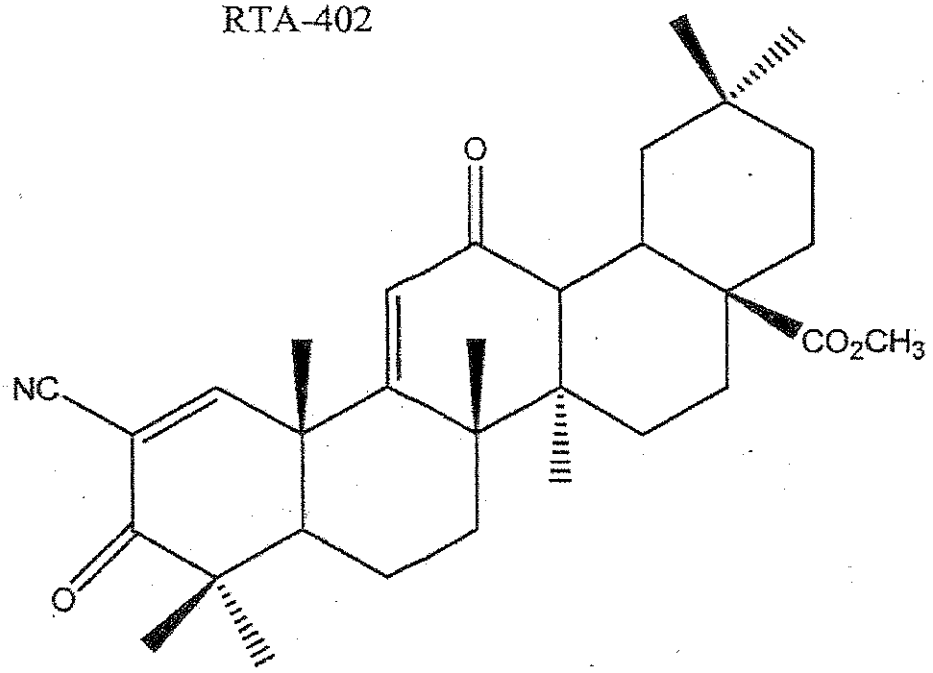
Figure 1 - Chemical structure of CDDO methyl ester

RTA-402



$C_{32}H_{43}NO_4$
Mol. Wt.: 505.69

Figure 2 – XRPD pattern of Form A (top) and Form B (bottom)
From top to bottom: unmicronized Form A (2A), micronized Form A (2B), and Form B (2C).

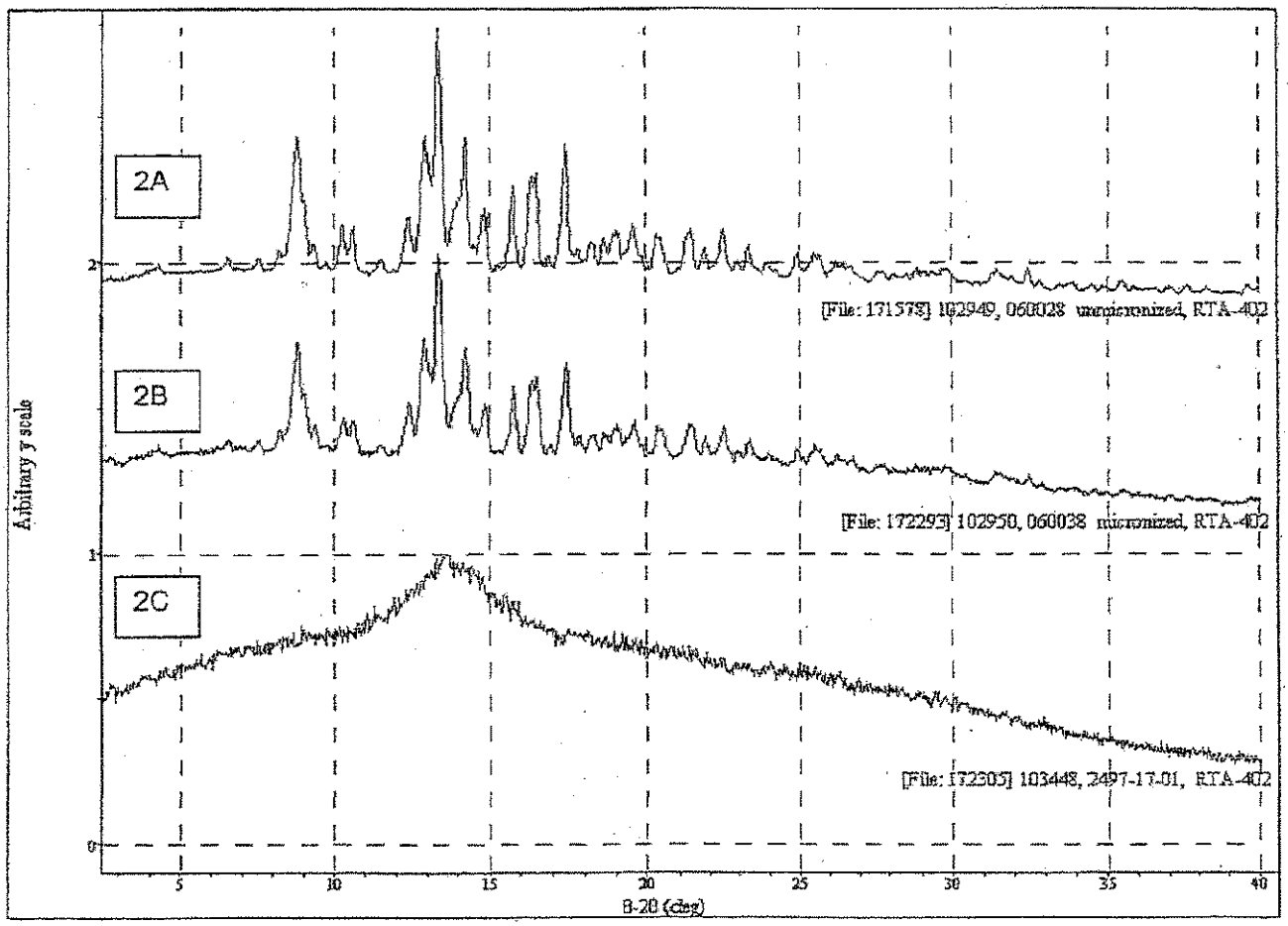
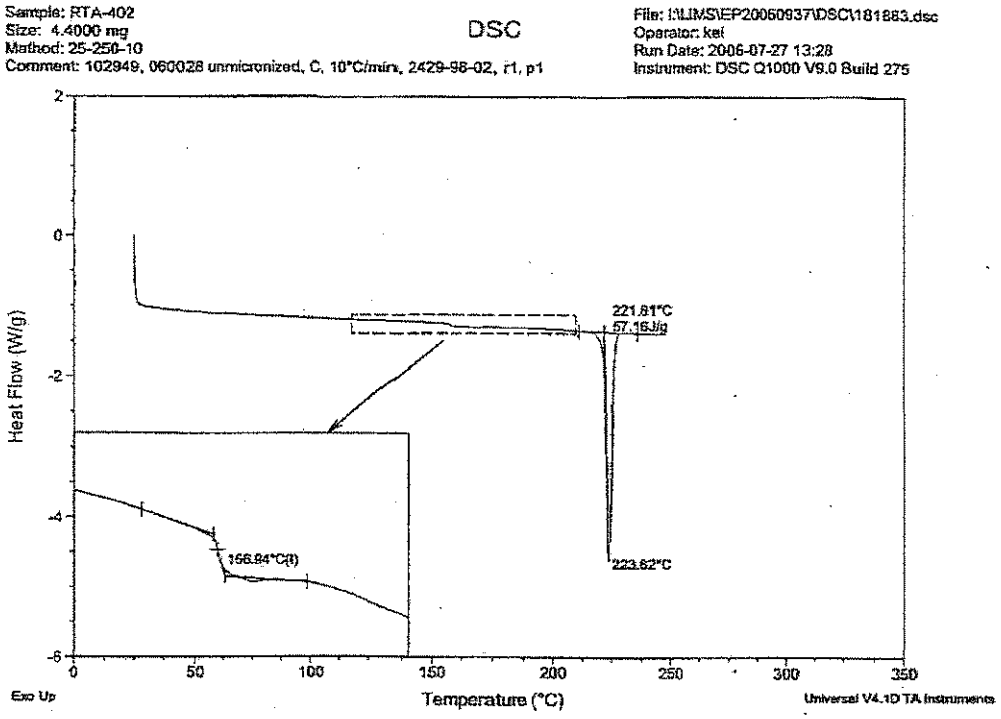


Figure 3 - DSC and TG curve of CDDO methyl ester.



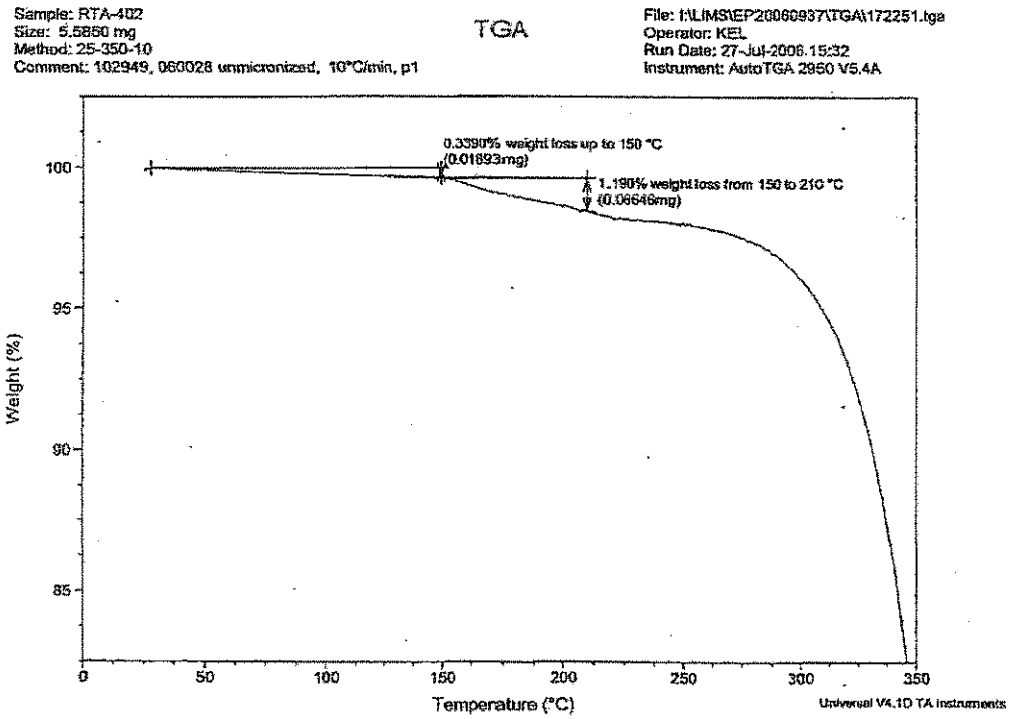


Figure 4 - Hot stage analysis of Form A - unmicronized

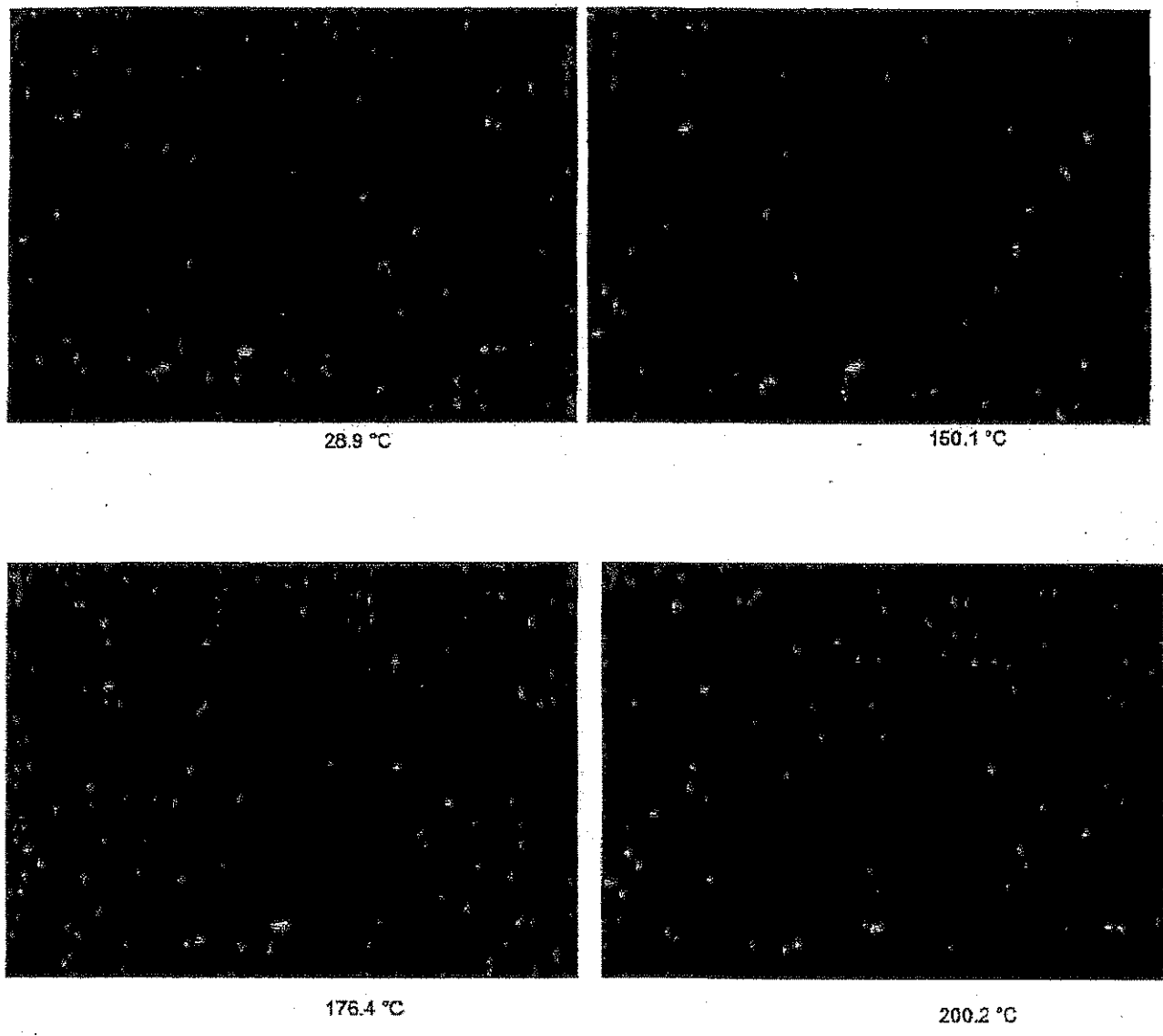
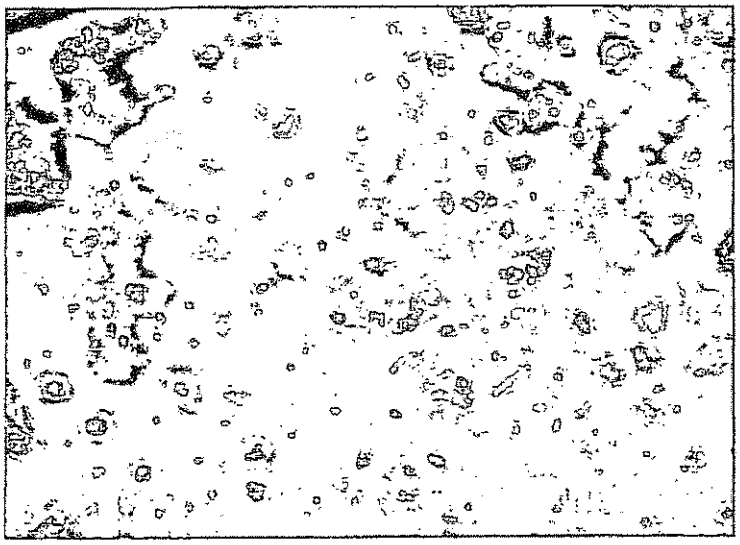


Figure 4 (continued) Hot stage analysis of Form A - unmicronized,



225.9 °C

Figure 5 - Dynamic vapor sorption isotherm of Form A - unmicronized

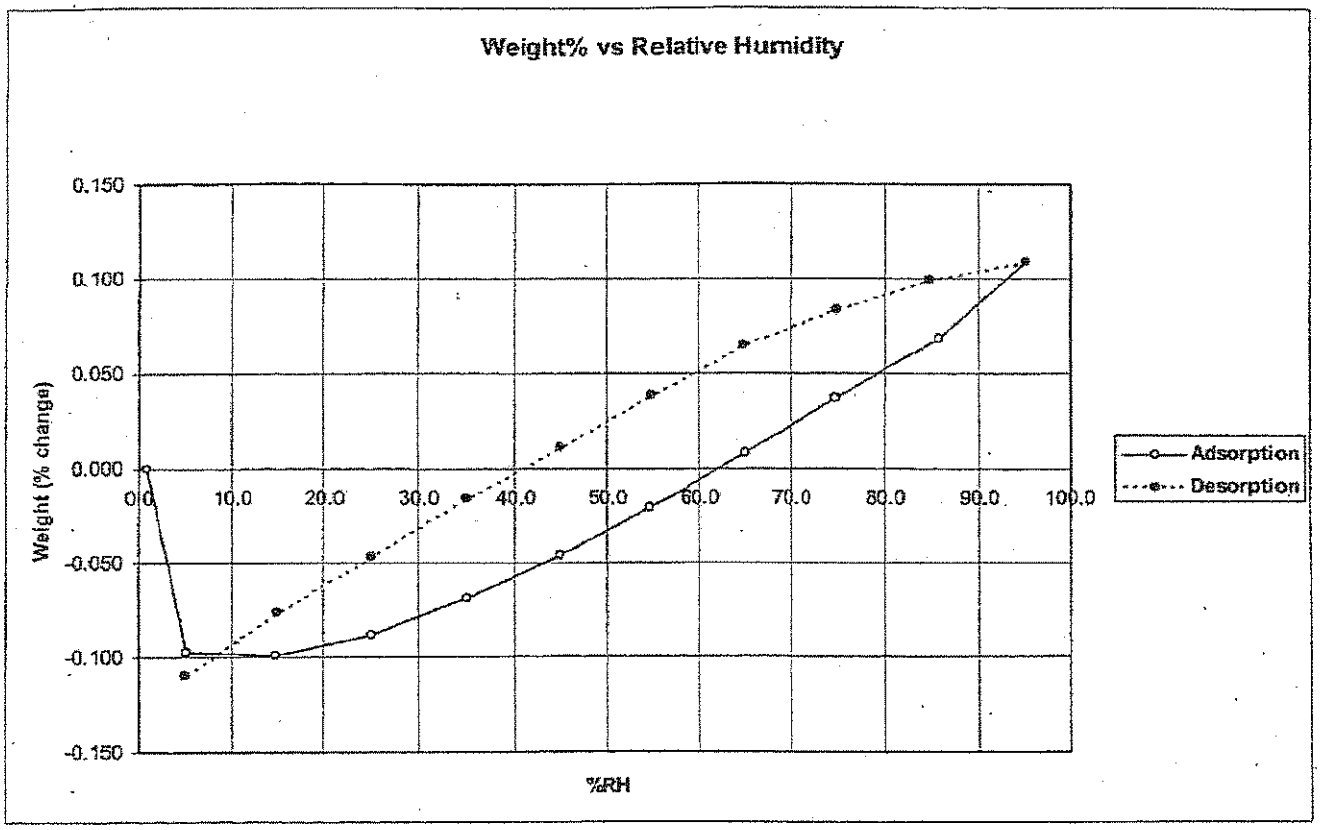


Figure 6- SEM images of Form A - unmicronized

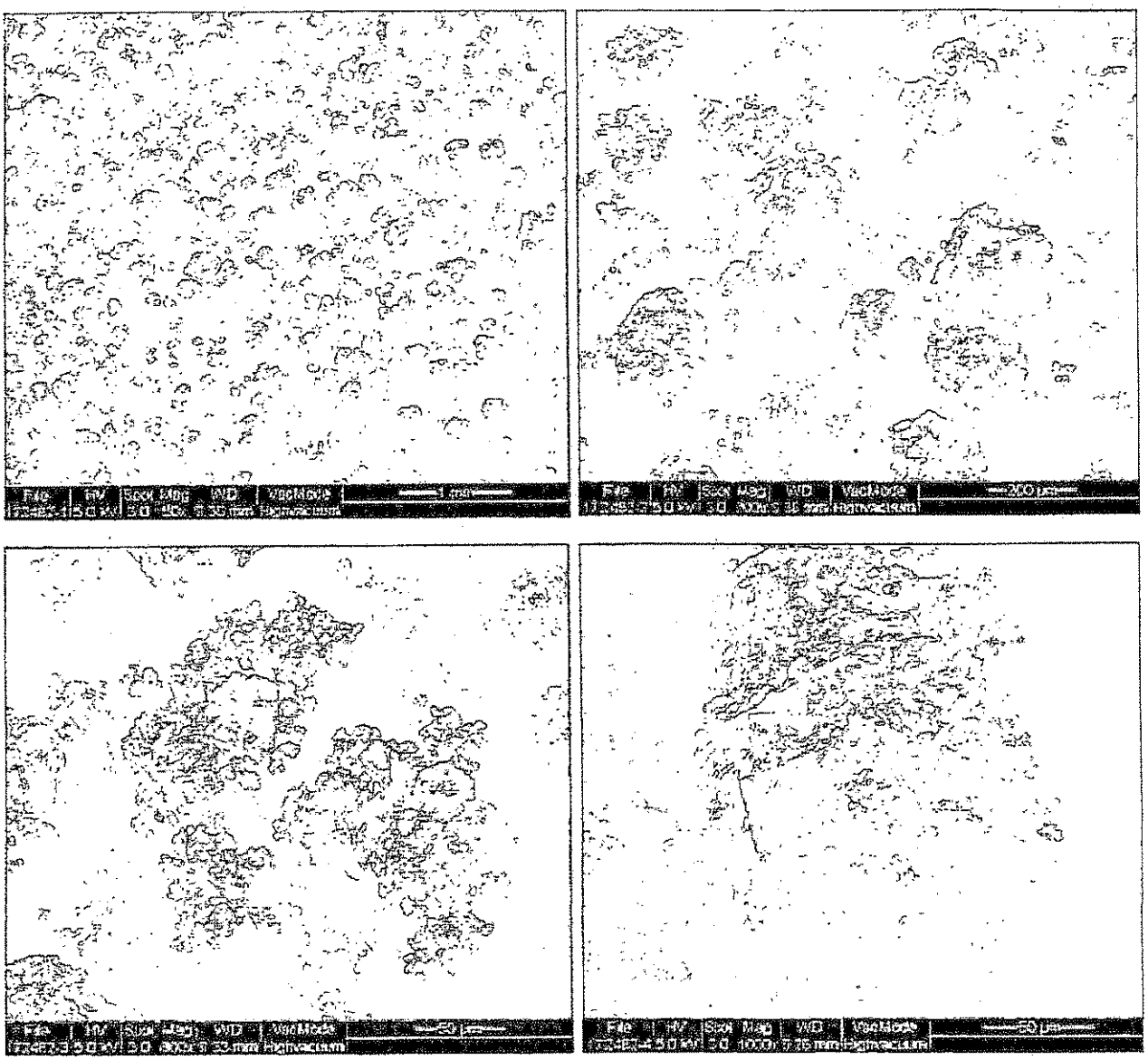


Figure 6 (continued) SEM IMAGES of Form A - unmicronized

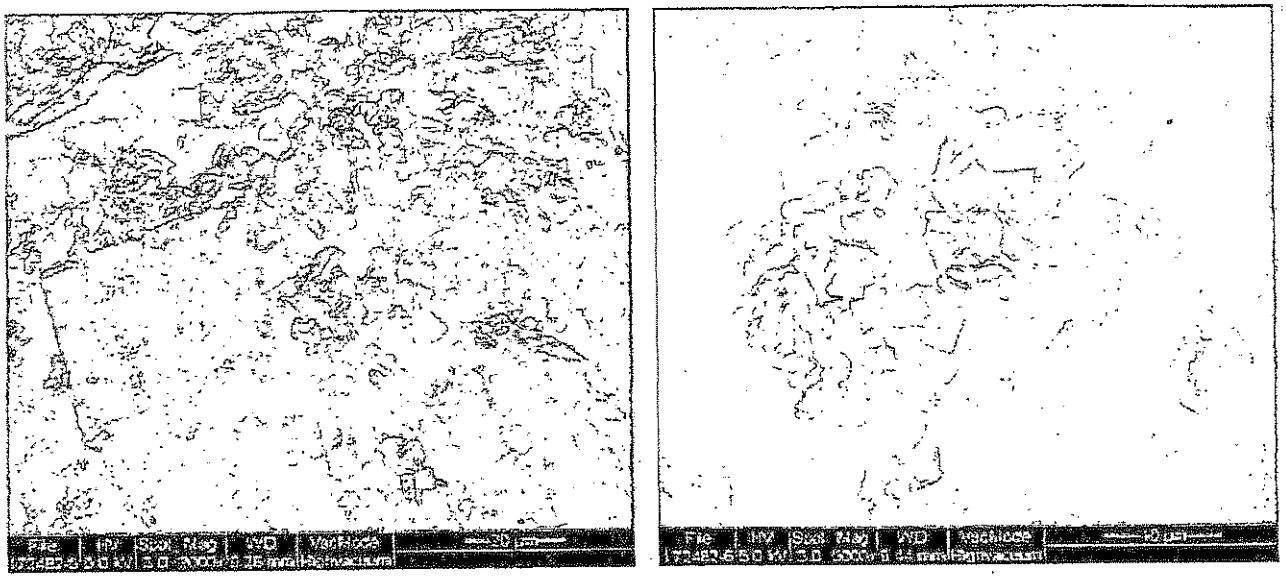


Figure 7 - Form A before (top) and after (bottom) stress at 195 °C.

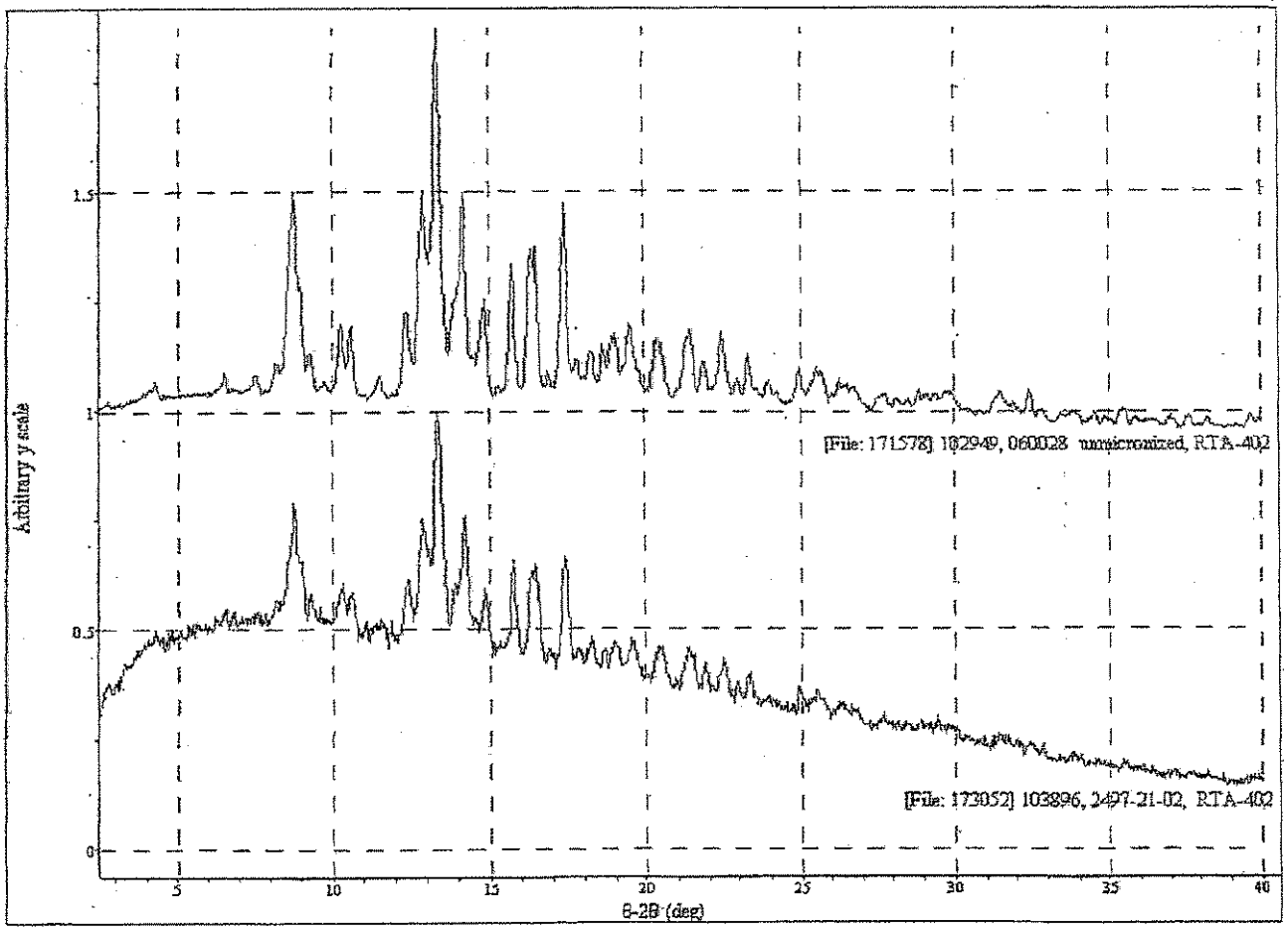


Figure 8 - NMR spectrum of Form A - unmicronized.

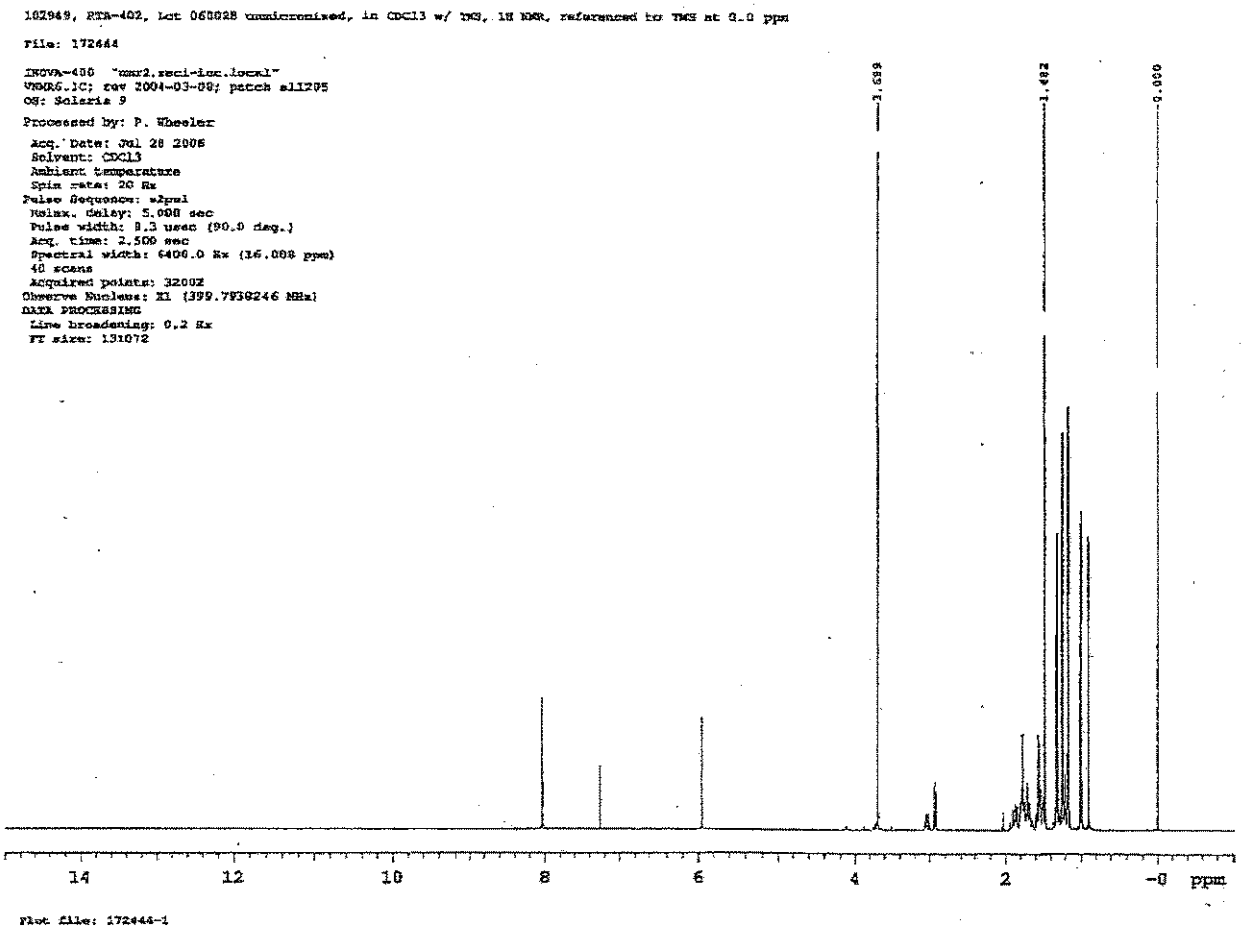


Figure 9 - MDSC curve of Form B CDDO methyl ester.

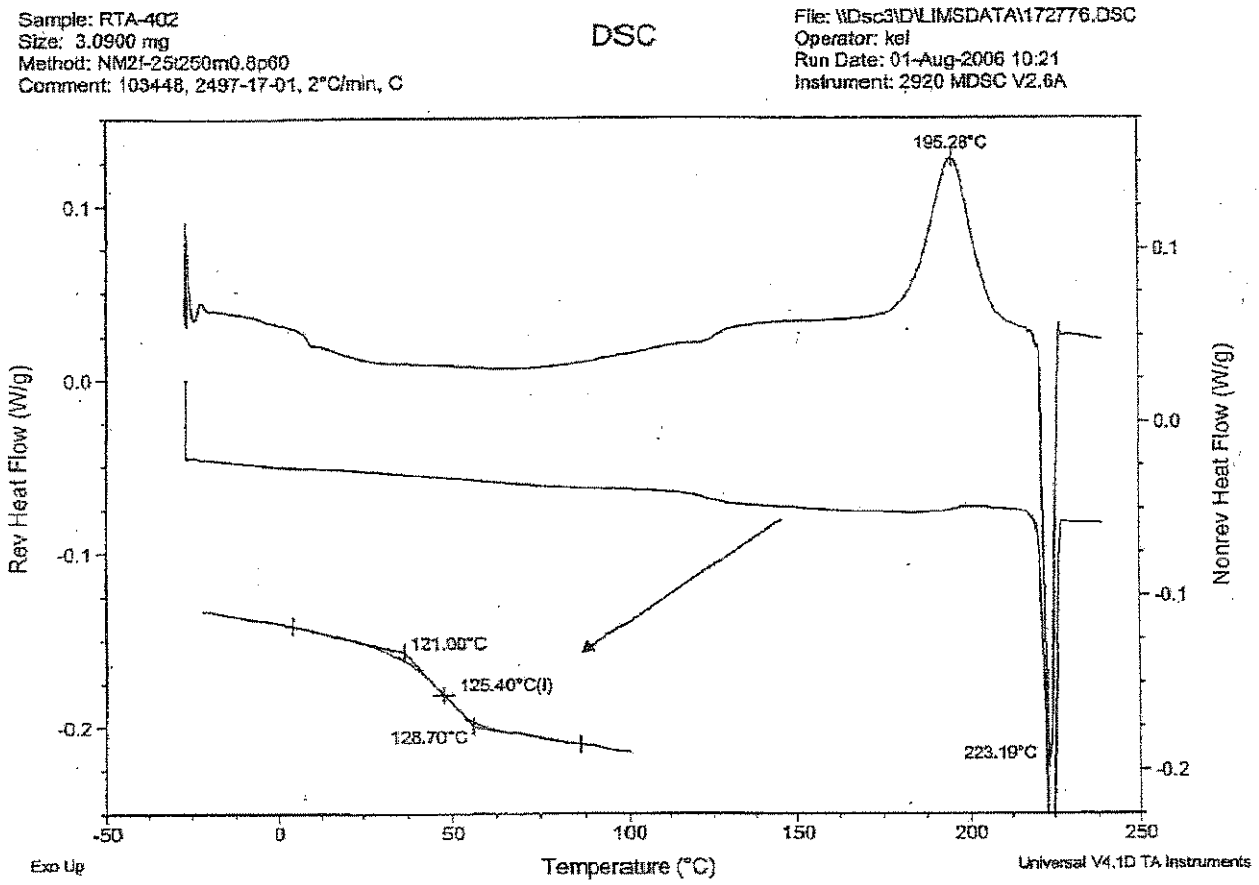


Figure 10 – Form B CDDO methyl ester before (top) and after (bottom) stress.

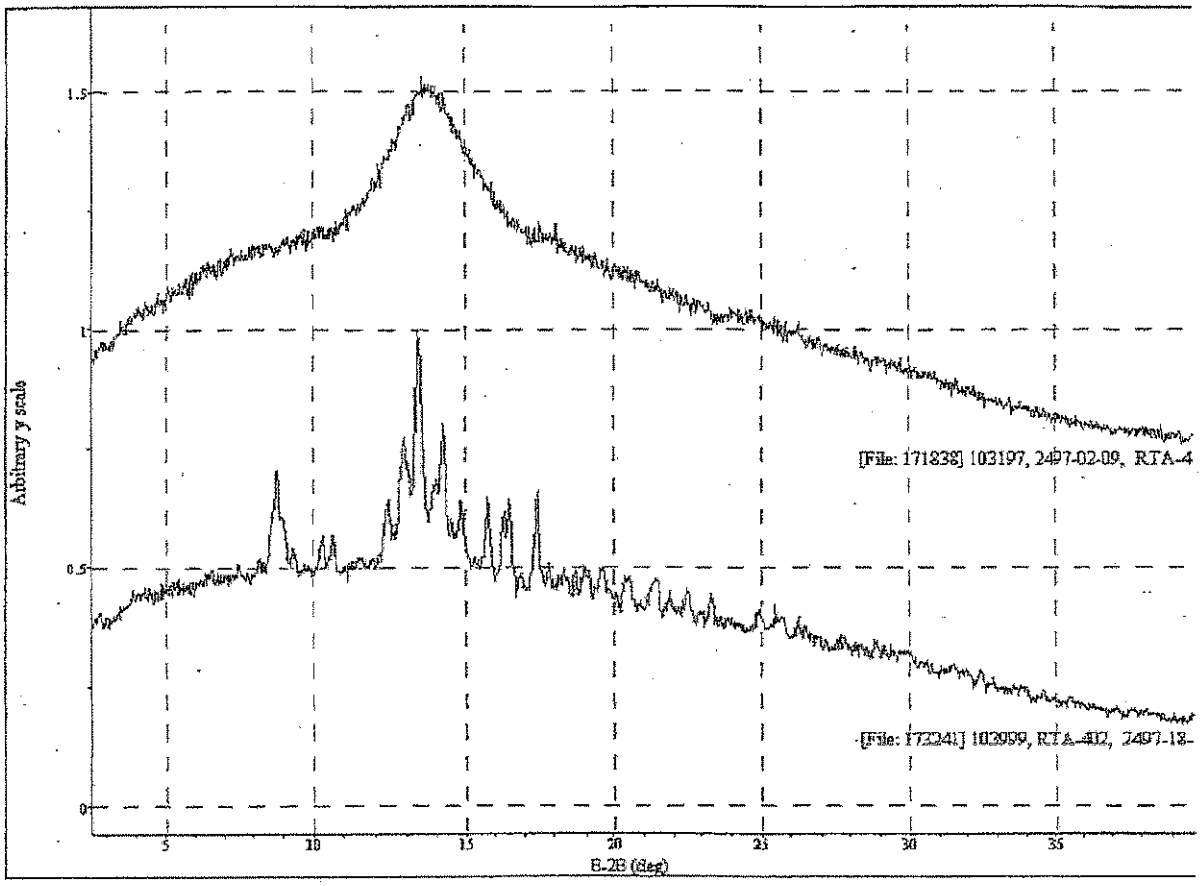


Figure 11 - NMR spectrum of Form B CDDO methyl ester.

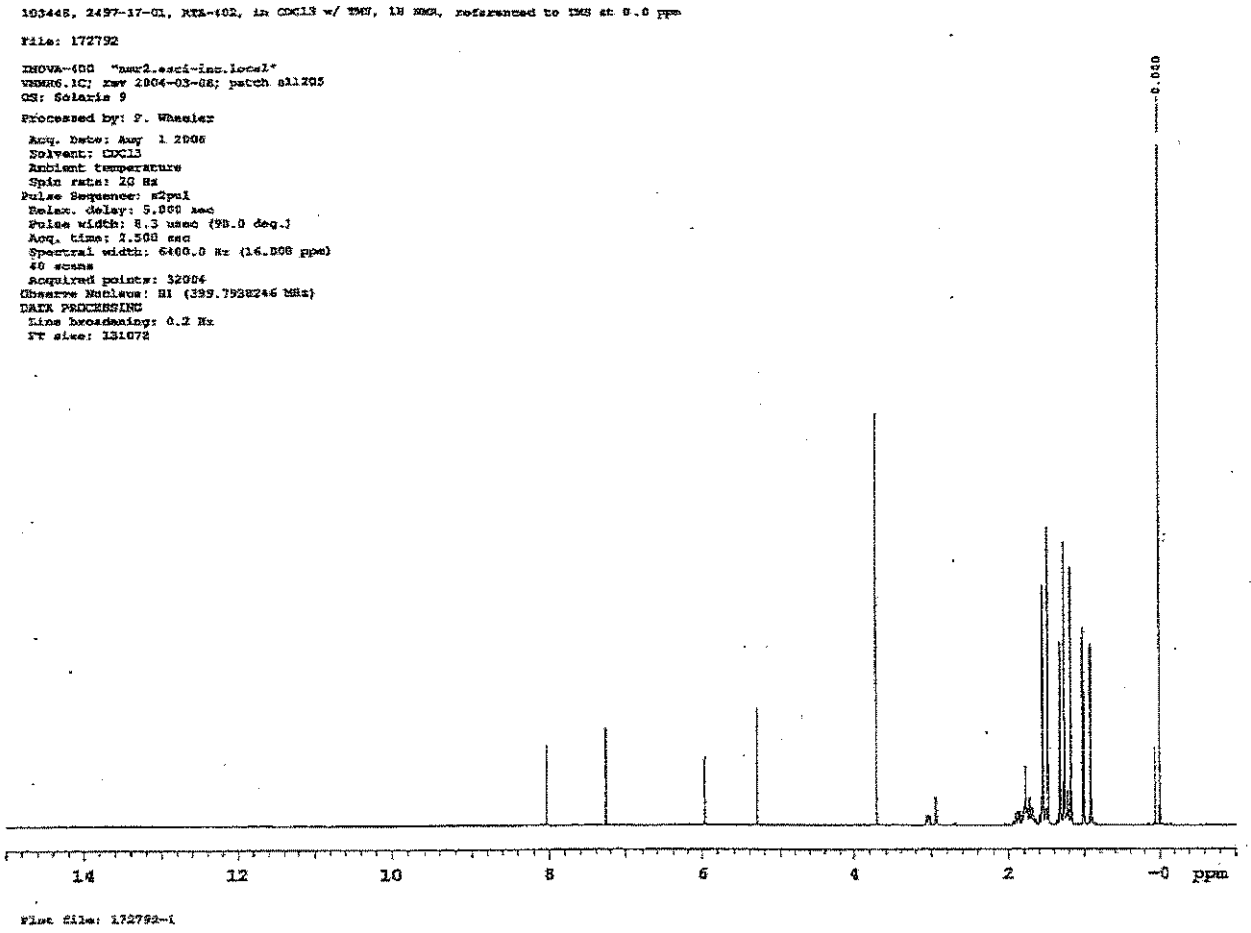


Figure 12 - ORTEP drawing of a single CDDO methyl ester molecule with labeling. Atoms are represented by 50% probability anisotropic thermal ellipsoids.

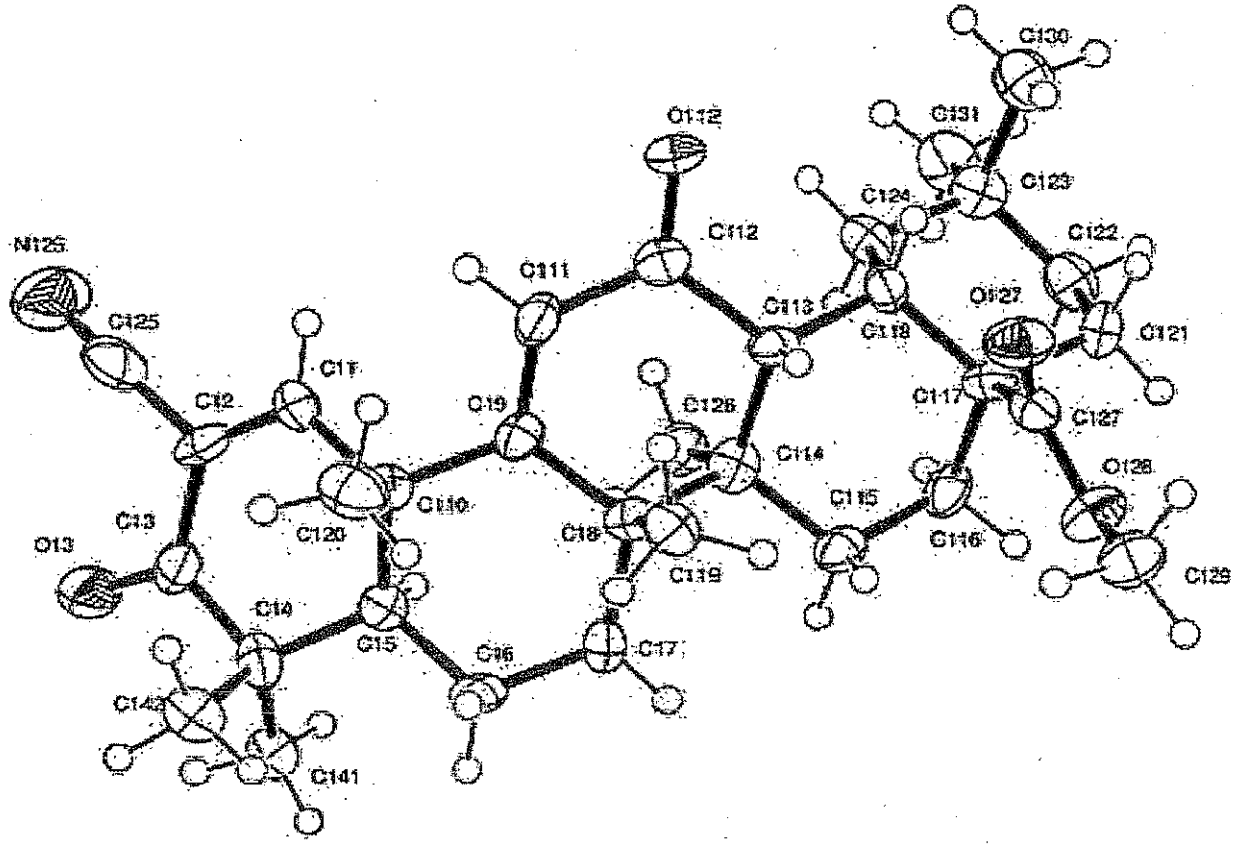


Figure 13 - ORTEP drawing of the contents of the asymmetric unit of Form A crystals. Atoms are represented by 50% probability anisotropic thermal ellipsoids.

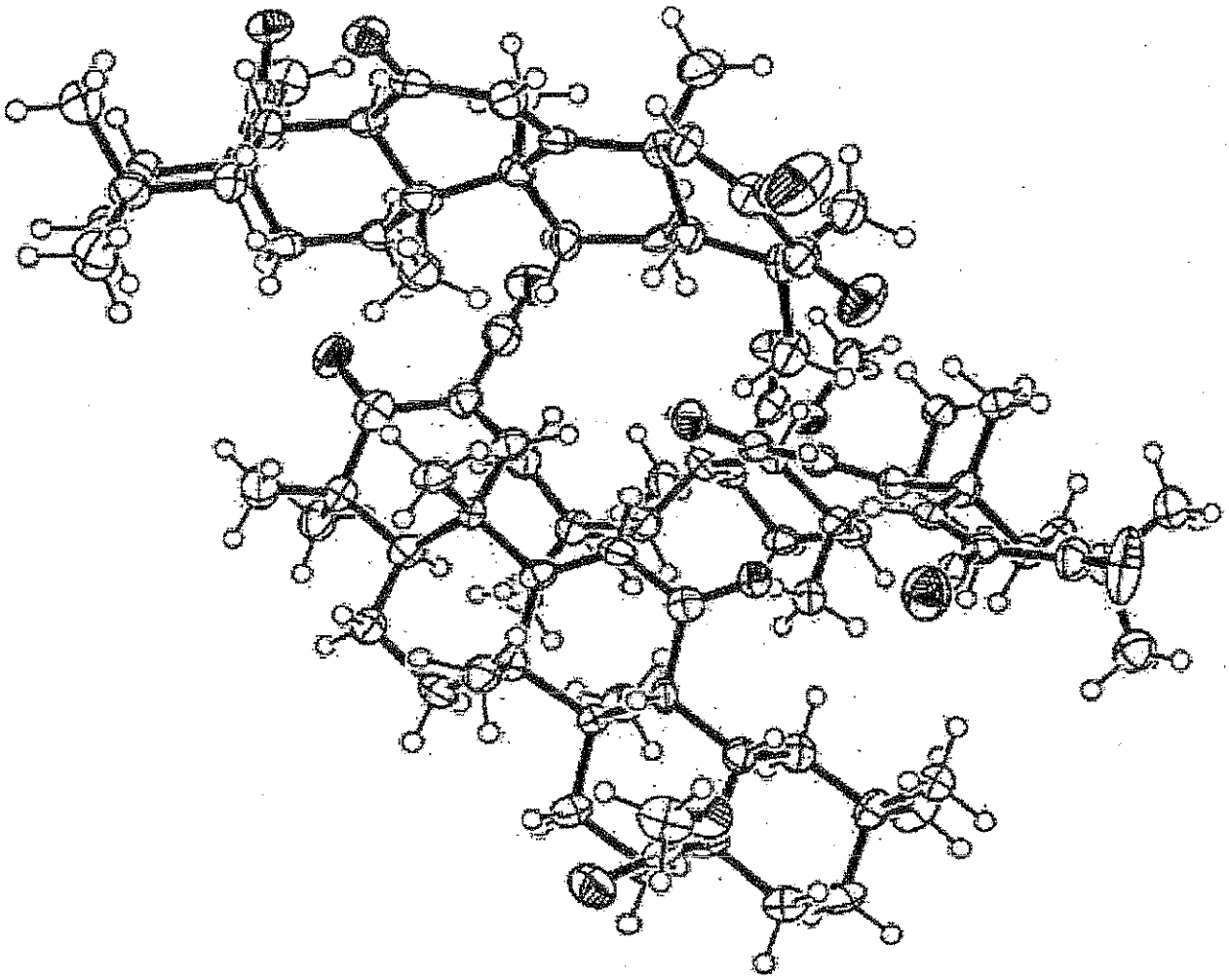


Figure 14 - Packing diagram of Form A crystals viewed down the crystallographic *a* axis.

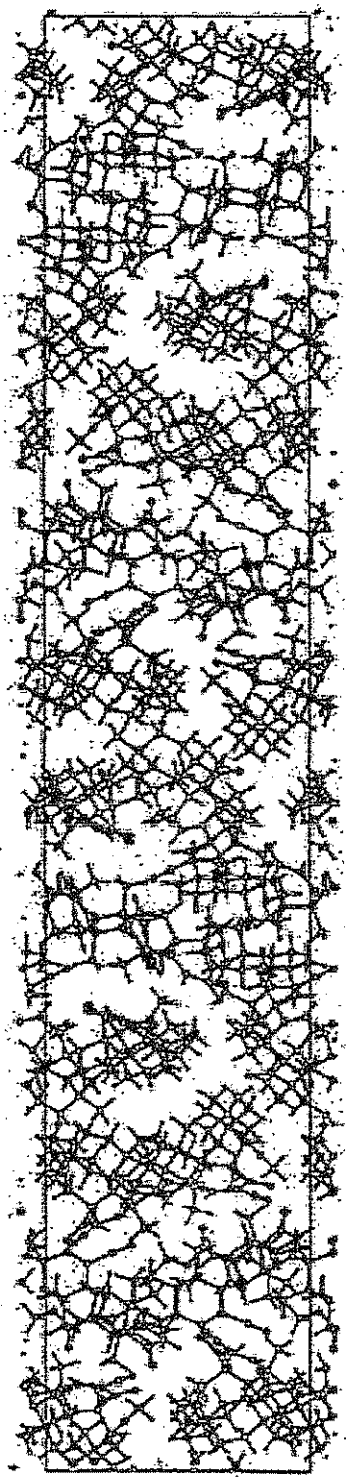


Figure 15 - Packing diagram of Form A crystals viewed down the crystallographic *b* axis.

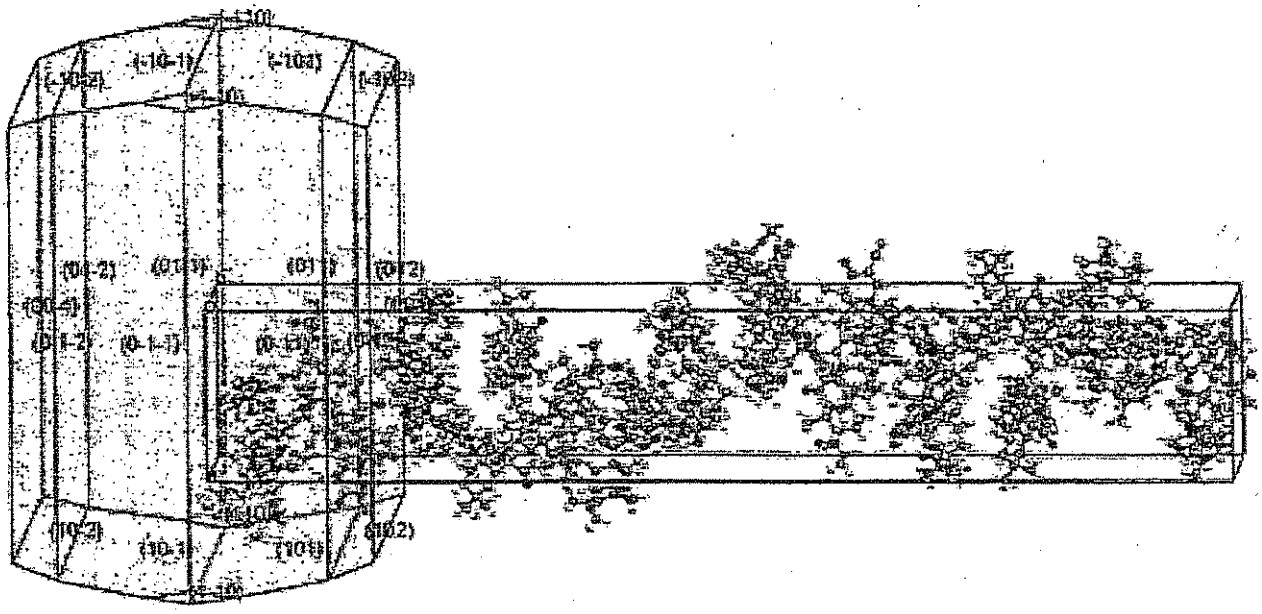


Figure 16 - Packing diagram of Form A crystals viewed down the crystallographic *c* axis.

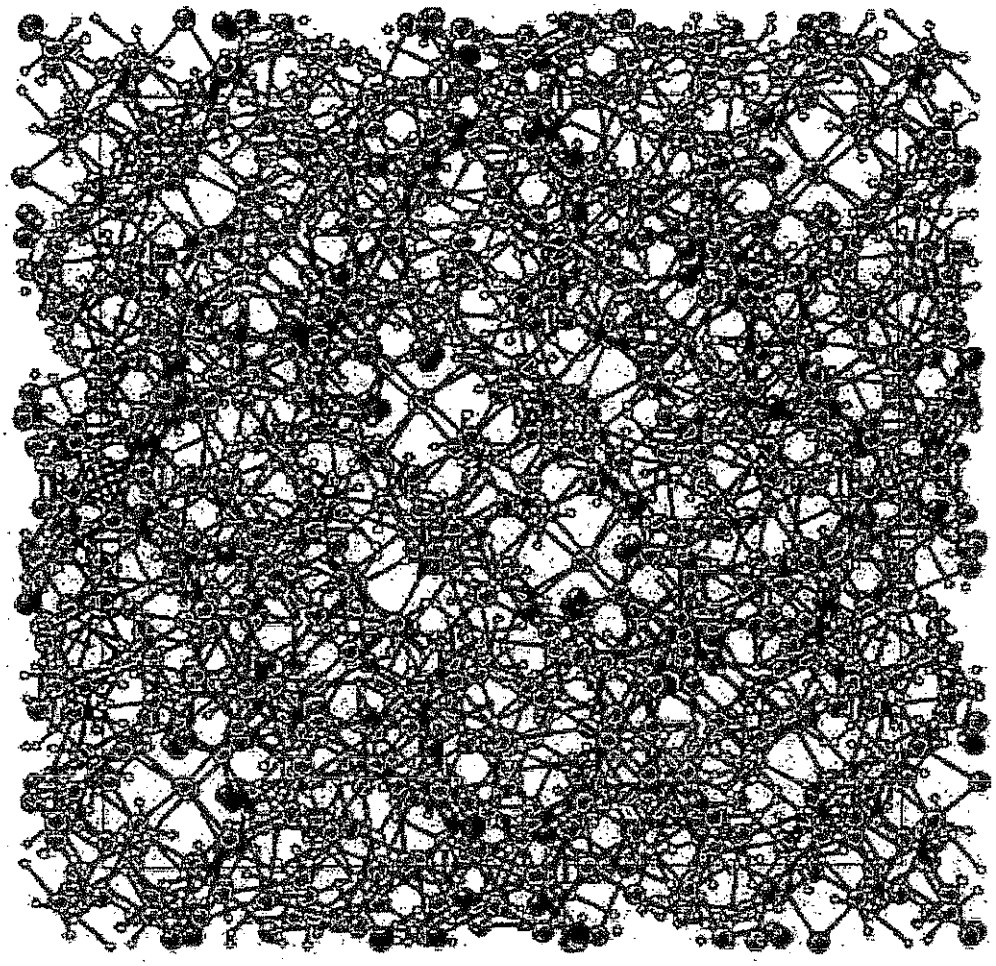


Figure 17 - Calculated X-ray powder pattern of Form A

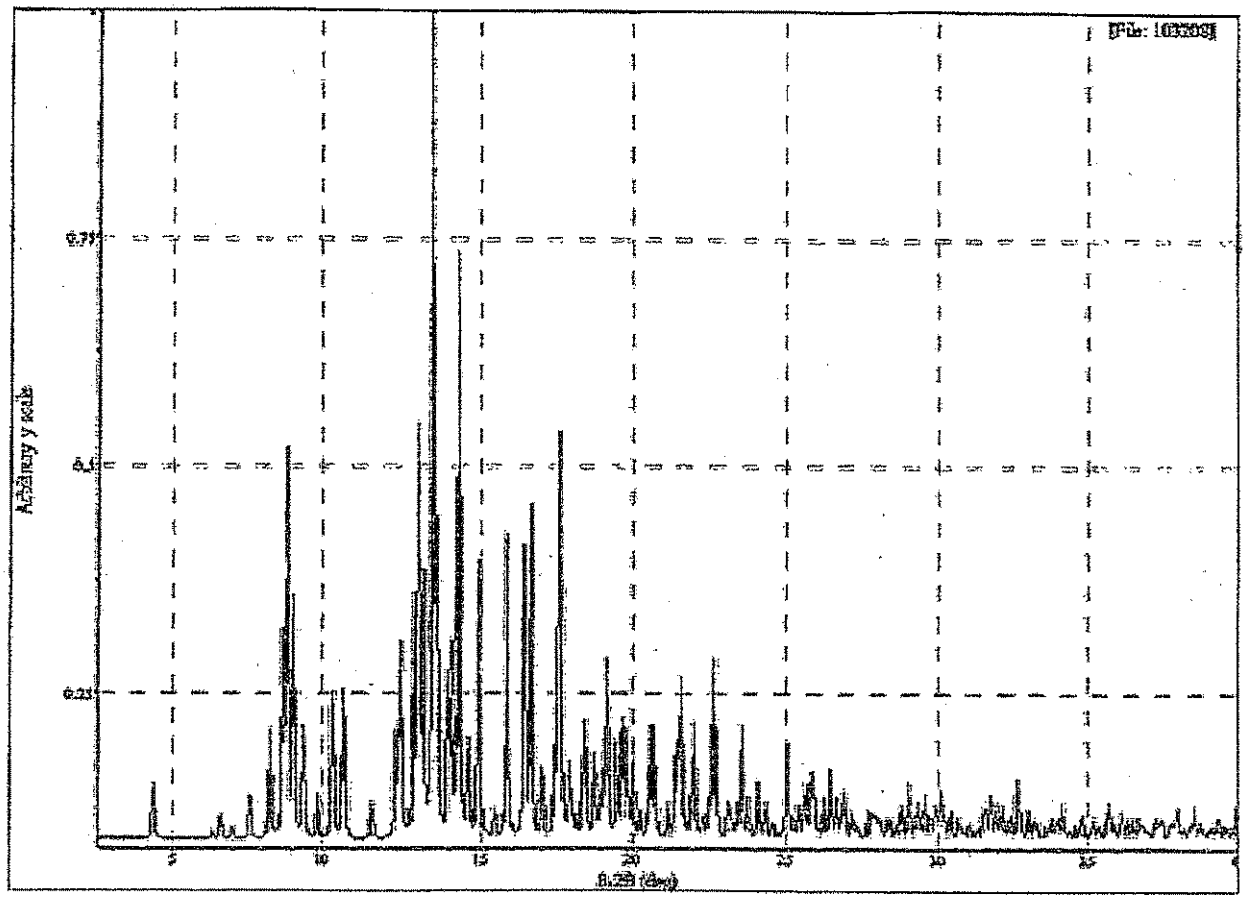


Figure 18 - Experimental XRPD of Form A

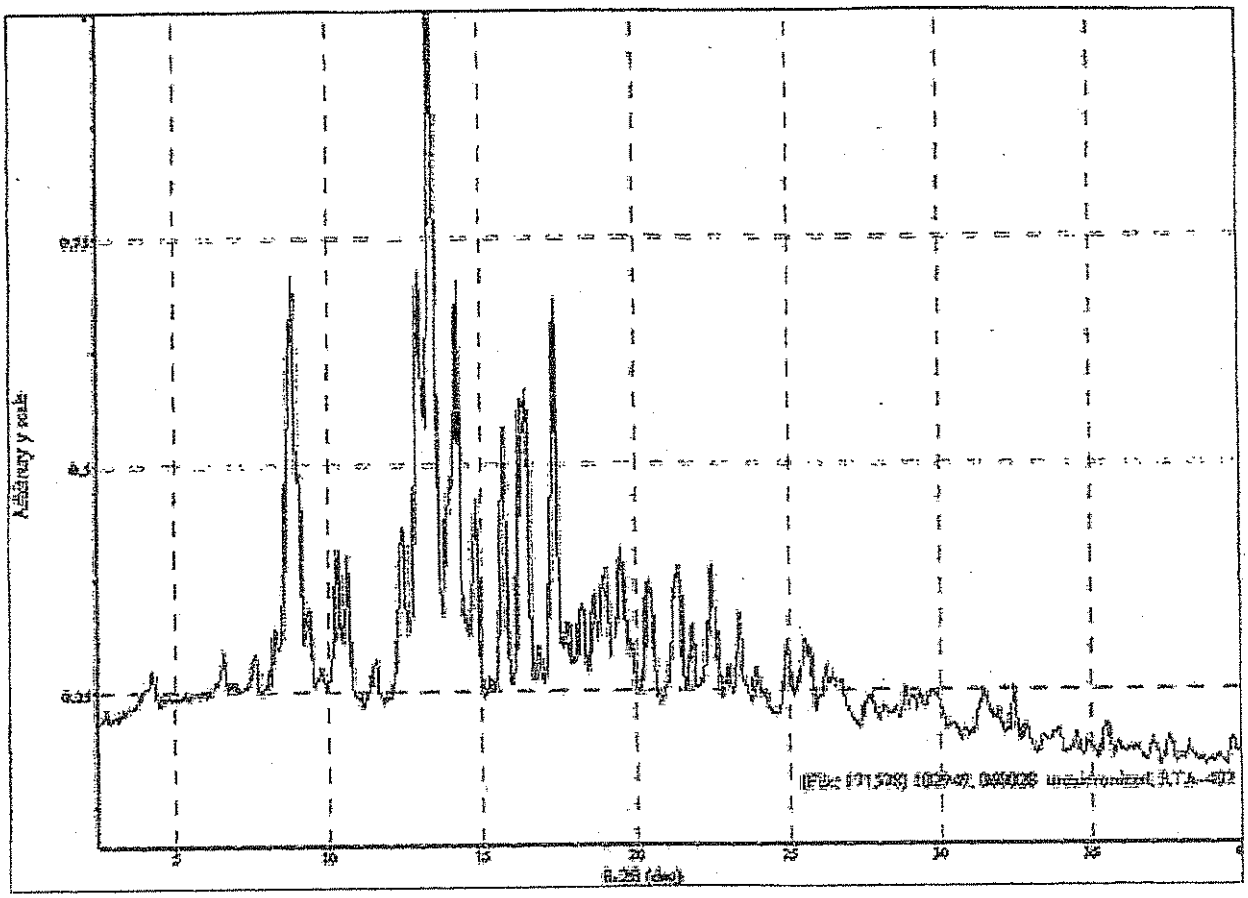


Figure 19 - Comparison of the calculated and experimental XRPD patterns of CDDO methyl ester to the XRPD pattern of CDDO methyl ester

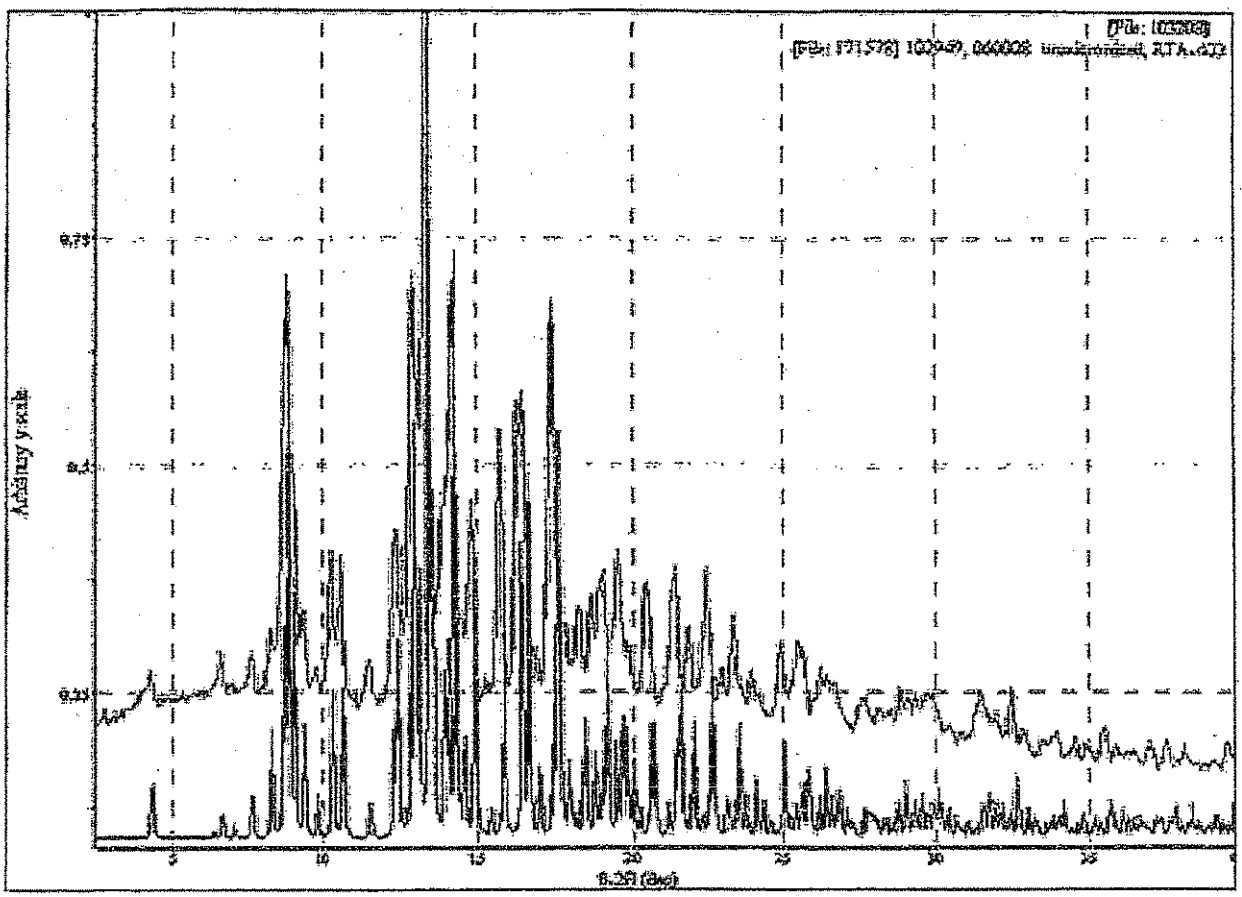


Figure 20. Representative plot of the area under the curve for Form A and Form B (amorphous), following a 4.1 mg/kg oral administration. Each data point represents the mean plasma concentration of CDDO methyl ester in 8 animals. Error bars represent the standard deviation within the sampled population.

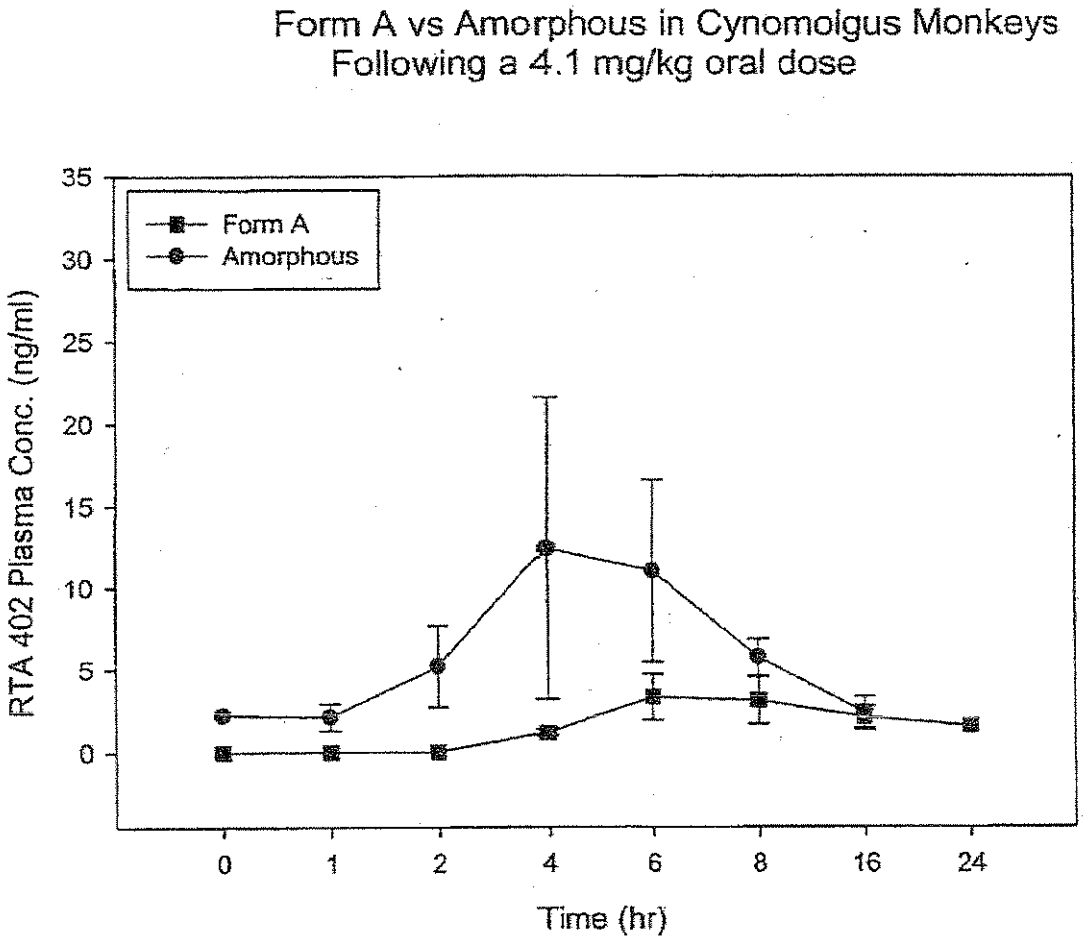
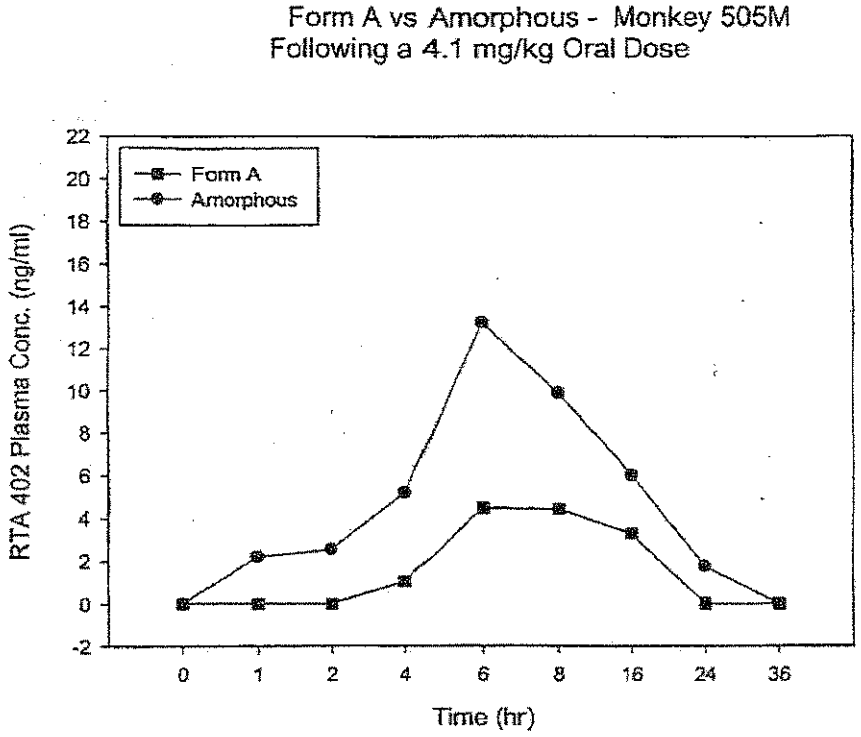


Figure 21. Animal #505M (top panel) and animal #507F (bottom panel)



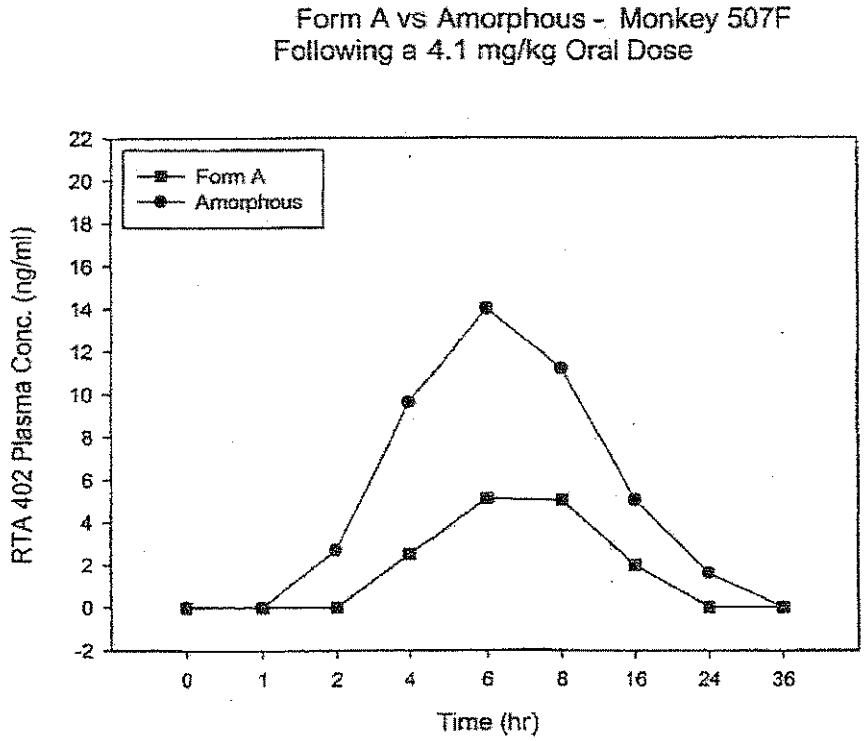


Figure 22. Animal #508F (top panel) and animal #502M (bottom panel)

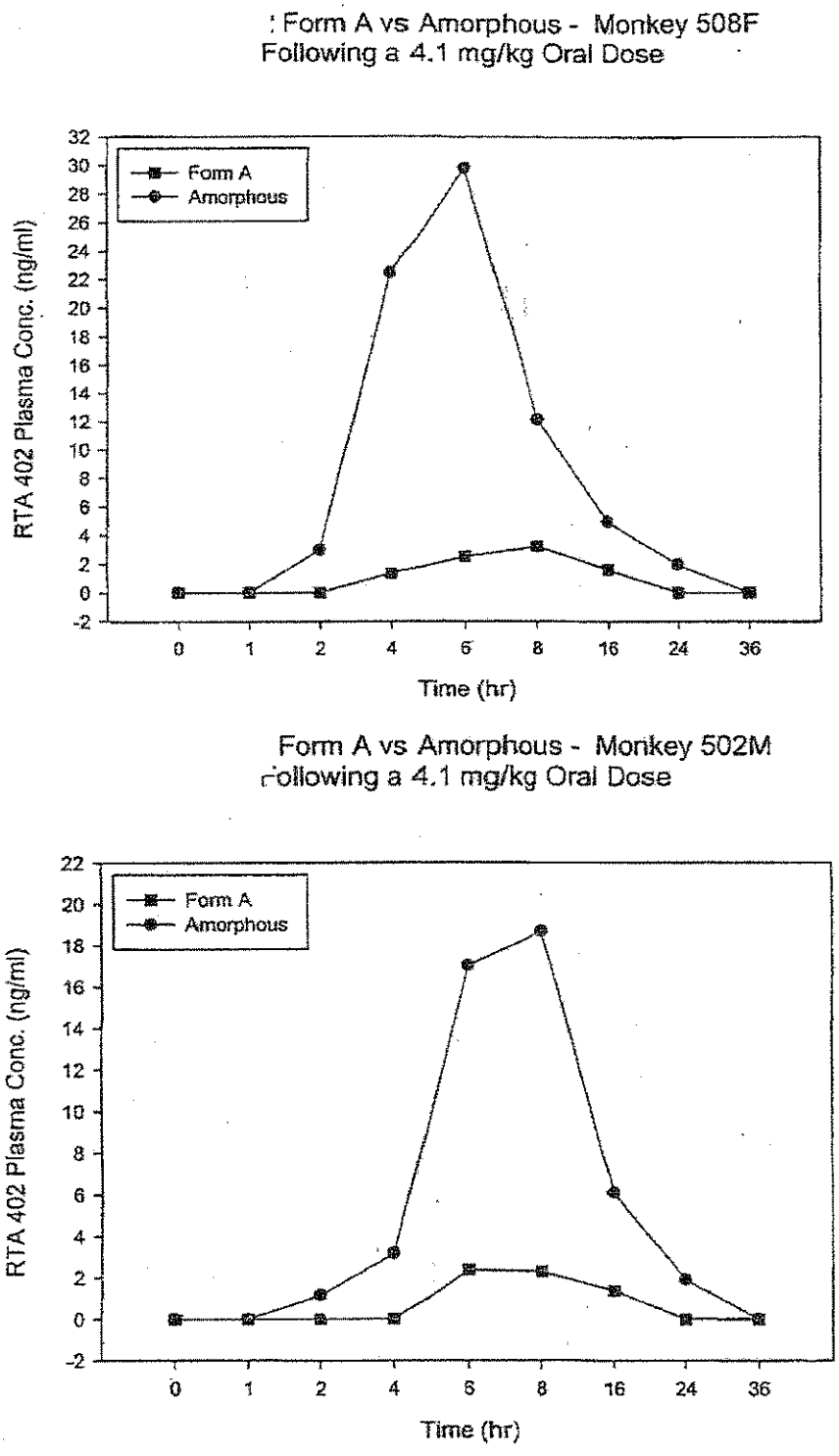
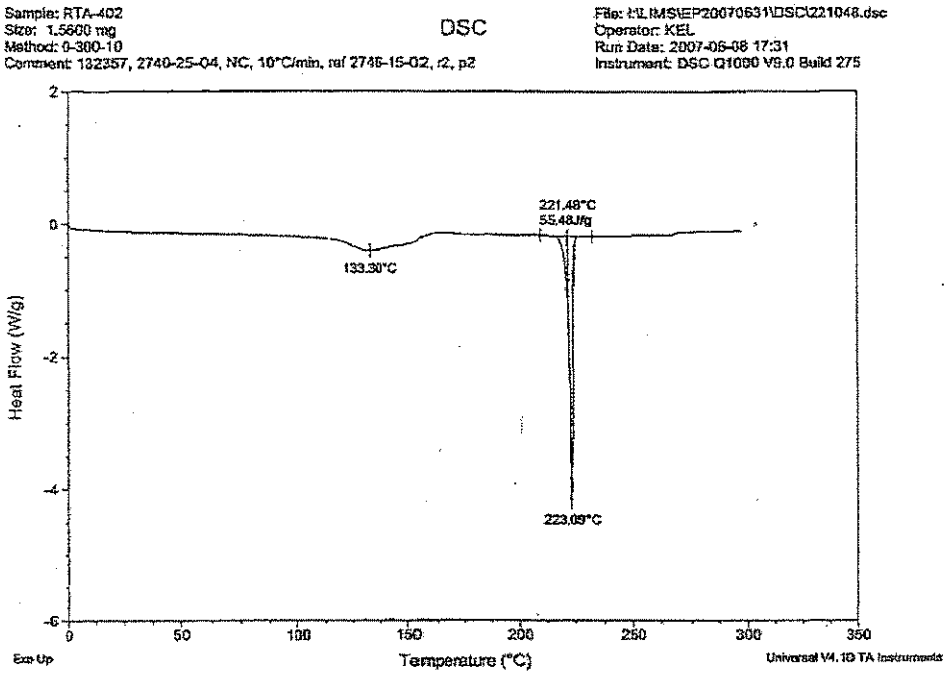


Figure 23. Thermograms of CDDO methyl ester hemibenzene solvate



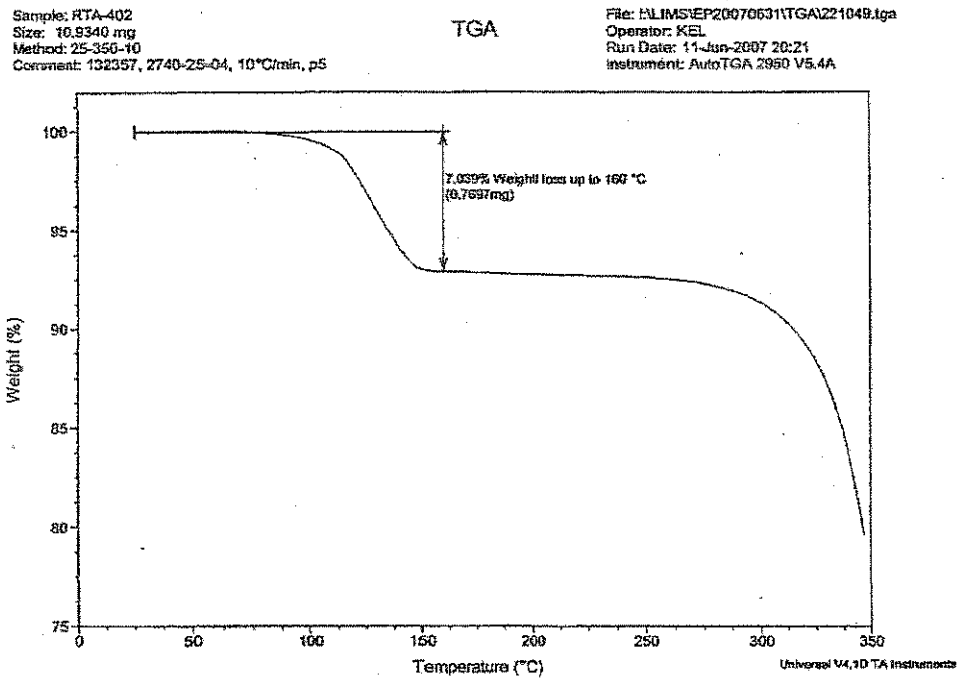
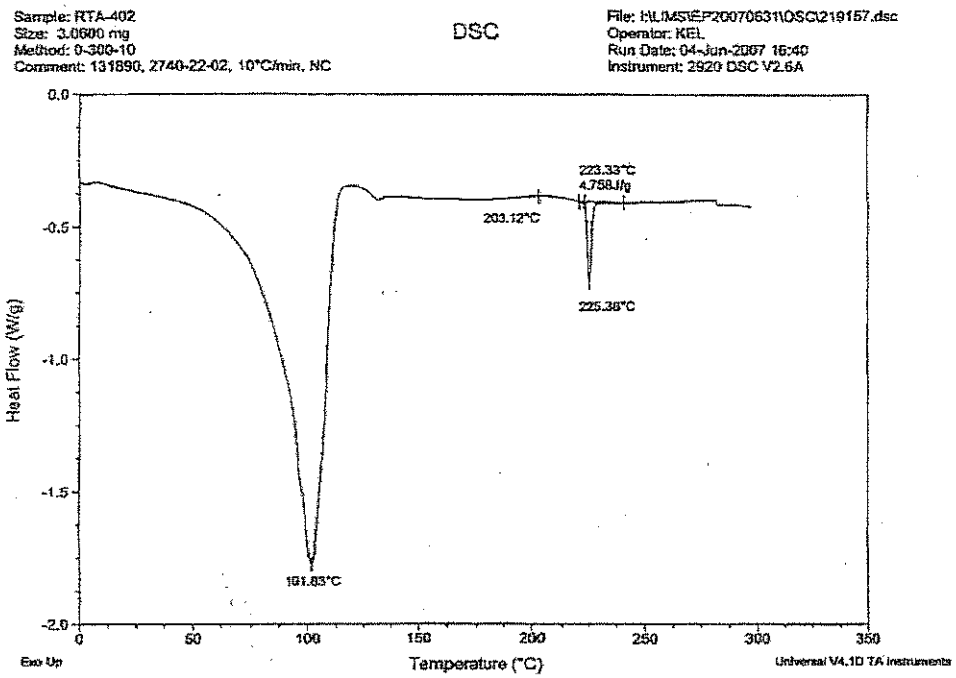


Figure 24 - Thermograms of CDDO methyl ester dimethanol solvate



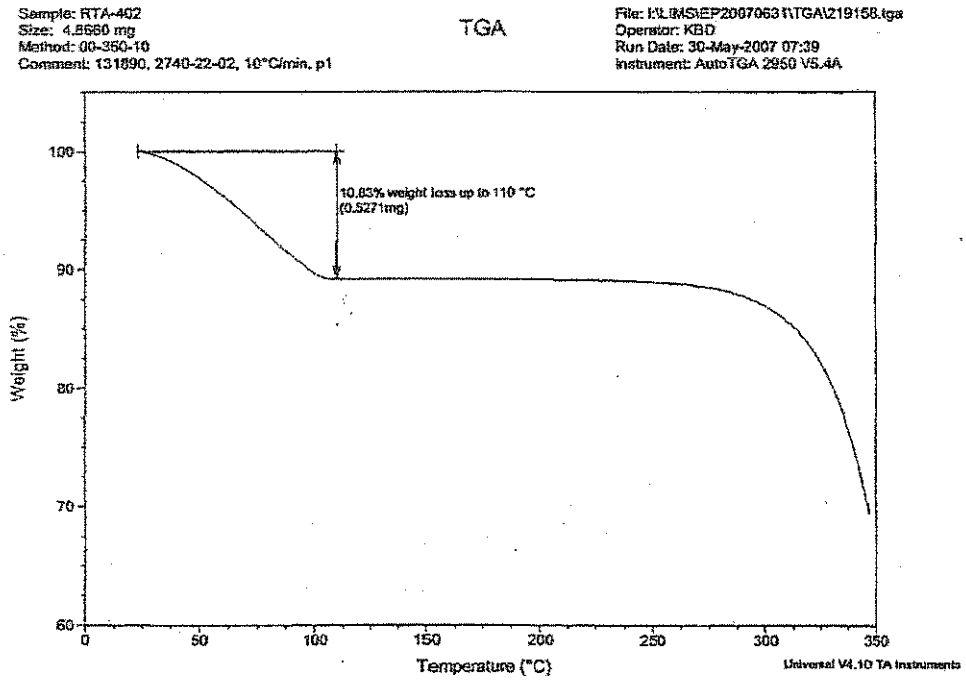


Figure 25 - TGIR data of CDDO methyl ester dimethanol solvate

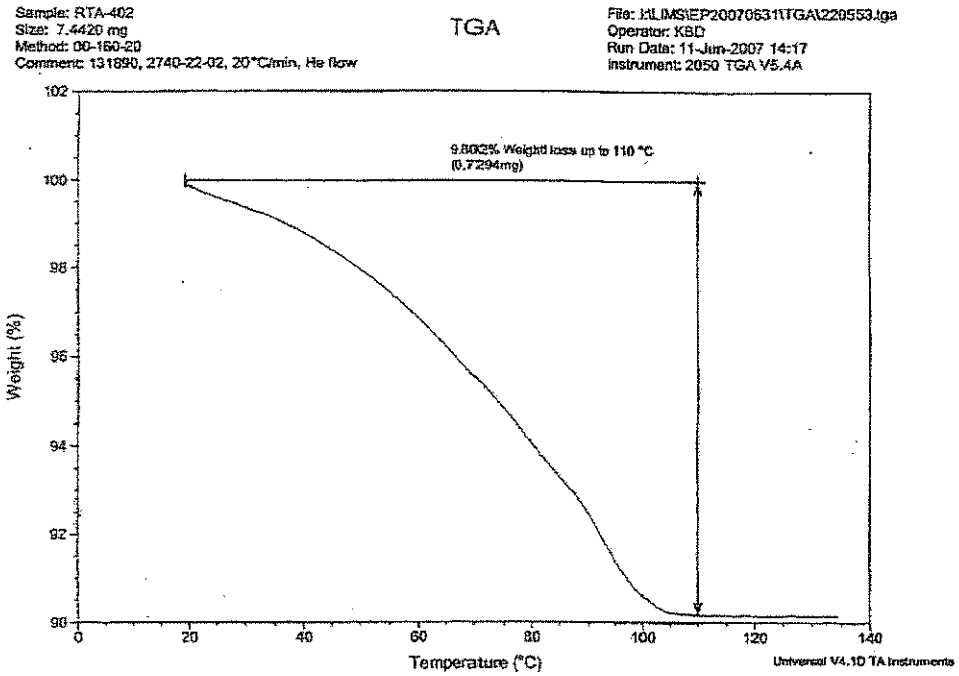


Figure 26 - XRPD patterns of CDDO methyl ester dimethanol solvate before (top) and after (bottom) TGIR analysis (up to 140 °C).

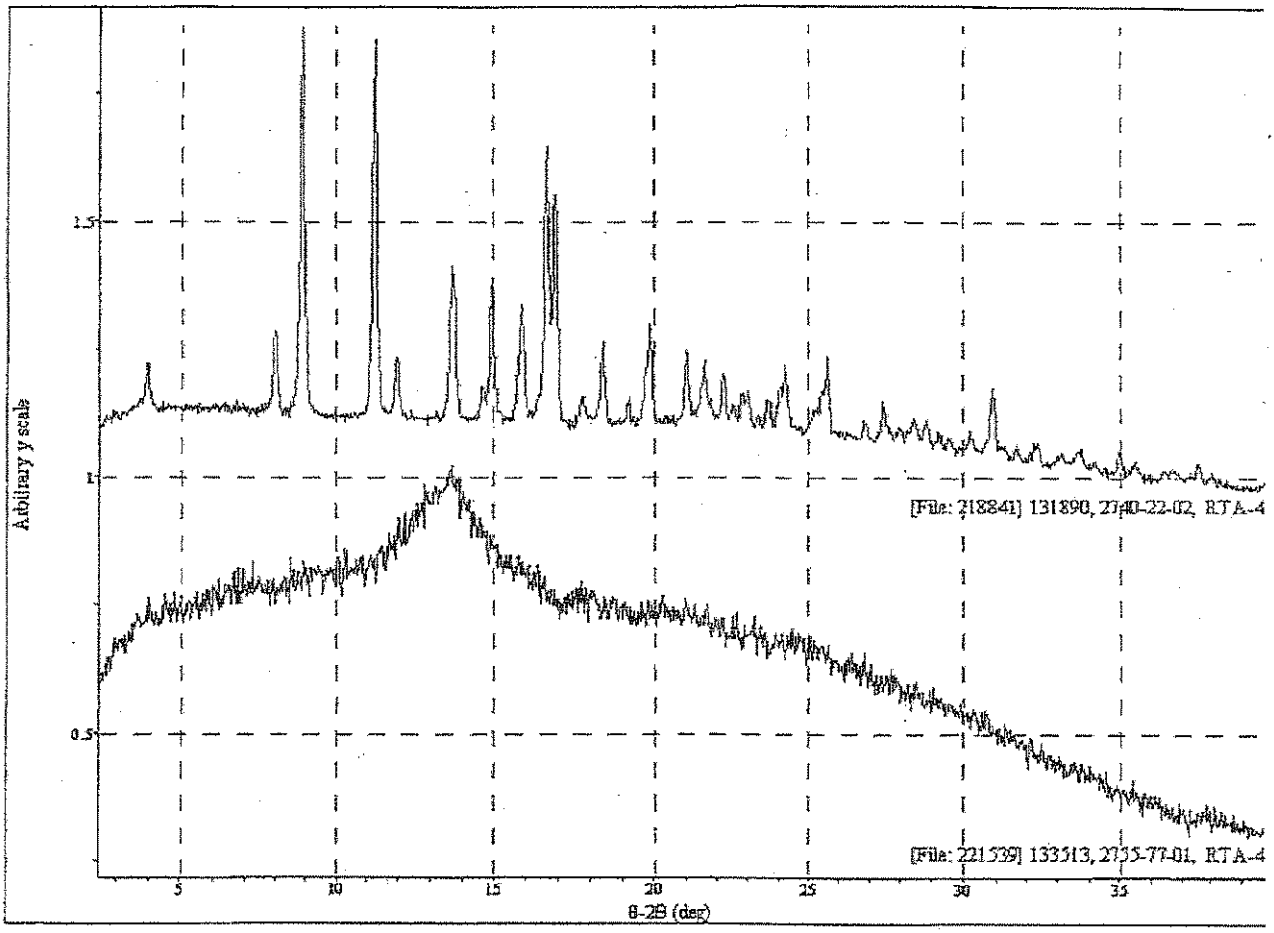


Figure 27 Overlay PDF, Form A vs. Form B. Local order similar from about 5 Å to about 20 Å.

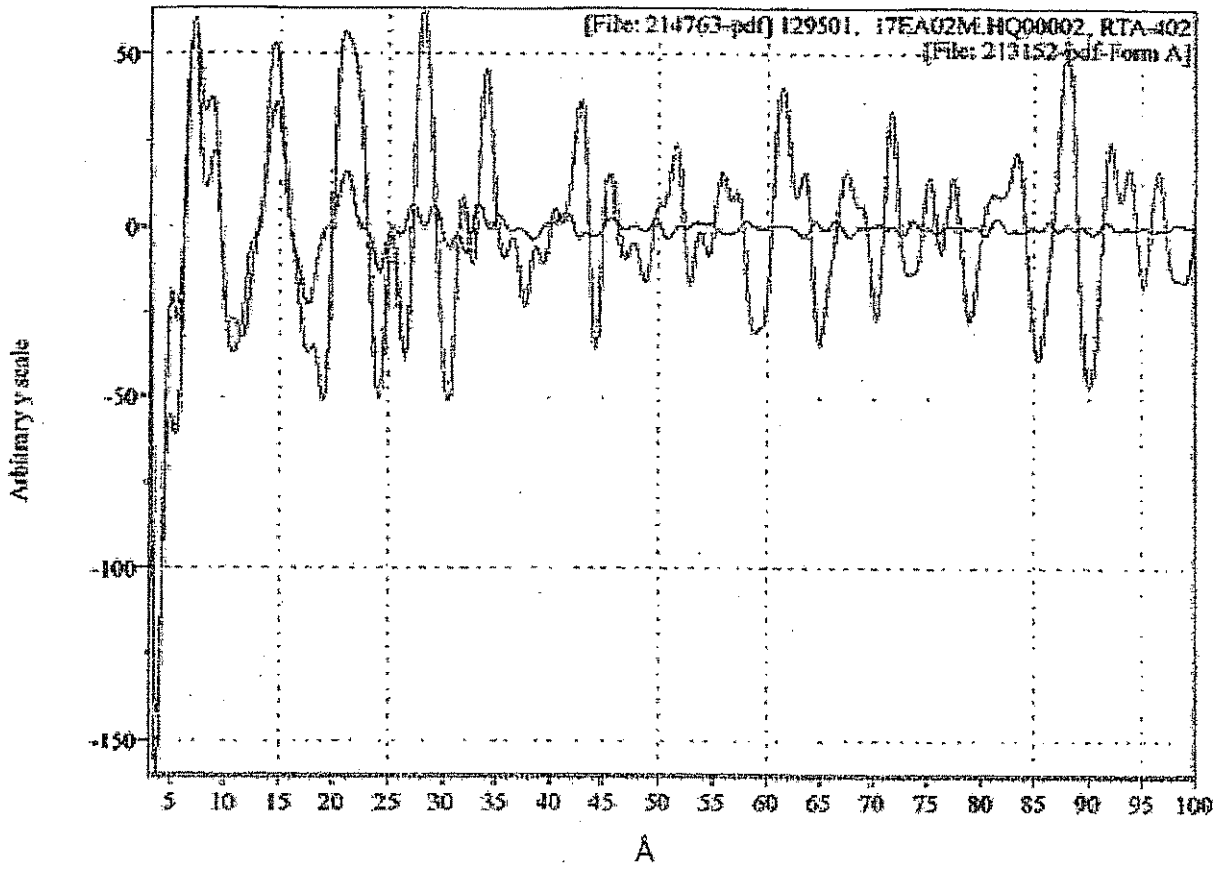


Figure 28 A PDF overlay of X-ray amorphous patterns for preparations of Form B

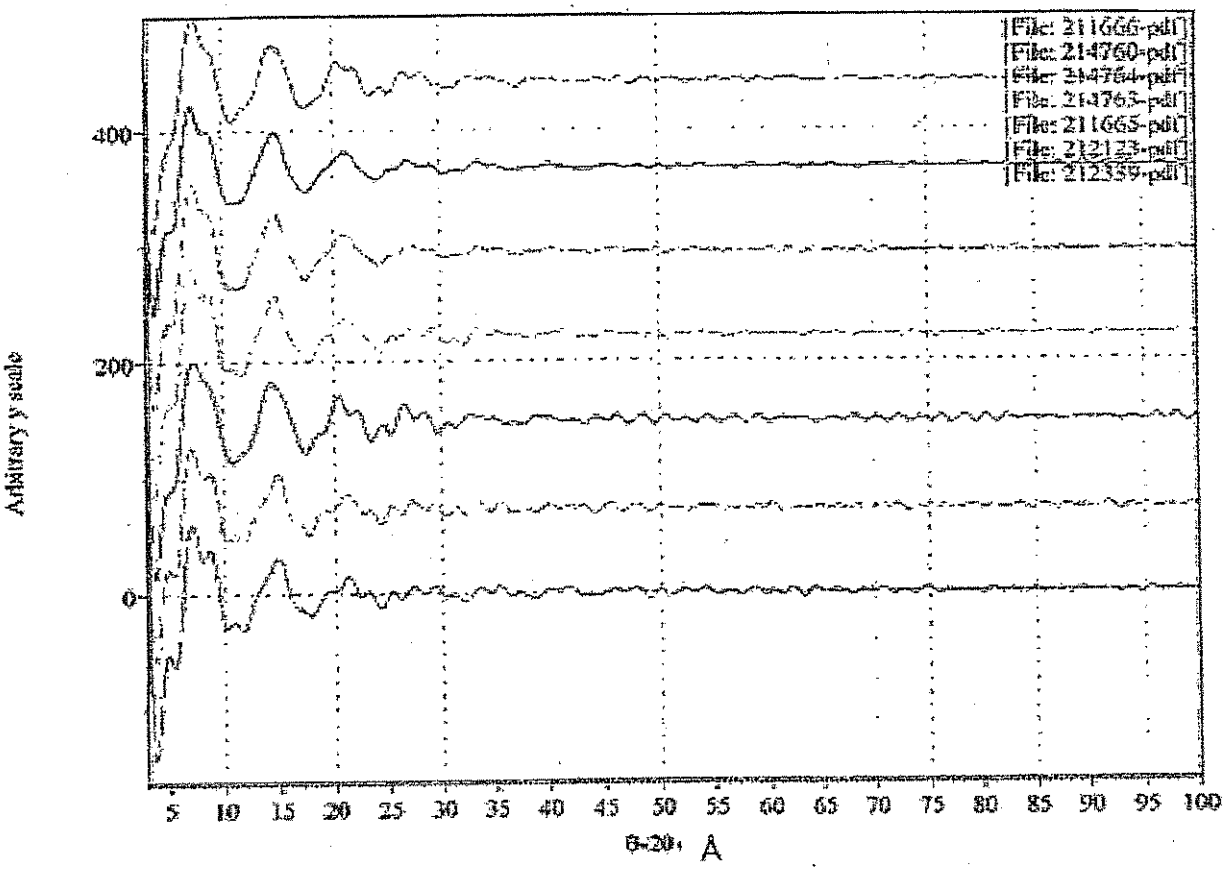


Figure 29 – A schematic representation of space group $P4_32_12$ (#96).

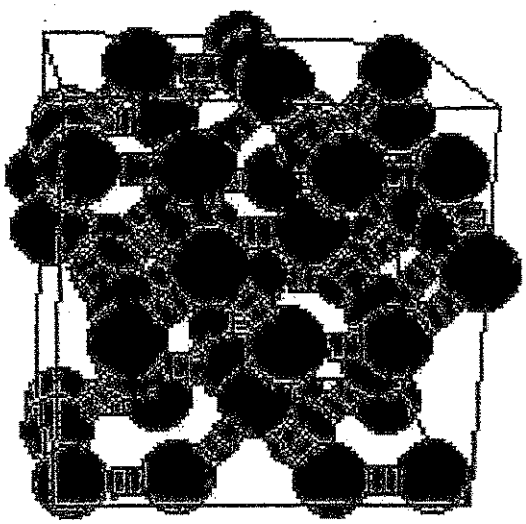
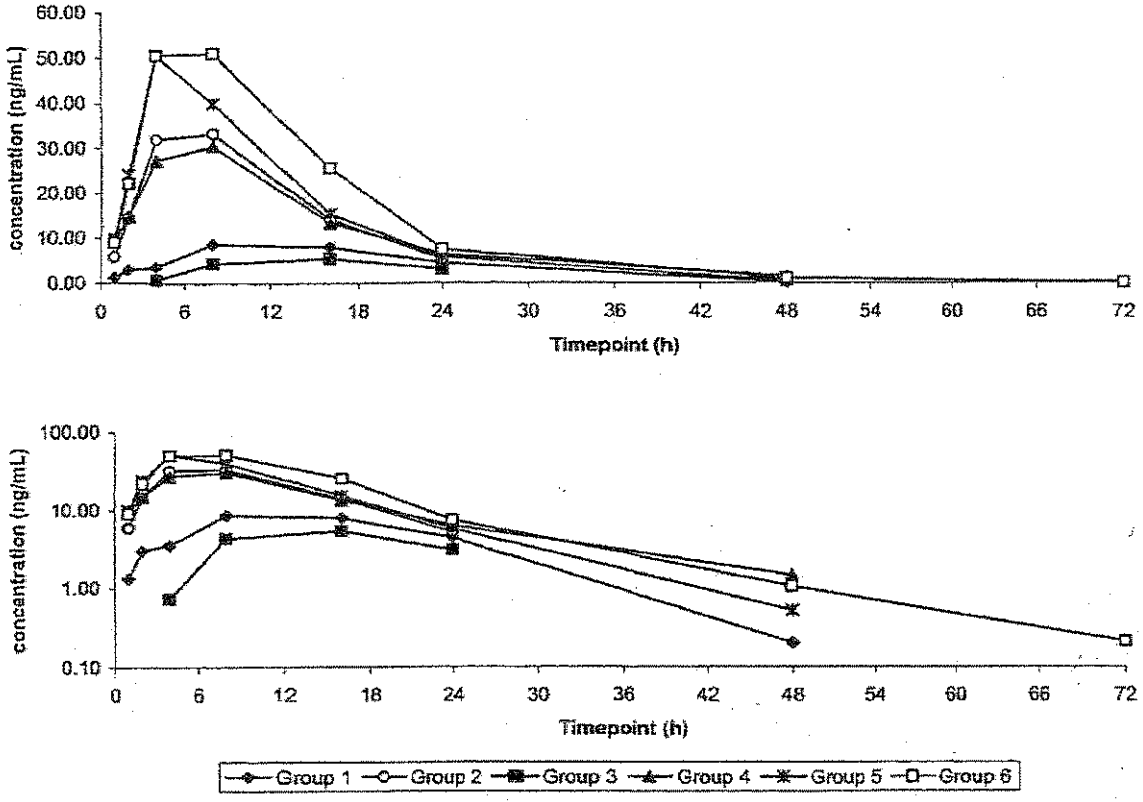


Figure 30 Mean blood concentrations of CDDO-methyl ester following single oral administrations of CDDO-methyl ester capsules to male Cynomolgus monkeys (Phases 2 and 3)



Group 1: (Phase 2), Animals received one capsule containing 30 mg of nanocrystalline Form A

Group 2: (Phase 2), animals received one capsule containing 30 mg of Form B micronized

Group 3: (Phase 2), animals received one capsule containing 30 mg of crystalline micronized Form A

Group 4: (Phase 3), animals received one capsule containing 30 mg of Form B - PVP/VA polymer matrix

Group 5: (Phase 3), animals received one capsule containing 30 mg of Form B - HPMCP polymer matrix (Hypromellose Phthalate)

Group 6: (Phase 3), animals received one capsule containing 30 mg of Form B - Eudragit L100-55 polymer matrix (methyacrylic acid copolymer Type C)