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Supporting information for article:

Two new polymorphic forms of combretastatin A-4, an antitumour agent

Anita M. Grześkiewicz, Tomasz Stefański, Zbigniew Dutkiewicz, Daria Buśko and Maciej Kubicki

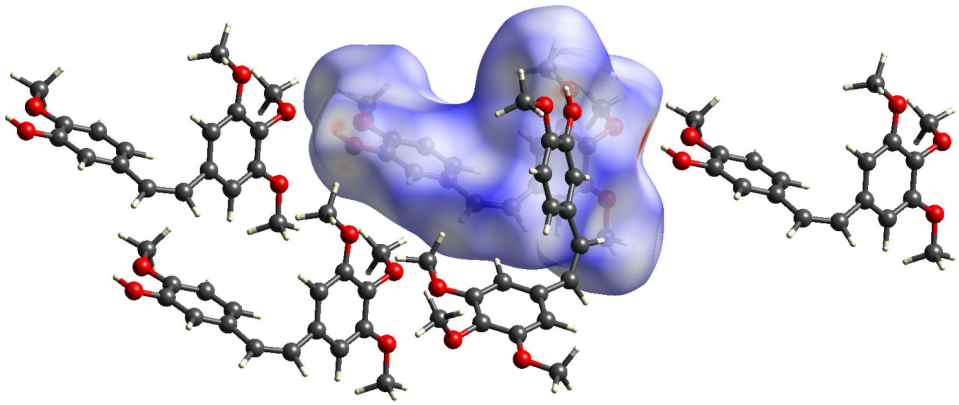

Fig. S1.

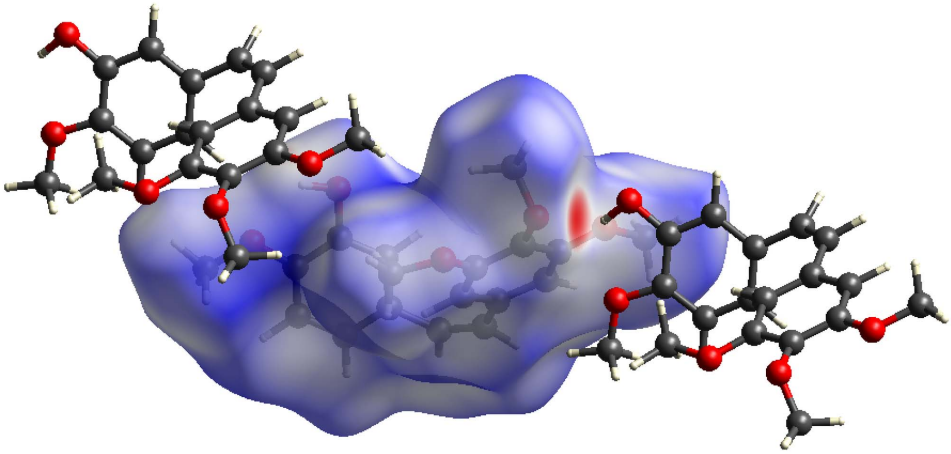

Fig. S2.

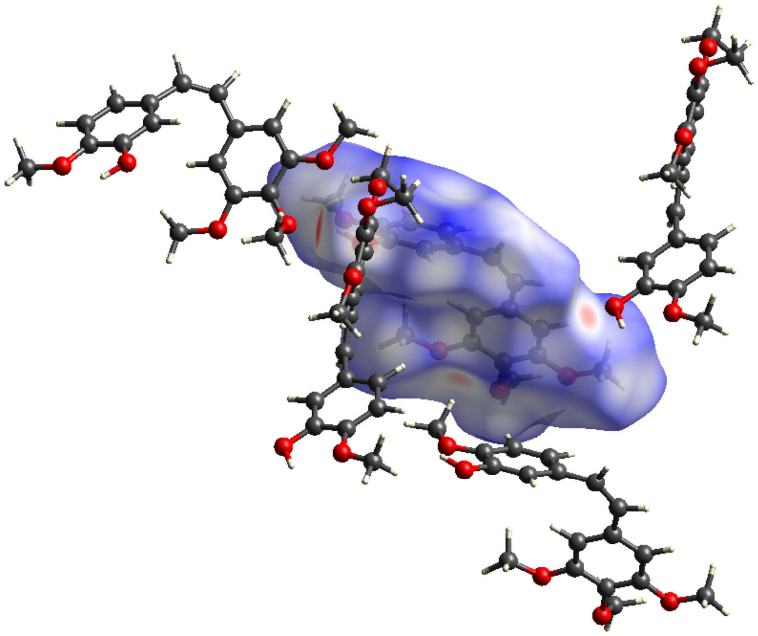

Fig. S3.

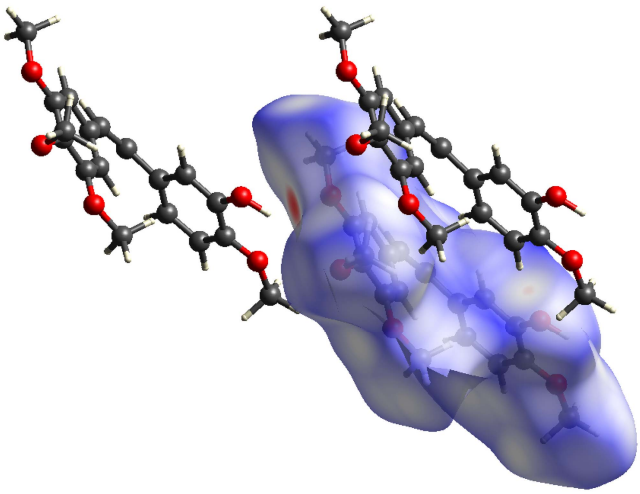

Fig. S4.

Crystallization procedurę and results

The initially obtained rough crystals were recrystallized from the mixture of ethyl acetate and petroleum ether. The crystals were dried and recrystallized again from different solvents: “plus” means the crystals of γ form, “minus” – no crystals.

1. Dichloromethane: hexane 1:1 (diffusion) +
2. Dichloromethane: hexane 1:1 +
3. Ethyl acetate: hexane 1:1 (diffusion) -
4. Ethyl acetate: hexane 1:1 +
5. Eter di izopropylowy +
6. Methanol +
7. Ethanol +
8. Izopropanol -
9. Acetonitrile: hexane 1:1 (diffusion) -
10. Acetonitrile: hexane 1:1 +
11. Tetrahydrofuran: hexane 1:1 (diffusion) -
12. Tetrahydrofuran: hexane 1:1 -
13. Acetone: hexane 1:1 (diffusion) oil
14. Acetone: hexane 1:1 +
15. Toluen +

Low temperature repetitions were performed for all successful solvents, with similar results. Finally, 1:1 mixture of hexane and dichloromethane was used, and the re-crystallization was performed in different lab. In the fridge crystals of β forms were finally obtained.

Table Suppl. 2 Interaction Energies (kJ/mol)
R is the distance between molecular centroids (mean atomic position) in Å.

Total energies, only reported for two benchmarked energy models, are the sum of the four energy components, scaled appropriately (see the scale factor table below)

Symop	R	E_ele	E_pol	E_dis	E_rep	E_tot
1						
x, -1+y, z	6.96	-9.4	-2.3	-52.0	28.4	-39.5
-1+x,1+y, z	12.11	-25.1	-6.3	-18.8	29.9	-29.1
1-x, -1/2+y, 3/2-z	7.25	-3.9	-1.8	-30.4	17.8	-21.0
-1+x, y, z	9.92	-5.3	-3.0	-23.4	14.6	-19.2
1-x, 2-y, 1-z	6.90	-0.4	-1.1	-22.4	11.1	-13.9
2-x, 1/2+y, 3/2-z	9.60	-3.5	-1.5	-14.0	6.4	-13.0
2						
A→B (x, 1+y, z)	10.98	-33.5	-8.5	-27.6	41.3	-40.2
A→B (x, y, -1+z)	7.21	-8.9	-2.5	-46.0	23.7	-36.7
A→B (1-x, -y, z-1/2)	6.25	-9.8	-1.5	-42.8	29.3	-30.7
A→B (1/2-x, y, -1/2+z)	6.80	-8.4	-3.6	-35.0	20.9	-29.1
B→B (x, -1+y, z)	8.87	-12.6	-3.2	-30.1	21.5	-28.7
A→B (x, y, z)	7.20	-5.3	-1.7	-39.6	21.6	-28.0
A→B (x, 1+y, 1+z)	11.85	-8.5	-1.8	-18.5	9.2	-20.8
A→B (1-x, 1-y, 1/2+z)	10.05	-4.3	-1.2	-15.5	7.3	-14.5
A→A (x, -1+y, z)	8.87	-0.4	-2.9	-19.6	7.9	-14.7
A→A (-x+1/2, y, z-1/2)	9.66	-2.8	-1.1	-13.1	6.6	-11.1
A→A (1-x, -y, z+1/2)	9.80	-4.3	-0.9	-8.2	4.8	-9.4
B→B (1-x, -y, 1/2+z)	9.28	-8.7	-2.1	-13.5	13.8	-14.0
B→B (1/2-x, -1+y, -1/2+z)	13.43	-0.7	-0.4	-6.7	5.1	-3.8
TIYJER						
-x, -y, 1-z	6.89	-24.0	-5.1	-41.3	25.7	-49.2

-1+x,y,-1+z	10.59	-22.4	-4.3	-30.4	24.0	-38.6
-1+x,y,z	6.82	-5.3	-2.7	-46.0	23.7	-33.0
x+1/2, -y+1/2, z+1/2	8.14	-6.8	-1.2	-29.8	15.1	-24.7
1-x,-y,1-z	7.30	-4.8	-1.2	-26.9	12.9	-21.4
3/2+x,1/2-y,1/2+z	11.73	-1.0	-0.5	-10.8	7.5	-6.2

Scale factors for benchmarked energy models

See C.F. Mackenzie, P.R. Spackman, D. Jayatilaka, M.A. Spackman, *IUCrJ*, 2017, 4 ,575-587

Energy Model	k_ele	k_pol	k_disp	k_rep
CE-HF ... HF/3-21G electron densities	1.019	0.651	0.901	0.811
CE-B3LYP ... B3LYP/6-31G(d,p) electron densities	1.057	0.740	0.871	0.618

Table Suppl. 3. Shares of different intermolecular contacts in the total of Hirshfeld surface

in	out	1	2A	2B	TIJYER
C	C	0.3	0	0.2	0.1
C	H	12.7	12.4	12.4	12.4
C	O	0.6	0.5	0.6	0.7
H	C	9.2	9.9	8.8	9.8
H	H	55.3	56.4	54.1	55.3
H	O	9.3	8.9	11.0	9.3
O	C	0.5	0.7	0.2	0.7
O	H	11.4	10.6	12.1	11.0
O	O	0.7	0.6	0.6	0.7

Table_Suppl_4. (3.-1) critical points data for intermolecular interactions in **1**.

Atom1	Atom2	symop	Gcp	Vcp	D_{12}	D_{1CP}	D_{2CP}	Rho	Lap	Hessian eigenvalues		
			kJ/mol			Å		e·Å^{-3}	e·Å^{-5}			
C10	C41	45501	8.15	-5.56	3.5274	1.7427	1.793	0.03159	0.394	-0.056	-0.025	0.476
H10	O5	45501	8.43	-5.17	2.867	1.2819	1.6194	0.02423	0.429	-0.066	-0.039	0.535
O11	H51B	45501	15.51	-11.03	2.5234	1.4821	1.0433	0.05079	0.734	-0.199	-0.157	1.091
H12C	H41B	46501	9.74	-6.69	2.2898	1.1497	1.1454	0.03569	0.47	-0.123	-0.071	0.664
O11	O3	46501	10.3	-6.45	3.2247	1.6487	1.5988	0.02926	0.519	-0.069	-0.016	0.604
H11	O4	46501	42.88	-48.47	1.9545	0.7245	1.2388	0.1804	1.369	-1.036	-0.957	3.363
C14	C121	54501	3.61	-2.12	3.9631	1.9655	1.9989	0.01252	0.187	-0.02	-0.014	0.221
C7	C12	54501	4.84	-3.1	3.7193	1.872	1.8893	0.0197	0.242	-0.033	-0.016	0.291
C2	H12B	54501	5.05	-3.39	3.1214	1.842	1.2827	0.02297	0.246	-0.065	-0.053	0.364
H8	O11	54501	5.05	-2.99	3.1248	1.4273	1.7693	0.01565	0.261	-0.034	-0.017	0.313
H31B	H13	54501	6.51	-4.12	2.4693	1.2367	1.2351	0.02277	0.327	-0.075	-0.04	0.442
C2	H51A	54501	6.71	-4.77	2.928	1.7224	1.2087	0.03067	0.318	-0.089	-0.058	0.465
C31	H41C	54501	7.52	-4.83	3.0442	1.8427	1.206	0.02599	0.375	-0.072	-0.048	0.495
H2	C13	54501	7.95	-6.05	2.7903	1.1379	1.653	0.03871	0.361	-0.104	-0.103	0.568
H31C	O5	54501	8.99	-6.33	2.8007	1.1656	1.6894	0.03592	0.428	-0.091	-0.039	0.557
C1	H14	55501	17.83	-13.11	2.6144	1.5505	1.1037	0.05901	0.828	-0.103	-0.073	1.005
C6	O11	64602	4.82	-2.88	3.6611	1.9213	1.7461	0.01584	0.248	-0.025	-0.023	0.295
H7	C8	64602	5.34	-3.61	3.0225	1.2394	1.7879	0.02398	0.26	-0.062	-0.037	0.359
C1	H10	64602	6.47	-4.12	3.127	1.8682	1.3148	0.02322	0.324	-0.036	-0.017	0.376
H8	C51	64602	6.83	-4.67	3.0327	1.1952	1.8424	0.02868	0.33	-0.095	-0.066	0.49
H51C	O11	64602	15.66	-12.36	2.465	1.0254	1.4411	0.06181	0.696	-0.245	-0.228	1.169
H12A	C31	66603	5.29	-3.56	3.0968	1.2645	1.8393	0.02367	0.258	-0.071	-0.062	0.39
C13	H31B	66603	7.82	-4.95	2.9892	1.7695	1.2255	0.02559	0.393	-0.058	-0.029	0.48

O12	H41A	67603	3.65	-2.31	3.2027	1.8711	1.3737	0.01608	0.183	-0.043	-0.021	0.248
H12A	H14	67603	6.17	-3.93	2.4551	1.2383	1.222	0.02257	0.309	-0.073	-0.05	0.431
H12C	O3	67603	8.16	-5.77	2.8398	1.1916	1.6995	0.03415	0.388	-0.096	-0.031	0.515
H13	H13	67603	10.34	-7.53	2.1672	1.0836	1.0836	0.04181	0.483	-0.176	-0.133	0.791
O5	H51B	74602	9.88	-6.53	2.8172	1.6926	1.1634	0.03288	0.486	-0.052	-0.04	0.578
H41A	H41A	76603	5.82	-3.53	2.5422	1.2711	1.2711	0.01866	0.298	-0.064	-0.016	0.378
C41	C31	76603	6.89	-4.23	3.7663	1.8777	1.8925	0.0215	0.351	-0.029	-0.022	0.402

Table_Suppl_5. (3.-1) critical points data for intermolecular interactions in **2**.

Atom1	Atom2	symop	Gcp	Vcp	D_{12}	D_{1CP}	D_{2CP}	Rho	Lap	Hessian eigenvalues		
			kJ/mol		Å			e·Å^{-3}	e·Å^{-5}			
C11A	H51E	54401	9.72	-7.66	2.8556	1.7666	1.1254	0.04625	0.433	-0.134	-0.07	0.637
H12D	C41B	54401	5.56	-3.93	3.1204	1.2696	1.8655	0.02709	0.264	-0.079	-0.047	0.391
H8A	H41E	54404	3.58	-2.69	2.5712	1.2678	1.3148	0.02347	0.164	-0.084	-0.079	0.327
H14A	O4B	54404	2.12	-1.27	3.3437	1.4917	1.8534	0.00962	0.109	-0.025	-0.022	0.157
H8A	O4A	54501	10.61	-6.86	2.803	1.3073	1.5682	0.0325	0.527	-0.093	-0.062	0.682
H8A	O5A	54501	5.24	-3.1	3.0212	1.3017	1.7231	0.01609	0.271	-0.028	-0.02	0.319
H41C	H51D	55401	5.3	-3.42	2.6002	1.3047	1.3173	0.02139	0.263	-0.069	-0.038	0.37
H51B	H41F	55401	5.29	-3.86	2.4603	1.216	1.2558	0.02809	0.246	-0.101	-0.087	0.434
H11A	C1B	55401	11.76	-9.74	2.6442	1.0429	1.6192	0.05609	0.506	-0.166	-0.113	0.786
O12A	H14B	55401	8.7	-5.74	2.7512	1.5995	1.1525	0.0304	0.428	-0.096	-0.074	0.599
H12E	H31F	55401	8.94	-6.84	2.2616	1.1438	1.1182	0.04183	0.406	-0.168	-0.12	0.694
H12F	H41D	55401	1.41	-0.79	3.2714	1.5979	1.6793	0.00572	0.074	-0.014	-0.003	0.091
O5A	H41E	55404	8.79	-5.55	2.8725	1.695	1.2161	0.02719	0.442	-0.04	-0.028	0.51
H51C	O3B	55404	18.58	-14.93	2.4043	0.9873	1.4185	0.07049	0.816	-0.294	-0.282	1.392
H14A	H12C	55404	3.23	-1.95	2.819	1.3837	1.4567	0.01284	0.166	-0.04	-0.018	0.223
C13A	H31E	55404	6.24	-4.06	3.0229	1.8041	1.2382	0.02409	0.309	-0.063	-0.02	0.392
H13A	H12C	55404	4.39	-2.65	2.6197	1.3	1.3332	0.01567	0.225	-0.054	-0.03	0.308
H12F	C7A	55404	7.16	-5	2.9582	1.1947	1.7712	0.03081	0.342	-0.091	-0.041	0.474
C121	H14A	55404	4.64	-2.74	3.328	1.9513	1.4651	0.01475	0.24	-0.024	-0.016	0.28
C7A	H12F	55504	7.16	-5	2.9582	1.7712	1.1947	0.03081	0.342	-0.091	-0.041	0.474
H14A	C121	55504	4.64	-2.74	3.328	1.4654	1.9513	0.01475	0.24	-0.024	-0.016	0.28
O3A	O12B	56501	10.43	-6.71	3.2052	1.6165	1.5977	0.03181	0.519	-0.046	-0.037	0.602

O4A	H8A	56501	10.61	-6.86	2.803	1.5682	1.3073	0.0325	0.527	-0.093	-0.062	0.682
O4A	H11B	56501	51.45	-57.25	1.8987	1.2173	0.6909	0.19786	1.676	-1.153	-0.998	3.826
O5A	H8A	56501	5.24	-3.1	3.0212	1.7231	1.3017	0.01609	0.271	-0.028	-0.02	0.319
C2A	H8B	65402	14.61	-10.78	2.7327	1.7147	1.0687	0.0527	0.677	-0.101	-0.048	0.826
H41A	C9B	65402	7.25	-5.45	2.9372	1.1887	1.8276	0.0358	0.332	-0.103	-0.06	0.495
H10A	H8B	65402	8.94	-6.41	2.3281	1.1283	1.2405	0.03713	0.421	-0.137	-0.095	0.654
O11A	H10B	65402	9.37	-6.71	2.6671	1.5519	1.1152	0.03809	0.442	-0.145	-0.138	0.725
O11A	H31C	65402	12.15	-8.66	2.6036	1.5187	1.0881	0.04408	0.574	-0.167	-0.147	0.888
H31C	O11A	65502	12.15	-8.66	2.6036	1.0881	1.5187	0.04408	0.574	-0.165	-0.149	0.888
O3A	H51F	66402	9.58	-6.3	2.7312	1.5791	1.153	0.03195	0.472	-0.108	-0.069	0.649
C41A	H31B	66402	5.93	-4.02	3.0895	1.8438	1.2495	0.02574	0.288	-0.082	-0.066	0.435
H41A	H51F	66402	2.43	-1.47	2.9178	1.4278	1.5005	0.01086	0.125	-0.028	-0.015	0.168
C41A	C6B	66402	4.01	-2.34	3.9409	2.0057	1.9448	0.01296	0.209	-0.023	-0.01	0.242
H41B	C7B	66402	5.39	-3.67	3.1216	1.2723	1.8585	0.02466	0.261	-0.076	-0.062	0.399
H31B	C41A	66502	5.93	-4.02	3.0895	1.2495	1.8438	0.02574	0.288	-0.082	-0.065	0.435

Table_Suppl_6. (3.-1) critical points data for intermolecular interactions in **TIYJER**.

Atom1	Atom2	symop	Gcp	Vcp	D_{12}	D_{1CP}	D_{2CP}	Rho	Lap	Hessian eigenvalues		
			kJ/mol		Å			e·Å^{-3}	e·Å^{-5}			
H3	H10	35404	7,13	-5,52	2,2814	1,127	1,1639	0,03734	0,321	-0,15	-0,137	0,608
H8	C15	35404	9,87	-6,37	2,9818	1,2682	1,7754	0,03103	0,491	-0,076	-0,05	0,617
H1	O3	45401	28,86	-25,24	2,1667	0,8393	1,3394	0,1041	1,193	-0,493	-0,376	2,062
O5	C7	45401	10,05	-6,8	3,2656	1,5963	1,6988	0,03521	0,488	-0,06	-0,027	0,575
H19	C5	45401	8,31	-5,8	2,9701	1,1704	1,8234	0,03366	0,397	-0,088	-0,037	0,522
C1	H11	45404	7,03	-5,38	2,8799	1,6979	1,1939	0,03625	0,319	-0,101	-0,08	0,501
C14	H2	45404	7,52	-5,83	2,9216	1,8033	1,1578	0,03857	0,338	-0,104	-0,057	0,5
C10	H5	45404	6,88	-5,06	2,886	1,7145	1,1756	0,03336	0,32	-0,096	-0,071	0,486
H6	C15	45404	4,38	-2,57	3,3083	1,3311	1,9772	0,01389	0,228	-0,027	-0,016	0,271
H15	C16	45501	7,91	-5,7	2,9347	1,1756	1,7675	0,0349	0,371	-0,113	-0,094	0,578
C18	O4	45501	7,78	-4,76	3,4782	1,8628	1,6177	0,02298	0,396	-0,044	-0,035	0,476
C1	H9	45501	6,79	-4,21	3,1239	1,8206	1,379	0,02214	0,344	-0,036	-0,028	0,407
C4	H14	45501	10,99	-7,43	2,8161	1,6905	1,1337	0,03704	0,534	-0,105	-0,052	0,691
H8	H6	45501	3,16	-1,96	2,7405	1,3448	1,4004	0,01396	0,16	-0,04	-0,025	0,224
H7	O4	45501	12,63	-9,42	2,546	1,0473	1,4989	0,04918	0,582	-0,195	-0,192	0,97
H8	C3	45501	4,07	-2,77	3,255	1,3085	1,954	0,02068	0,197	-0,041	-0,026	0,264
H19	C18	45503	1,37	-0,76	3,7702	1,6189	2,1967	0,00532	0,073	-0,01	-0,006	0,088
H4	C10	55501	23,22	-17,86	2,5062	1,0302	1,4957	0,07495	1,049	-0,187	-0,063	1,3
O1	H18	55603	12,96	-9,17	2,5788	1,5033	1,0786	0,04517	0,615	-0,167	-0,143	0,926
C13	H16	55603	8,71	-6,2	2,8351	1,6866	1,1553	0,03604	0,412	-0,098	-0,053	0,563
H15	H15	55603	8,19	-4,99	2,6729	1,3365	1,3365	0,02346	0,418	-0,066	-0,003	0,487
H16	H12	65603	9,37	-6,9	2,3592	1,2734	1,1496	0,04023	0,435	-0,141	-0,095	0,67

H13	O5	65603	2,8	-1,72	3,2441	1,4548	1,7937	0,01251	0,143	-0,033	-0,032	0,208
C17	C17	65603	6,74	-4,32	3,6981	1,849	1,8491	0,02422	0,336	-0,05	-0,012	0,398
O2	H13	75703	2,62	-1,51	3,2683	1,8296	1,4486	0,00937	0,137	-0,026	-0,017	0,18