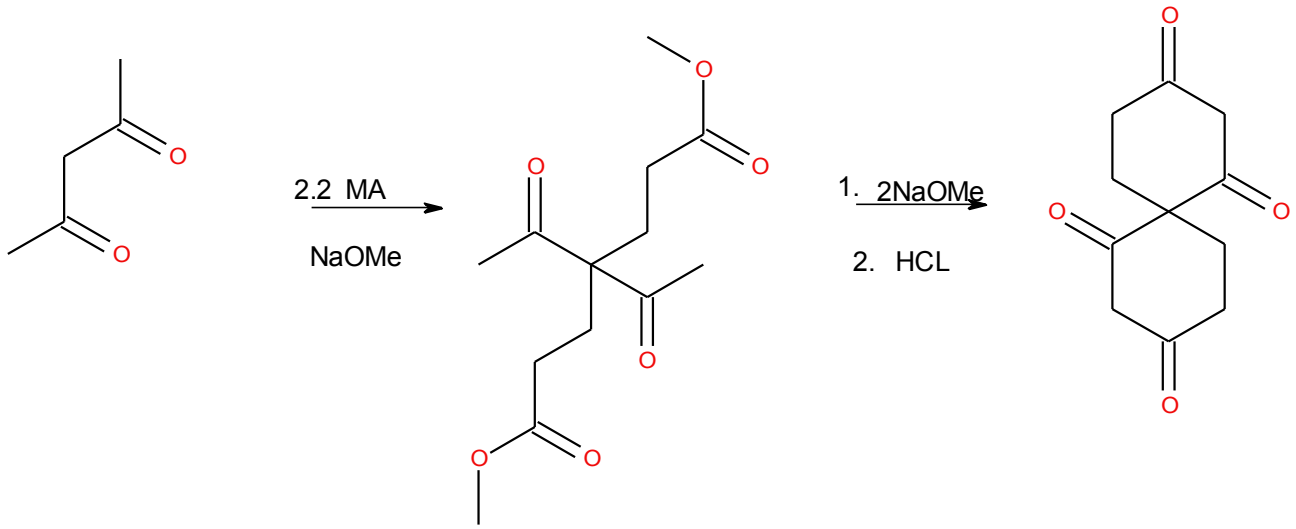
Spiro-bis-cyclohexane-1,3-dione (spiro[5.5]undecane-3,5,9,11-tetrone)

By: Robert B. Login

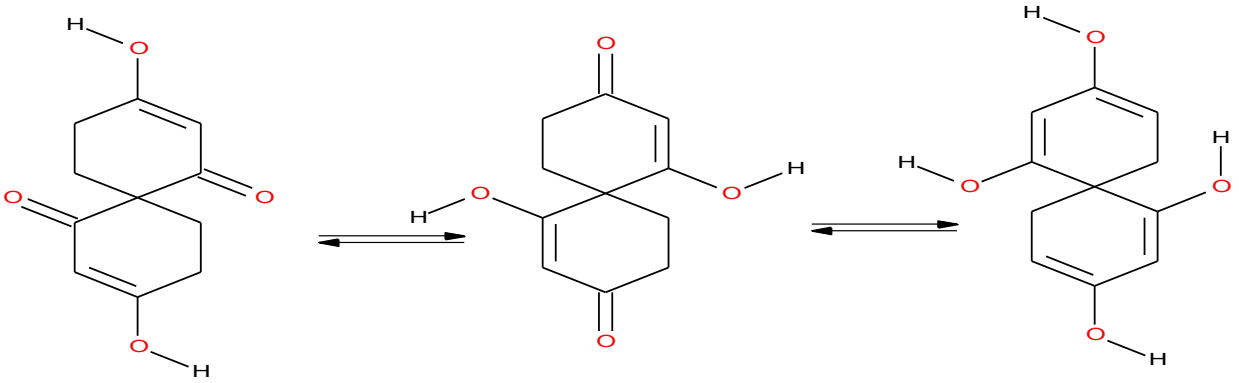
Abstract:

A unique dimedone spiro dimer can be readily prepared in good yield from inexpensive 2,4-pentanedione and methyl acrylate. It can be employed as a synthon for the preparation of molecules like those numerous examples found for dimedone but as unique spiro dimer derivatives. Medicinal chemist and those interested in new specialty compounds might find significant uses for these spiro-bis-cyclohexane-1,3-dione derivatives.

After exploring the chemistry of the di-adduct of methyl acrylate(MA) and diethyl malonate, to produce dimethyl-diethyl-1,3,3,5-pentanetetracarboxylate, (a low mp crystalline compound that can be recrystallized from methanol), I explored the same Michael reaction with 2,4-pentanedione (acetylacetone). This reaction can be run neat or in methanol. I found the best yields are obtained by mixing 2.2 moles of MA with a mole of the dione, neat at ice bath temperatures and, catalyzed with the minimum of NaOMe(25% in MeOH) which indicates its activity by turning the mixture a light yellow color. The stirred mixture is allowed to increase in temperature to RT then slowly raised to 80C. A slight exotherm was noticed but nothing like the exotherm from the reaction of diethyl malonate and MA. Mixing is continued for usually two hours at 80C or until GC analysis confirms diadduct formation(dimethyl 4,4-diacetylpimelate). As the mixture cools, it crystallizes to a crystalline mush that is then recrystallized from MeOH affording better than 70% yield of product (MP 95-96C) lit. 97-98C. (R.Cheng and P.S. Clezy, Aust. J. Chem., 1967,20, 123-130.)

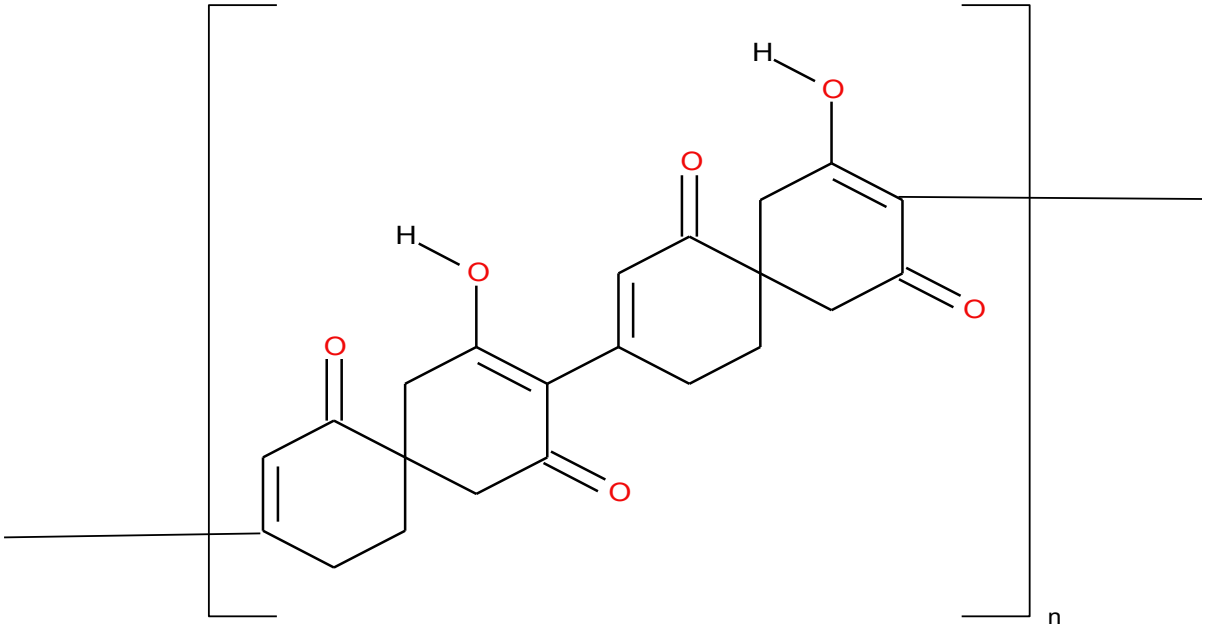


The spiro bis-cyclohexane-1,3-dione was obtained by following an analogous procedure for a related compound from Organic Syntheses(Coll. Vol. 6, p774(1988). The resulting compound was insoluble in the usual solvents such as water, methanol, CH2CL2, ethyl acetate etc. It is however soluble in DMSO. It was crystallized out of DMSO and MeOH. Its IR was very difficult to obtain but cast from DMSO as a film or as a nujol mull shows no carbonyl at the usual absorptions but absorptions at 1570, 1500 that I ascribe to enols or carbonyl's? This solid compound does not melt but decomposes at high temperatures(>300C). The nmr taken in d6 DMSO, eliminating the water related peaks at approx. 3.33 and 2.5 ppm, reveals peaks at 11.07(1H), 5.19(1H), 2.3(3H) and 1.71(1H) ppm and all are singlets. I conclude that the best fit for the spectral data is the following;

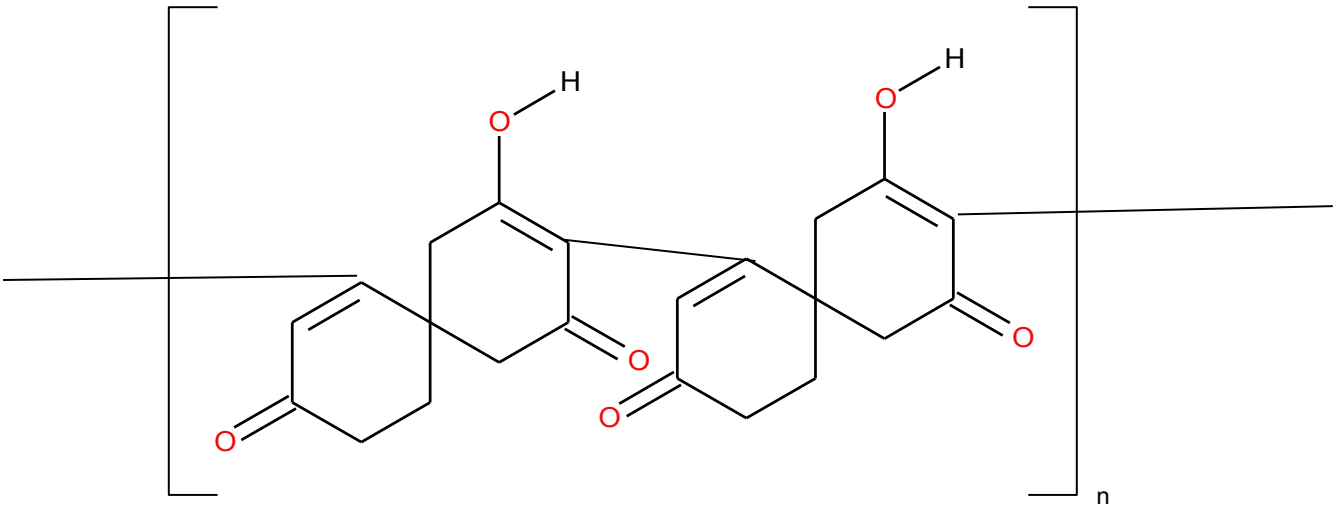


This structure agrees with the nmr because when compared to known cyclohexane-1,3-diones, it has peaks in identical positions as concerns the enols. A model shows that three of the methylenes are in the shielding cone of the carbonyls while one is not, accounting for 1.71ppm peak. The integrations are as expected. There is a lack of coupling patterns and the insoluble nature and decomposition instead of a mp still needs to be explained. This compound maybe so polar that it has these observed properties! The broad singlets may result from the rapid isomerism of the enols as any of the carbonyls can enolize, hence many tautomers are possible. Another possibility is that both carbonyls are in the enol form; however this does not fit the nmr which is a solution in d6dmso while the IR is a nujol mull so the compound is really in the solid form where an all enol structure is possible; however, when the IR is run as a solution in dmso, the IR now reveals carbonyl bands at 1640 and 1600 cm-1, this suggests that my interpretation is correct. Finally, extensive hydrogen bonding can explain the insolubility and decomposition.

I thought that this intermediate under the reaction conditions would polymerize to afford the following structures;



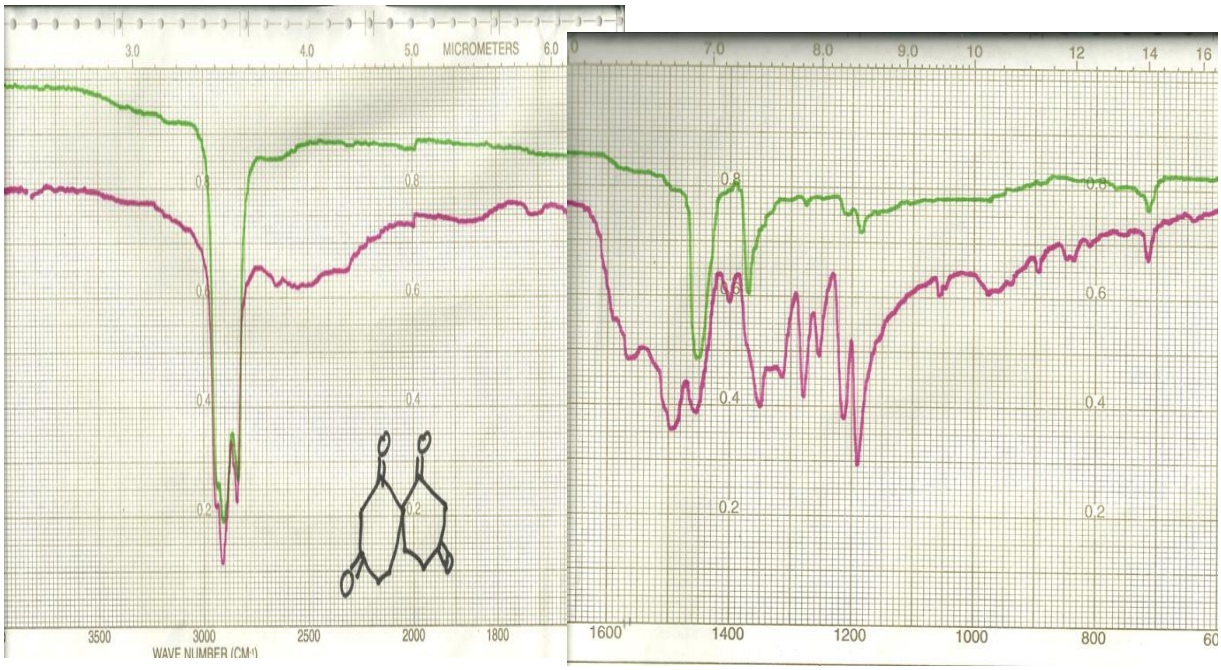
This shows two repeat units for clarity. The enol would be favored because of the extended unsaturation. An alternative structure would be;



I would think both are possible? However the evidence doesn't support a polymeric structure.

A search of the literature did not reveal any matches for bis-spiro-cyclohexane-1,3-dione and therefore, I believe this is a new compound.

Dimedone is a well known synthon with many examples of its use in the literature. Bis-cyclohexane-1,3-dione being a dimer of dimedone should be of value especially to the pharmaceutical science affording entre to many new medicinals.



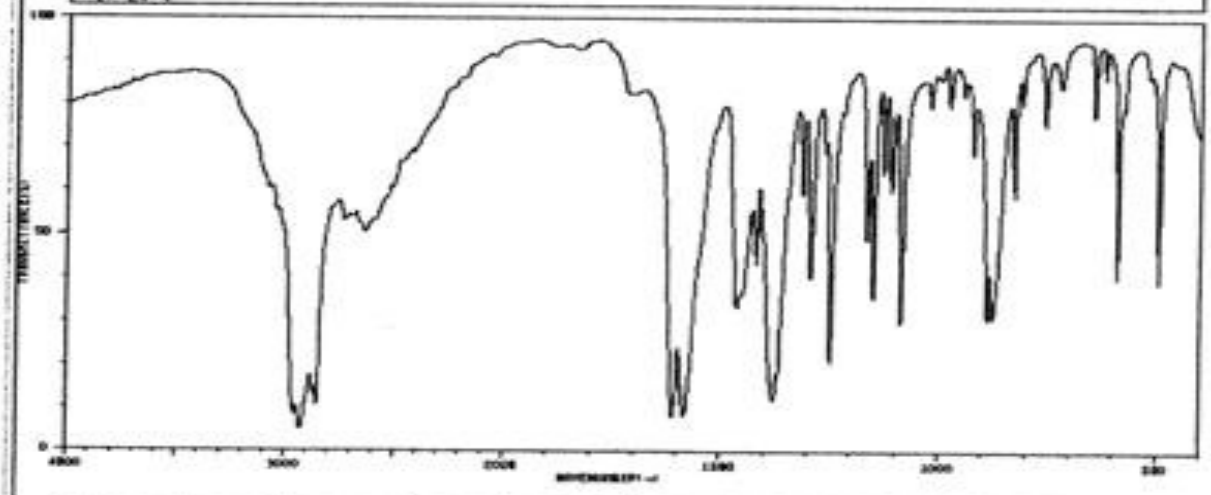
aFig. 1 Nujol(green trace) mull of bis-spirocyclohexane-1,3-dione

ethyl-2-

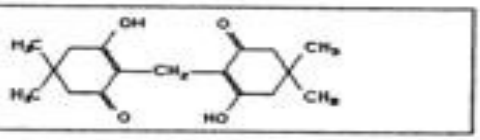
HIT-NO=15673 | SCORE= ( ) | SDBS-NO=31597 | IR-NIDA-68856 : NUJOL MULL

2,2'-METHYLENEBIS(3-HYDROXY-5,5-DIMETHYL-2-CYCLOHEXEN-1-ONE)

$C_{17}H_{24}O_4$



2967	8	1463	32	1263	66	1021	77	812	77
2924	4	1453	35	1242	50	979	77	759	72
2864	10	1413	42	1166	47	943	79	646	74
2730	60	1378	11	1151	34	923	68	590	38
2633	49	1363	15	1120	62	869	29	584	72
1611	7	1315	57	1111	58	676	29	577	77
1582	7	1296	38	1086	29	627	67	496	37



AIST:RIO-DB Spectral Database for Organic Compounds,SDBS

Spectral Database for Organic Compounds SDBS

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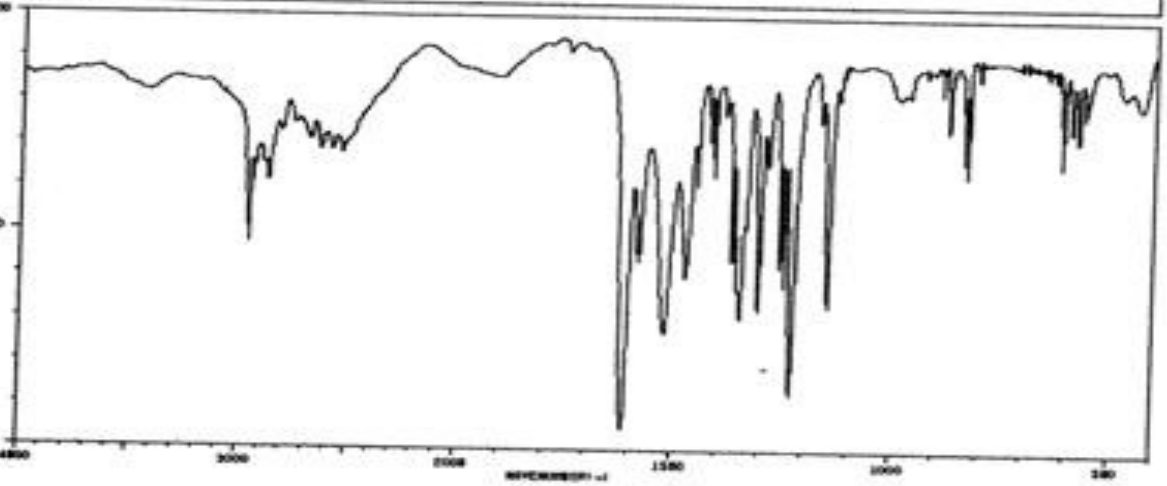
HIT-NO=2296 | SCORE= ( ) | SDBS-NO=3075 | IR-NIDA-24630 : KBR DISC

5,5-DIMETHYL-1,3-CYCLOHEXANEDIONE

$C_8H_{12}O_2$



2972	60	2682	68	1474	38	1337	49	1147	32
2954	46	2632	65	1449	50	1308	31	974	70
2940	55	2586	66	1425	86	1288	64	937	64
2890	64	2534	65	1412	60	1258	41	829	60
2868	60	1813	4	1368	42	1248	36	613	64
2814	70	1582	42	1356	35	1235	28	593	72
2760	72	1520	28	1348	29	1230	12	578	70

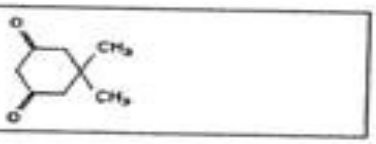


Fig. 2&3 above were selected to show that known cyclohexane-1,3-diones show little absorption in the -OH region and have carbonyls(enols) at 1611 & 1682(top spectra) and 1613 & 1582(bottom spectra).

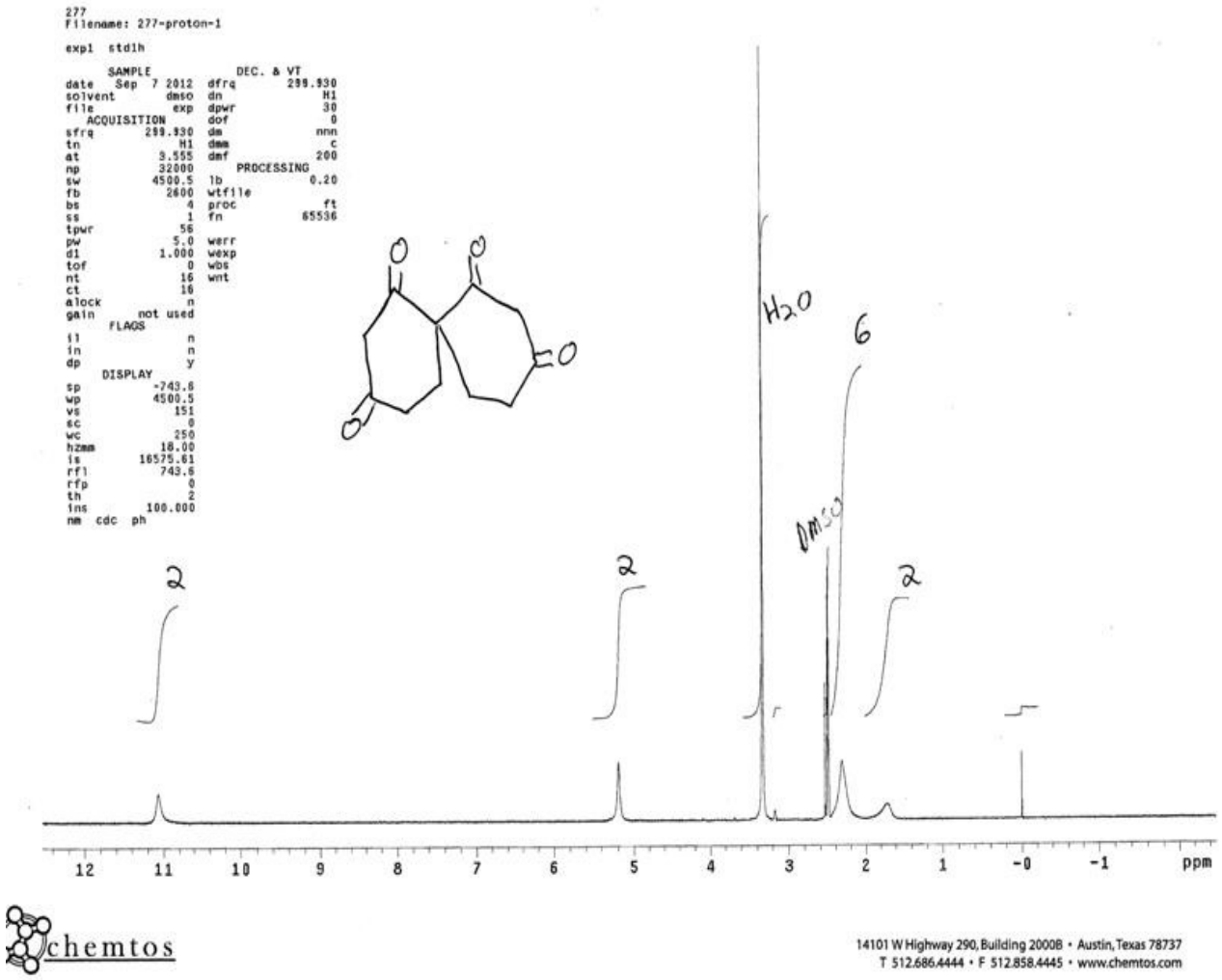


Fig. 4 bis-spirocycloheane-1,3-dione(spiro[5.5]undecane-3,5,9,11-tetrone) in d6dmso

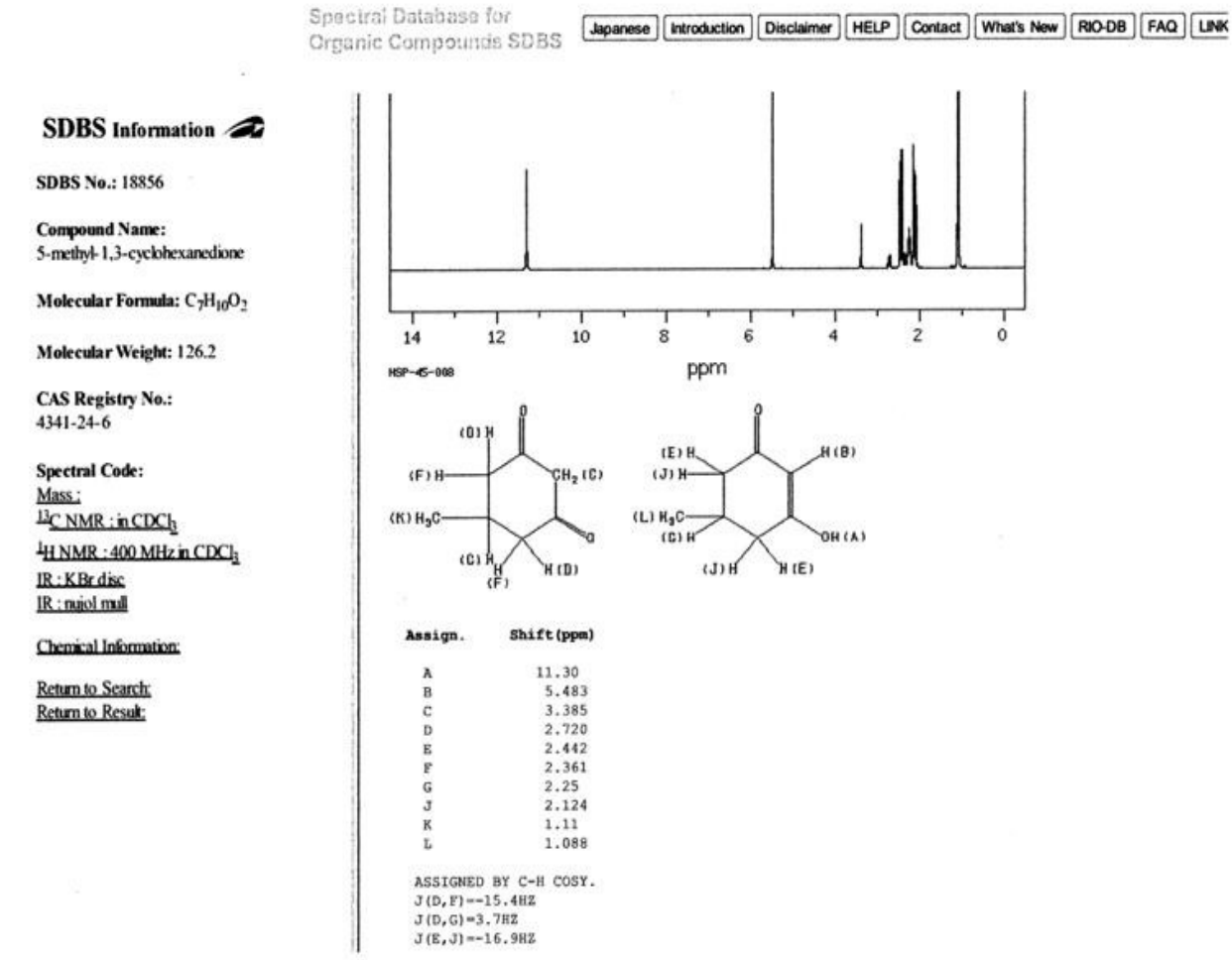


Fig. 5 nmr of 5-methyl-cyclohexane-1,3-dione for comparison.

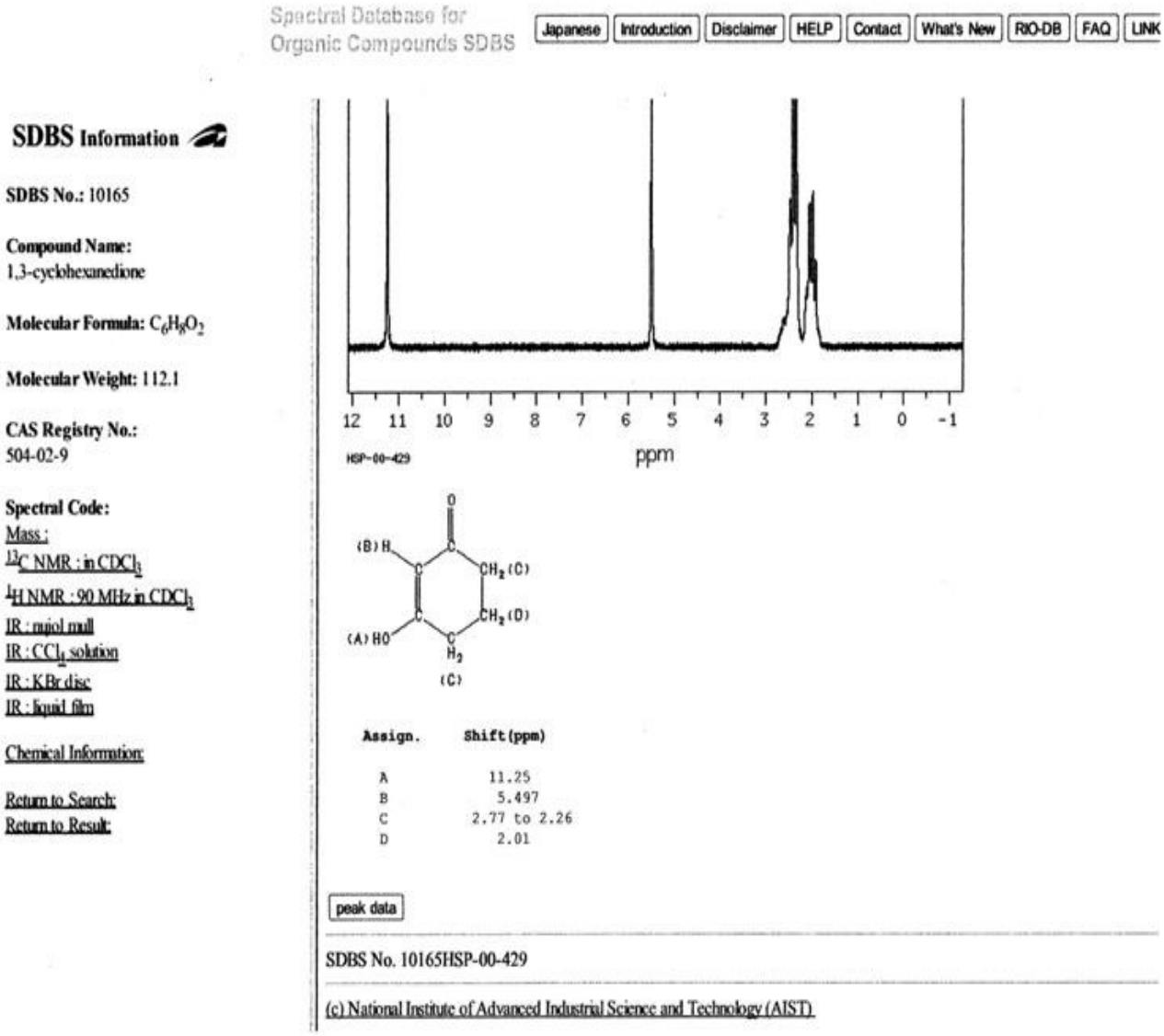


Fig. 6 cyclohexane-1,3-dione nmr for comparison