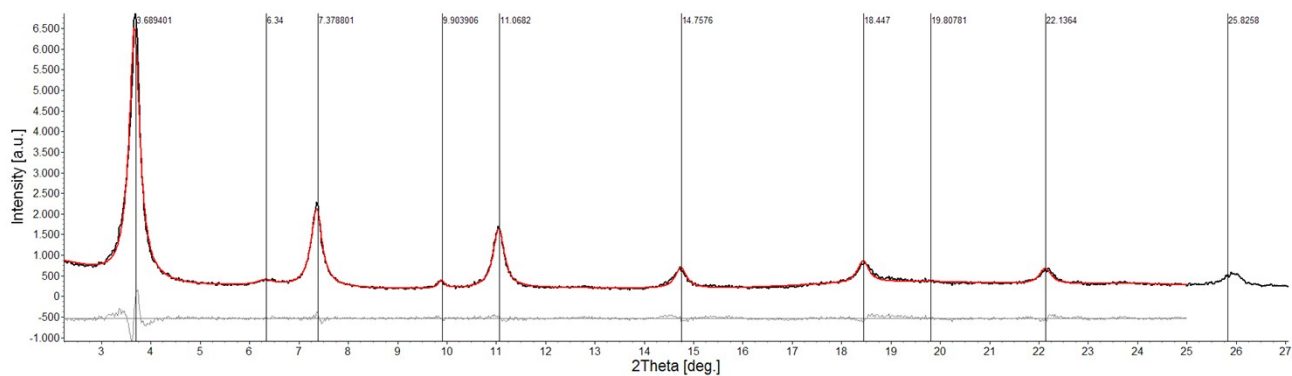


Figure SI3: XRPD pattern (in black) and Single peak fit (in red) of LDH_FLUR obtained by LAG intercalation. The peaks of the intercalated phase are visible up to the seventh order (at 3.69° and multiples). The peaks of LDH_NO₃, falling at 9.90° (003) and 19.81° (006) are almost invisible.

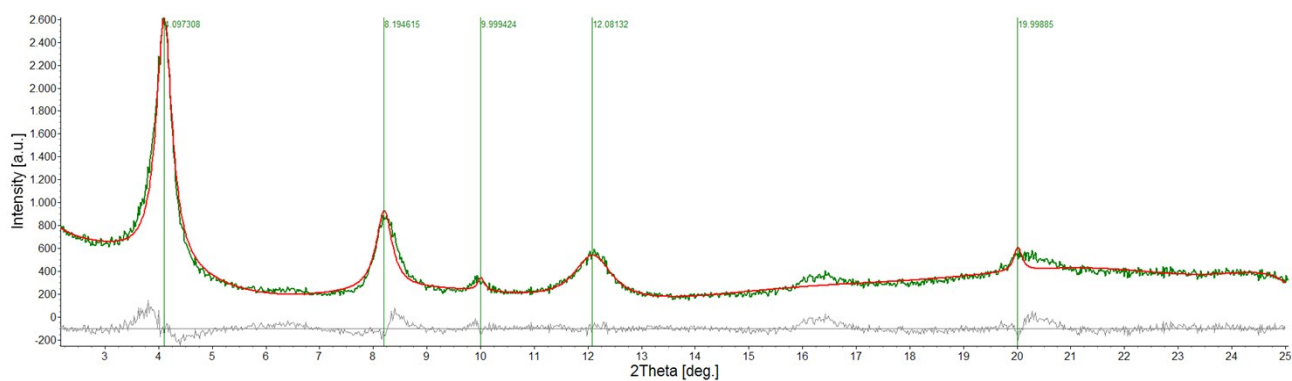


Figure SI4: XRPD pattern (in green) and Single peak fit (in red) of LDH_TIAP obtained by LAG intercalation. Peak assignment: 4.10° , 8.15° and 12.10° LDH_TIAP. 10° and 20° LDH_NO₃

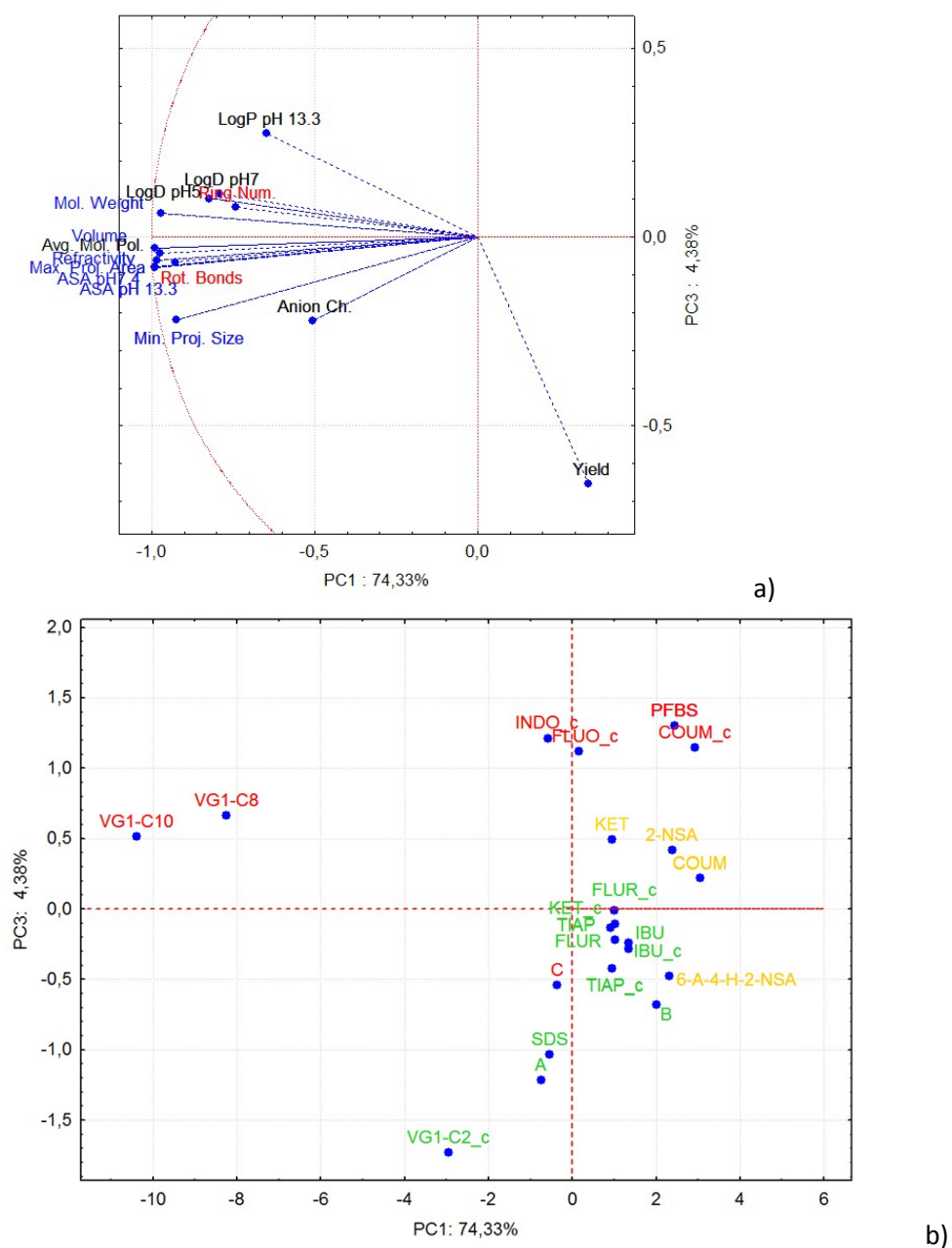
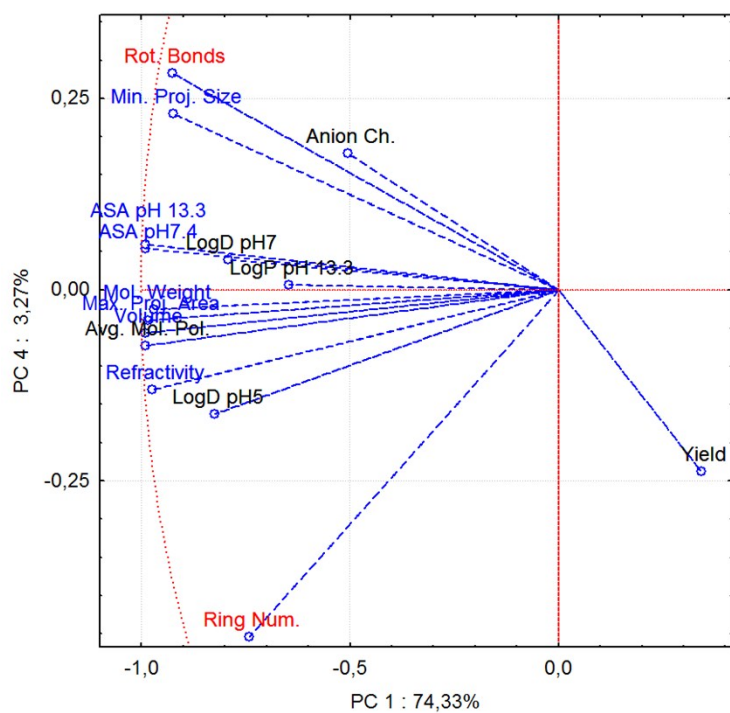
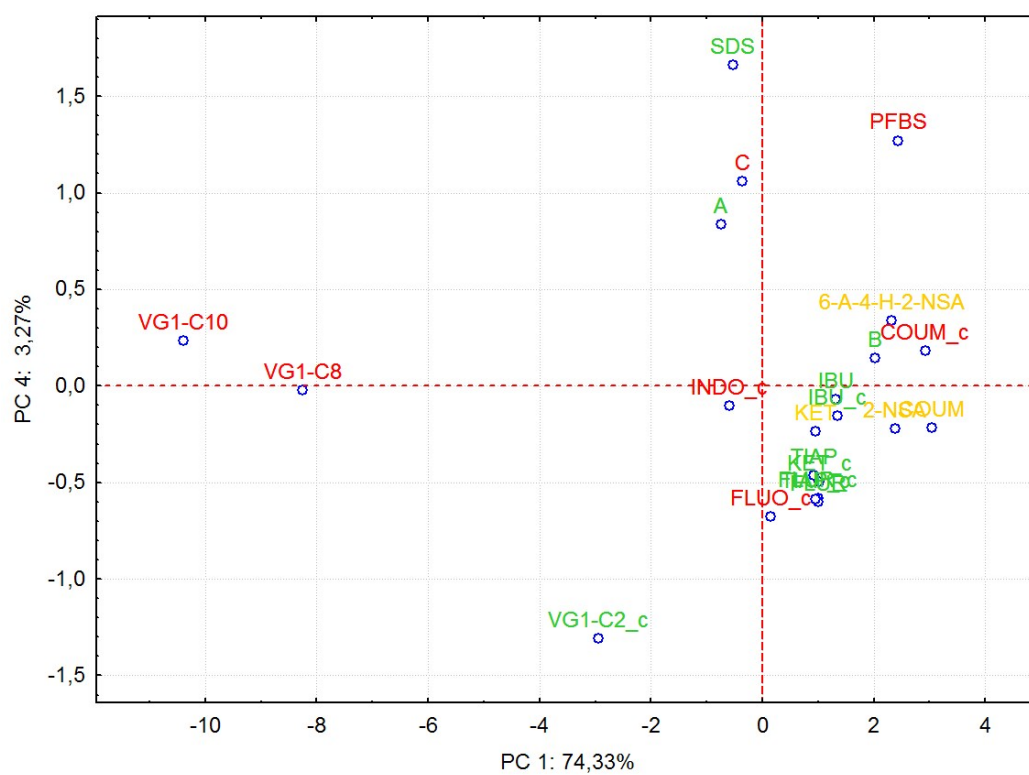


Figure S15: a) Loading plot reporting variables projection on PC1 vs. PC3. b) Score plot reporting the samples on the PC1 vs. PC3 axes. Sample color codes were used to highlight the fully intercalated ones (green) the partially intercalated (yellow) and the poorly or not intercalated (red).

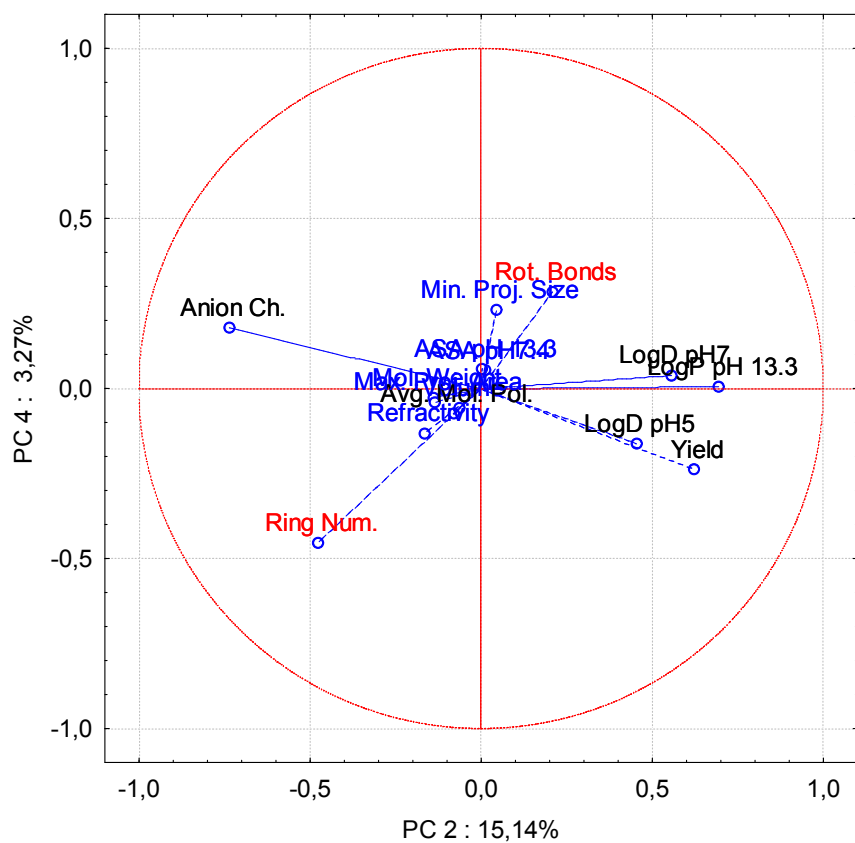


a)

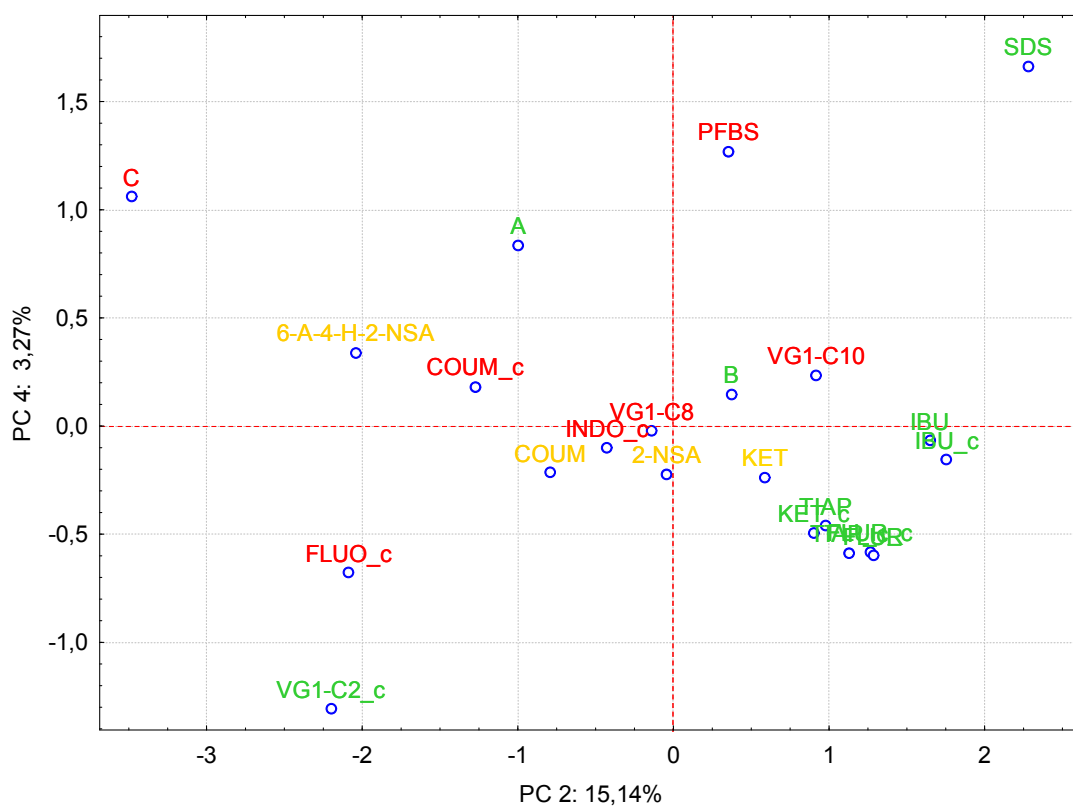


b)

Figure S16: a) Loading plot reporting variables projection on PC1 vs. PC4. b) Score plot reporting the samples on the PC1 vs. PC4 axes.

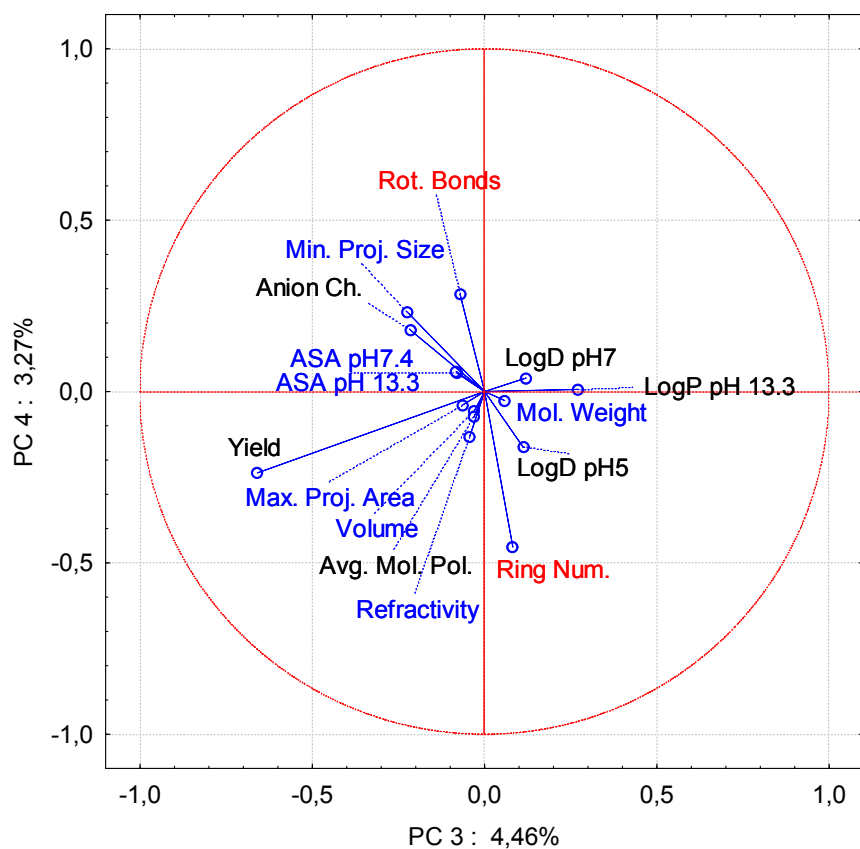


a)

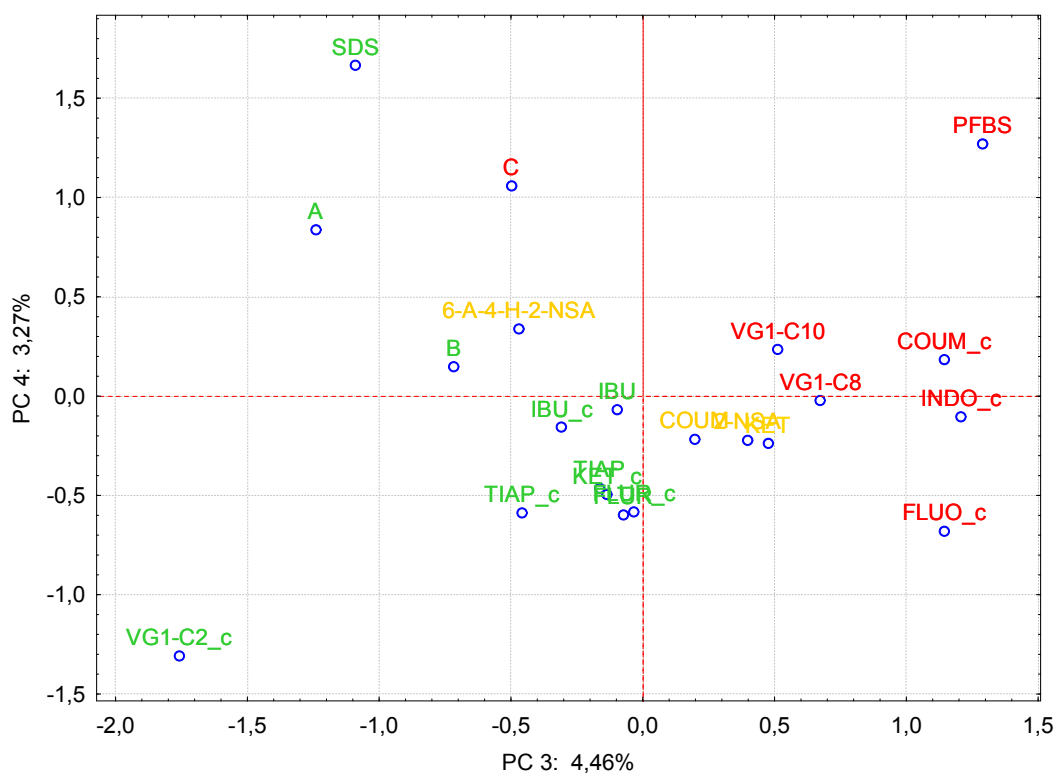


b)

Figure S17: a) Loading plot reporting variables projection on PC2 vs. PC4. b) Score plot reporting the samples on the PC2 vs. PC4 axes.



a)



b)

Figure S18: a) Loading plot reporting variables projection on PC3 vs. PC4. b) Score plot reporting the samples on the PC3 vs. PC4 axes.

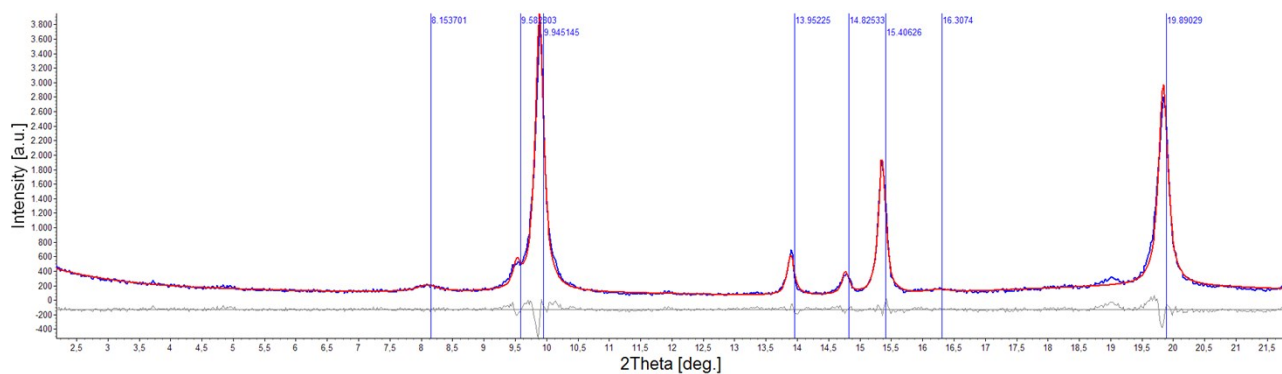


Figure SI9: XRPD pattern (in blue) and Single peak fit (in red) of LDH_PABA obtained by LAG intercalation.

Peak attribution: 8.14° and 16.298° LDH_PABA. 9.58° , 13.95° ,14.82° and 15.41° PABA. 9.95° and 19.90° LDH_NO₃

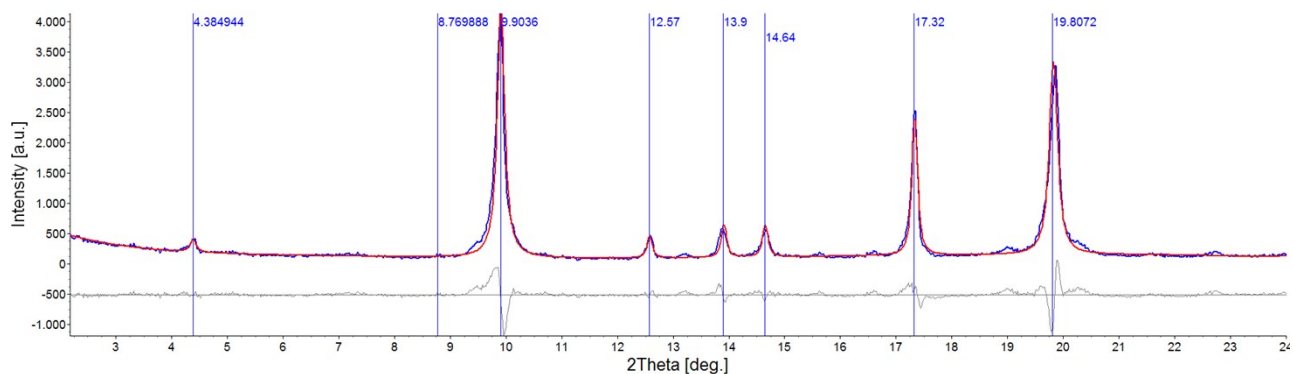


Figure SI10: XRPD pattern (in blue) and Single peak fit (in red) of LDH_TOLU obtained by LAG intercalation.

Peak attribution: 4.38° and 8.77° LDH_TOLU. 12.57° , 13.9° ,14.64° and 17.32° TOLU. 9.90° and 19.81° LDH_NO₃