Electron spin resonance studies of substituent effects. Part 6. Experimental and theoretical studies of ortho substituent-induced cis-trans isomerization in 1-phenyl-1,2-propanesemidiones[1]

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Dedicated to Professor Henry J. Shine on the occasion of his 80th birthday

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Abstract

Cis- and *trans*-1-(2′-methoxyphenyl)- and 1-(2′,4′-dimethoxyphenyl)-1,2-propanesemi-diones were made by oxidation of ketones and studied by esr. The hyperfine splitting constants and *cis*, *trans* ratios of these and related radicals were investigated by *ab initio* calculations.

Keywords: Semidiones, esr, anion radicals, *ab initio* calculations

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Introduction

Semidione free radicals (anion radicals of alpha diketones) were discovered by Russell and Strom nearly 40 years ago.[2] Alkyl semidiones were found to occur in both *cis* and *trans* orientations.[3] Monophenyl semidiones also were found to have both *cis* and *trans* orientations.[4,5] However, we found that a variety of *meta*- and *para*-substituted 1-phenyl-1,2-propanesemidiones formed only one radical, presumably the *trans*.[6,7] In this study we investigate the effect of *ortho*-substitution on this system, using the methoxy group. We also have performed *ab initio* calculations on the parent system and the *ortho*-substituted compound as well as phenylglyoxal anion radical. The only previous *ab initio* study on semidione systems of which we are aware is over ten years old.[8]

Results and Discussion

The semidiones studied were the 2′-methoxy and 2′,4′-dimethoxy compounds. The radicals were formed by potassium t-butoxide catalyzed oxidation of *ortho*-methoxybenzylmethyl ketone and

2′,4′-dimethoxypropiophenone, respectively, using normally dissolved oxygen in either pure dimethylsulfoxide (DMSO) or 80% DMSO-20% t-butyl alcohol (t-BuOH).

The oxidation of 2′,4′-dimethoxypropiophenone in DMSO gives rise to a spectrum consisting of a quartet of quintets. Additional small multiplets could be discerned, however, on the wings and partially overlapping the inner two quintets. The observed ratio of radicals is approximately 40:1 in this case, but when the oxidation is carried out in 80-20 DMSO-t-BuOH, the ratio of the main radical to the longer radical decreases to approximately 2:1. The radical with the longer spectrum has a multiplet structure consisting of a quartet of quartets. The analysis of the spectrum is as follows:

Long radical $A^H(3) = 6.52$ gauss (G), $A^H(2) = 0.44$ G, $A^H(1) = 0.55$ G,
g-value = 2.00515 +/- .00005.
Short radical $A^H(3) = 4.81$ G, $A^H(2) = 0.33$ G, $A^H(1) = 0.60$ G,
g-value = 2.00530 +/- .00005.

We attribute the short and long spectra to the *cis*- and *trans*- isomers of 1-(2’,4’-dimethoxyphenyl)-1,2-propanesemidione (**1a** and **1b**). It is well known that *cis*-semidiones have lower g-values and larger hyperfine proton splitting constants than the *trans*-isomers.[3,4] The presence of an *ortho*-substituent somehow results in the formation of some *cis* radical. The larger splitting from three protons in both radicals is obviously from the methyl group of the semidione side chain. In the shorter radical the 0.60 gauss splitting is assigned to the *ortho* proton and the 0.33 gauss splitting to the two *meta* protons. In the longer radical the 0.53 and 0.42 gauss splittings are assigned in an analogous manner.

Similarly, oxidation of *ortho*-methoxybenzyl methyl ketone in 80-20 DMSO-t-BuOH gives a spectrum resulting from two radicals with non-identical g-values. The radical of shorter total spectrum length is about 3.5 times as abundant as the longer radical. The multiplet structure of the shorter radical consists of a quartet of septets, while that of the longer radical is a quartet of quintets. The septet arises from two pairs of protons, one pair of which has approximately twice the splitting of the other. This is expected on the basis of the previous analysis. The quintet results from four protons which are approximately equivalent under these conditions of resolution and component line width. A consistent analysis of the experimental results is as follows:

Long radical $A^H(3) = 6.44$ G, $A^H(4) = 0.48$ G, g-value = 2.00510 +/- .00005
Short radical $A^H(3) = 4.69$ G, $A^H(2) = 0.57$ G, $A^H = 0.34$ G,
g-value = 2.00525 +/- .00005.

By analogy, these radicals are clearly the *cis*- and trans- isomers of 1-(2′methoxyphenyl)-1,2-propanesemidione (**2a** and **2b**). We doubt that the long (*cis*) radical really has identical splitting constants for the *ortho*, *para* and *meta* protons. The large width of the lines, 230 milligauss, probably from unresolved methoxy hydrogen splitting, makes it impossible to resolve the differences. For all four radicals there are probably differences between the two *meta* splittings and the *ortho*, *para* splittings that cannot be discerned at this level of resolution.

Both analyses were confirmed by simulating the experimental spectra using the two g-value program of Snowden and Strom.[9] The experimental and simulated spectra for the *ortho*-methoxy radical are shown in Figure 1. The input line width of the components was 230 milligauss.

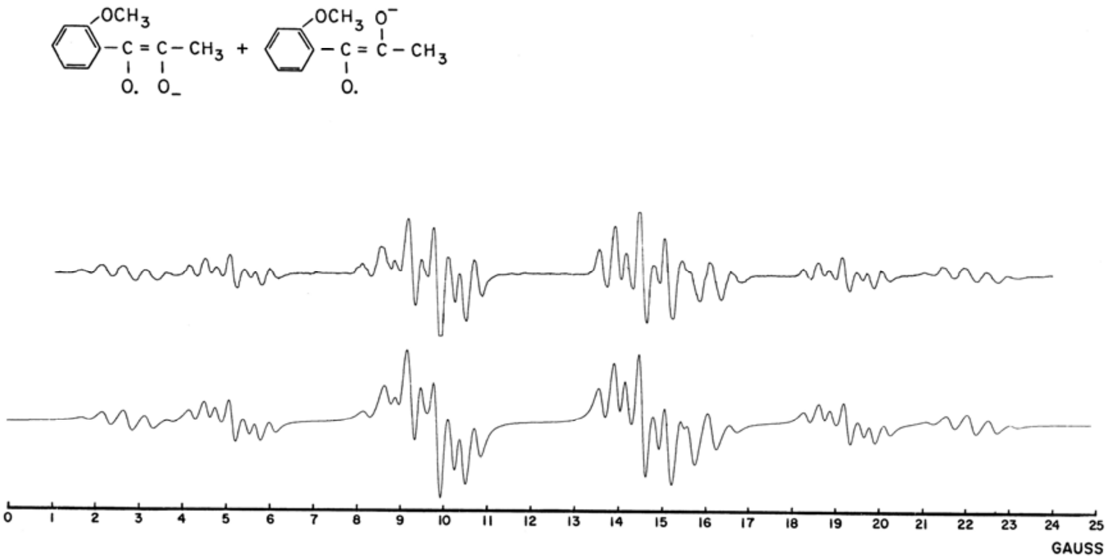
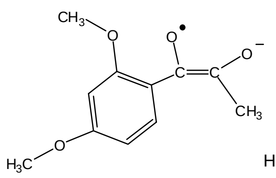
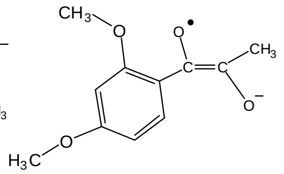


Figure 1. Experimental (top) and simulated (bottom) esr spectra of *cis*- and *trans*- isomers of 1-(2'methoxyphenyl)-1,2-propanesemidione.

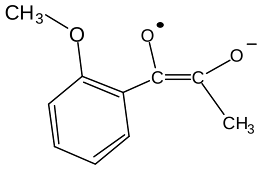
Our *ab initio* calculations were designed to give insight into two significant aspects of these radicals--the reason for the appearance of *cis* radical when an *ortho*-substituent is placed on the benzene ring of a 1-phenyl-1,2-propanesemidione and the variations in spin density between *cis* and *trans* radicals. Calculations were carried out on the *cis* and *trans* isomers of 1-phenyl-1,2-ethanesemidione (phenyl glyoxal anion radical) (**3a** and **3b**), the *cis* and *trans* isomers of 1-phenyl-1,2-propanesemidione (**4a** and **4b**), and the *cis* and *trans* isomers of 1-(2'methoxyphenyl)-1,2-propanesemidione (**2a** and **2b**). No calculations were performed for the 2',4'-dimethoxyphenyl system (**1a** and **1b)** because of the increased length of time for the calculation and the fact that the experimental data indicates that the second methoxy has a minimal impact on the spin distribution.



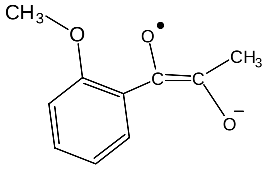
1a



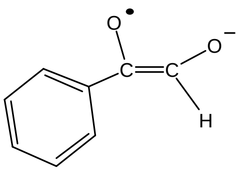
1b



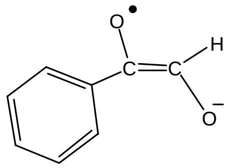
2a



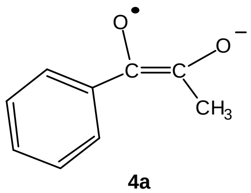
2b



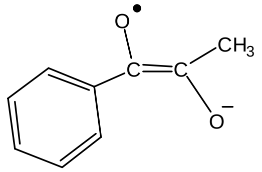
3a



3b



4a



4b

Two types of calculations were used for this system: B3LYP/6-31+G**// B3LYP/6-31+G** and B3LYP/TVP//MP2/6-31+G** (see Calculations). So far as energetics are concerned, the two systems gave essentially identical results. Therefore, we will only discuss calculations for energetics at the first level. However, the energy results for the two sets of calculations are given in Table 1. The second type of calculation is superior for probing spin distributions, so our hyperfine splittings were calculated at the B3LYP/TVP//MP2/6-31+G** level.

The calculations for the *cis*- and *trans*-phenylglyoxal anion radicals indicate the *trans* semidione is the more stable. The calculated energy difference is 4.9 kcal/mol. The twist angle of the semidione side chain with the benzene ring for the *cis* radical is 11.5 ^{0}. The corresponding twist angle for the *trans* semidione is 0.0^{0}. The energy differences are not terribly large, nor is the twist angle for the *cis* radical very large. There appears to be a weak repulsive interaction between the aldehydic hydrogen and the *syn ortho* hydrogen in the *cis* radical, because both hydrogens have some positive charge. Analogously, there is a weak attractive interaction between the alpha carbonyl oxygen and the *syn ortho* hydrogen in the *trans* radical, because the two atoms have opposite charges.

Nevertheless, the small difference between the two isomers means that ion pairing can significantly change the ratios. For example, Russell *et al*[4] could form the *cis* radical exclusively in DMSO when potassium was used as the counter ion, presumably because of simultaneous ion pairing of the potassium with both oxygens, while the bulky cesium counter ion gave only *trans* radical.

When the corresponding geometric isomers are studied for the 1-phenyl-1,2-propanesemidione system, it is quite clear that the exclusive preference for the *trans* isomer is caused by repulsive steric interactions in the *cis* isomer between the side chain methyl and the *syn ortho* hydrogen. This results in a twist angle at the minimum of 28.5 ^{0}, while the *trans* radical has a zero degree twist angle. In this instance the energy difference favors the *trans* semidione by 9.8 kcal/mol.

When we pass to the situation where the methyl phenyl semidione has an *ortho*-methoxy substituent, we have to consider not only the twist angle of the semidione side chain with the benzene ring, but also the twist angle of the methoxy group with the benzene ring.

There are two significant minima calculated for the *cis* semidione system. One has the methoxy unit in a *syn* position to the alpha carbonyl oxygen. This orientation has twist angles of 58.9 and 5.4 degrees, respectively, for the semidione side chain and methoxy group. The energy of this conformation is 8.3 kcal/mol greater than the lowest energy *trans* radical system. The other minima has the methoxy unit in an *anti* alignment with the alpha carbonyl oxygen. Here the twist angles are 47.5 and 1.6 degrees. The energy is 6.3 kcal/mol.

The *trans* semidione system has three significant minima. The lowest energy minimum, which we take as zero kcal/mol, has the methoxy group in an *anti* alignment with the alpha carbonyl oxygen. The side chain and methoxy group have twist angles, respectively, of 43.7 and 59.1 degrees. Another minumum with an energy of 0.9 kcal/mol also has the *anti* alignment, but the methoxy tilts toward the beta carbonyl oxygen as a result of a small attractive interaction. The twist angles here are 53.4 ^{0} for the semidione side chain and 29.9 ^{0} for the methoxy group. A *syn* alignment of the methoxy group with the alpha carbonyl oxygen has an energy of 2.0 kcal/mol. The methoxy group has a small twist angle of 3.5 ^{0}, while the side chain is twisted by 37 ^{0}.

Clearly one cannot choose among these three minima. However, these calculations on the *cis* and *trans* radicals demonstrate that the *ortho* substituent has induced a significant twist in the *trans* radical as well as in the *cis* and the previous 9.8 kcal/mol difference for the unsubstituted compound has dropped to 4-6 kcal/mol for the substituted compound. Therefore, ion pairing can help promote the formation of *cis* radical. Note that our results showed that the proportion of *cis* radical in the 2′,4′-dimethoxy compound increased in going from pure DMSO to an 80-20 mixture of DMSO-t-BuOH. The reduction in polarity in going to the mixture would be expected to facilitate potassium ion pairing.

In Tables 2-4 we give the comparison of our *ab initio* calculations with the experimental hyperfine splitting constants. The experimental splitting constants for the *ortho*-methoxy derivative come from this work. The values for *cis*- and *trans*-phenylsemidione in DMSO were determined by Russell *et al*.[5] The values for *trans*-phenylmethylsemidione in 80% DMSO-20% t-BuOH are those of Strom and Norton.[7] Our past experience has been that this difference in solvent has no impact whatsoever on the ring splitting constants and an effect of only a few milligauss on the side chain splitting.

Our *ab initio* calculations are for a minimum energy conformation. Consequently, the calculations give two different *ortho* and *meta* splittings and three different methyl hydrogen splittings. We will just cite the average of these values. For the *cis ortho*-methoxy derivative the values given are for the lower energy *syn* methoxy orientation. There are no differences in splitting constants compared to the results for the *anti* orientation. For the *trans ortho*-methoxy derivative the values are those for the lowest energy *anti* orientation. Here the calculated methoxy hydrogen splitting constants give us additional justification for this choice. The *syn* alignment gives a methoxy hydrogen splitting of essentially zero. The *anti* alignment tilted toward the beta carbonyl carbon gives a value of 1.15 G, in contradiction to the experimental results. The regular *anti* alignment gives a value of 0.25 G. The 0.23 G component lines we measured for this radical are consistent with an unresolved methoxy hydrogen splitting close to this magnititude.

Table 1. Calculated energies for the semidione systems

Semidione	B3LYP 6-31+G**		B3LYP/TVP	
	E[1]	ΔE[2]	E[1]	ΔE[2]
3a	-458.95643	4.9	-459.08446	4.6
3b	-458.96423	0.0	-459.09187	0.0
4a	-498.26929	9.8	-498.40818	9.8
4b	-498.28493	0.0	-498.42372	0.0
2a syn	-612.78443	8.3	-612.95858	8.4
2a anti	-612.78756	6.3	-612.96154	6.5
2b syn	-612.79442	2.0	-612.96851	2.2
2b anti	-612.79764	0.0	-612.97196	0.0
2b anti-tilted	-612.79622	0.9	-612.97050	0.9

[1] Atomic Units [2] kcal/mol.

Table 2. Experimental and theoretical splitting constants for *cis*- and *trans*-1-phenylethanesemidione

Proton Position	Experimental(G)		Theoretical(G)	
	cis	*trans*	*cis*	*trans*
ortho	1.50	1.34	-0.73	-1.18
meta	0.52	0.45	+0.28	+0.39
para	1.70	1.52	-0.95	-1.50
aldehydic	6.88	5.59	-5.43	-5.00
Absolute Sum of Ring H's	5.74	5.10	2.97	4.65

Table 3. Experimental and theoretical splitting constants for *trans*-1-phenyl-1,2-Propanesemidione

Proton Position	Experimental(G)	Theoretical(G)
ortho	1.59	-1.14
meta	0.54	+0.37
para	1.84	-1.43
methyl	3.43	3.16

Table 4. Experimental and theoretical splitting constants for *cis*- and *trans*-1-(2′methoxyphenyl)-1,2-propanesemidione

Proton Position	Experimental		Theoretical	
	cis	*trans*	*cis*	*trans*
Methoxy	----	-----	+0.08	+0.25
3′	0.48	0.34	+0.51	+0.32
4′	0.48	0.57	-0.79	-.055

5′	0.48	0.34	+0.32	+0.32
6′	0.48	0.57	-0.54	-0.46
Side Chain Methyl	6.44	4.69	+4.72	+4.36
Absolute Sum of Ring H’s	1.92	1.82	2.16	1.65

The theoretical hyperfine splittings for the *trans*-phenylsemidione and *trans*-(2′methoxyphenyl)-1.2-propanesemidione are rather good. The other results are not as good, but the calculations do reproduce many of the important experimental trends. They do predict the order of splitting constants *meta* < *ortho* < *para*, and they predict side chain proton splittings greater for *cis* radical than *trans* radical. For the methoxy-substituted radicals, the calculations predict the sum of the ring proton splittings greater for cis-radical than *trans*-radical, as is found. However, for the phenylsemidione system, the calculations also predict the sum of ring proton splitting greater for *cis*-radical than for *trans*-radical, contrary to the experimental result.

In future work we hope to investigate the effect of other *ortho* substituents on the *cis*, *trans* ratios of these radicals.

Experimental Section

The ketone starting materials and potassium t-butoxide were purchased from Aldrich Chemical Co. and used without further purification. The DMSO was also an Aldrich product and was dried over molecular sieves. The concentrations of base and ketone were 0.1 and 0.05 *M*, respectively. The apparatus was the H-cell of Russell and coworkers.[10] Esr spectra were obtained with a Varian V-4500-10 esr spectrometer equipped with a 12-in. magnet and 100 kc/sec field modulation. Sweep rates were calibrated from the spectrum of *p*-benzosemiquinone in 1-butanol.[11] For the g-value determination the magnetic field was measured with a gaussmeter and the frequency calibrated with a wavemeter.

Calculation Section

All geometries were initially optimized at the DFT/6-31+G** level using the B3LYP[12,13] functional (B3LYP/6-31+G**//B3LYP/6-31+G**). Subsequently, geometries were reoptimized at the MP2 level using the same basis set. Recent theoretical work has indicated that MP2 geometries are superior to those of DFT for the calculation of contact spin densities[14]. Final spin densities were calculated using the B3LYP functional and a TZVP quality basis set[15], supplemented by tight s functions to better describe the core s orbitals[14] and diffuse functions taken from the standard 6-31++G** basis set (B3LYP/TVP//MP2/6-31+G**).

Acknowledgements

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References

1. Part 5. Strom, E. T. *J. Org. Chem.* **1995**, *60*, 5686.
2. Russell, G. A.; Strom, E. T. *J. Am. Chem. Soc.* **1964**, *86*, 744.
3. Russell, G. A.; Stephens, R. D. *J. Phys. Chem.* **1966**, *70*, 1320.
4. Corvaja, C.; Nordio, P. L.; Giacometti, G. *J. Am. Chem. Soc.* **1967**, *89*, 1751.
5. Russell, G. A.; Lawson, D. F.; Ochrymowycz, L. A. *Tetrahedron* **1970**, *26*, 4697.
6. Strom, E. T. *J. Am. Chem. Soc.* **1966**, *88*, 2065.
7. Strom, E. T.; Norton, J. R. *J. Am. Chem. Soc.* **1970**, *92*, 2327.
8. Calle, P.; Martin, J.; Garcia de la Vega, J. M.; Siero, C. *J. Mol. Struct.* **1992**, *269*, 163.
9. Snowden, B. S., Jr.; Strom, E. T. *QCPE* 1970 *11*, 160.
10. Russell, G. A.; Janzen, E. G.; Strom, E.T. *J. Am. Chem. Soc.* **1964**, *86*, 1807.
11. Segal, B. G.; Kaplan, M.; Fraenkel, G. K. *J. Chem. Phys.* **1965**, *43*, 4191.
12. Lee, C.; Yang, W.; Parr, R. G. *Phys Rev.* **1988**, *B37*, 785.
13. Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648
14. Nguyen, M. T.; Creve, S.; Vanquickenborne, L. G. *J. Phys. Chem. A* **1997,** *101*, 3174.
15. Goodbout, N.; Salahub, D. R.; Andzelm, J.; Wimmer, E. *Can. J. Chem.* **1992**, *70*, 560.