

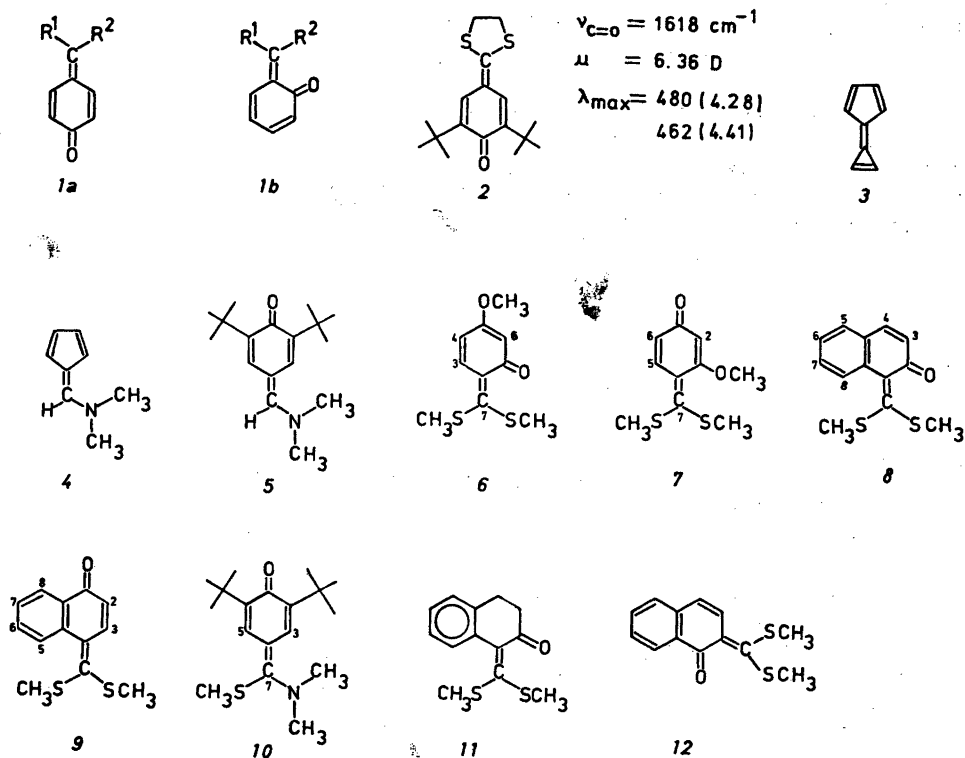
Barriers to Rotation about the Exocyclic Carbon—Carbon Bond in some Quinone Methides with Donor Substituents on the Exocyclic Carbon

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Four ω,ω -bis(methylthio)quinone methides and one ω -dimethylamino- ω -methylthioquinone methide have been prepared from the corresponding 2- and 4-hydroxyaryldithioesters and hydroxy-*N,N*-dimethylthiobenzamides by methylation on the sulfur atom and subsequent deprotonation. The quinone methides are un-

stable but can be studied in solution. The barriers to rotation around the exocyclic double bond have been determined by ^1H and ^{13}C NMR techniques. Low barriers are observed indicating a high degree of stabilization of the transition state.



Scheme 1.

Quinone methides, with the general formula $1a-b$ (Scheme 1), represent a group of compounds of considerable theoretical interest. The parent compounds ($R^1 = R^2 = H$) have not been isolated, and attempts to prepare them have usually resulted in dimers and trimers.¹ The monomers have been spectroscopically detected in solutions^{2,3} and some derivatives were recently isolated.⁴

Quinone methides with electron-donating substituents on the exocyclic carbon are usually more stable. Their reactivity towards nucleophiles and electrophiles is high, but they show no tendency to polymerize. Gompper *et al.*⁵ have isolated some ω,ω -bis(alkylthio)quinone methides of the type 2, and estimated the contribution of the dipolar resonance structures to the ground state, as reflected by IR, UV and dipole moments, to be 10–20%.⁵

Incorporation of the exocyclic double bond π -electrons into the ring results in the creation of an aromatic phenolate system, and a dipolar stabilization of the twisted transition state to rotation around the exocyclic double bond might be envisaged in the same way as for push-pull substituted ethylenes, which show low rotational barriers.⁶

In calicene, 3, incorporation of the double bond π -electrons into the cyclopentadienyl ring results in the creation of two aromatic systems, thus giving a transition state to rotation of low energy. Barriers in the order of 75–84 kJ mol⁻¹ have been reported for derivatives with formyl groups in the cyclopentadiene ring.⁷ Similarly, a C(1)=C(6) barrier in 6-dimethylaminofulvene (4) of 92.5 kJ mol⁻¹ and a moderately high barrier to rotation about the C(6)–N bond of 56.5 kJ mol⁻¹ have been reported.⁸

A zwitterionic transition state in 3 and 4 is supported by a decrease in the barriers to rotation about the double bond with increasing solvent polarity.^{7,8} A polar solvent will stabilize the zwitterionic transition state better than the less polar ground state, and the difference in stabilization energy between the two states will increase with increasing solvent polarity.

Mannschreck *et al.* observed a low C=C barrier ($\Delta G^\ddagger = 60.7$ kJ mol⁻¹) and a significant C–N barrier ($\Delta G^\ddagger = 51.9$ kJ mol⁻¹) in the quinone methide 5.⁹

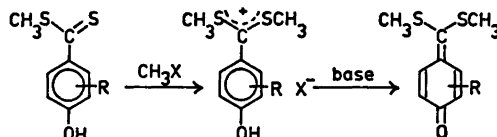
In order to acquire further understanding of the importance of dipolar resonance con-

tributions in these types of systems, and to compare the stabilities of *ortho* and *para* quinonoid structures, we have investigated some quinone methides (6–10) with electron donating substituents [CH_3S and $(CH_3)_2N$] on the exocyclic carbon atom. The ketene mercaptal 11 has been studied as a non-quinonoid reference compound.

EXPERIMENTAL

NMR Spectra. The ¹H NMR spectra were recorded on Varian A60 or XL-100 spectrometers and the ¹³C NMR spectra on a Jeol FX-60 spectrometer working at 15.03 MHz. A flip angle of 45° was used, the number of data points was 8 K and spectral widths were 5000, 2500 and 1000 Hz. All spectrometers were equipped with standard variable-temperature attachments. The temperatures were measured by external thermocouples, which were calibrated by means of a thermocouple held inside a spinning dummy tube. The bandshape analyses were performed by visual curve fitting with spectra calculated on a Hewlett-Packard 9820A desk calculator equipped with a 9862A plotter, and by use of the coalescence approximation.¹⁰ The determination of T_2 was performed as described previously.¹¹

Assignments of the ¹³C resonances were made on the basis of expected chemical shifts, substituent effects and intensities, and were in agreement with calculated charge densities.



Scheme 2.

Preparations. The synthesis of the ω,ω -bis(alkylthio)quinone methides was carried out according to Gompper *et al.*⁵ from *ortho*- and *para*-hydroxydithiobenzoates *via* the bis(methylthio)(hydroxyaryl)carbenium salts. The quinone methide systems 6–10 are less stable than the analogs of type 2, and it was in general not possible to isolate them in pure form. The precursor salts, on the other hand, are reasonably stable and crystalline compounds, and they can be purified by conventional methods and stored for months under dry conditions. The deprotonation step was carried out directly in the solution used for the spectroscopic experiment. The resulting triethylammonium salt was filtered off and the solution used immediately. Since the rotational barrier of these systems is very sensitive to acid catalysis,

a 5 % excess of triethylamine was always used. Control experiments showed the addition of a small amount of triethylamine to effectively eliminate the catalytic influence of traces of acidic impurities.¹²

The general procedure for the preparation of an NMR sample was performed according to the following description:

The dry and ground salt (0.5–1 mmol) was weighed into a test tube and supplied with ca. 1 ml of the dry solvent (CS₂, CS₂+CH₂Cl₂ or C₆D₆). Triethylamine (5 % excess) was added, the tube stoppered and placed in a desiccator for ca. 30 min with occasional stirring. An intensely red-coloured solution was immediately formed and a pale precipitate separated. The solution was filtered through a piece of predried cotton-wool, and transferred to the NMR tube. The ω,ω -bis(methylthio)quinone methides were characterized by spectroscopic methods and through their precursor salts.

ω -Dimethylamino- ω -methylthioquinone methides should in principle be available by an analogous route. 2- and 4-hydroxy-*N,N*-dimethylthiobenzamides are easily methylated on the sulfur atom. The addition of triethylamine to a suspension of the salt in an inert polar solvent, such as acetonitrile, instantaneously produced a bright orange or red coloured solution. An NMR spectrum indicated that the quinone methide was produced, but the spectrum also contained unidentified signals. Despite the use of combinations of several different anions, bases and solvents, all attempts to prepare sufficiently pure and concentrated quinone methide solutions were unsuccessful. However, evaporation of a carbon disulfide solution of 2,6-di-*tert*-butyl-4-[(dimethylamino)-(methylthio)methylene]-2,5-cyclohexadien-1-one (*10*) gave a pure and stable product after recrystallization from ligroin.

Bis(methylthio)(2-hydroxy-4-methoxyphenyl)-carbenium methyl sulfate, (*6a*) was prepared from methyl 2-hydroxy-4-methoxydithiobenzoate¹³ (0.8 g, 3.7 mmol) by heating with dimethyl sulfate (2.5 ml) for 20 min at 120 °C. After cooling to room temperature dry ether (25 ml) was added. On scratching, the oily product slowly crystallized and was recrystallized from acetonitrile; yield 1.0 g (78 %) red crystals, m.p. 97–99 °C. Anal. C₁₁H₁₆O₆S₃: C, H, S.

Bis(methylthio)(4-hydroxy-2-methoxyphenyl)-carbenium iodide, (*7a*) was prepared from methyl 4-hydroxy-2-methoxydithiobenzoate¹² (0.9 g, 4.2 mmol) by reflux with methyl iodide (4 g) for 30 min. The solution was treated with several portions of dry ether with scraping, and a crystalline product separated. After recrystallization from acetonitrile 1.0 g (67 %) of red crystals was obtained; m.p. 117–119 °C (decomp.). Anal. C₁₀H₁₃O₂S₂I: C, H, S.

Bis(methylthio)[4-hydroxynaphthyl-(1)]carbenium methyl sulfate, (*9a*) was prepared from methyl 4-hydroxy-1-dithionaphthoate⁵ by the

same procedure as *6a*. Yield: 33 %; m.p. 195–197 °C. Anal. C₁₄H₁₆O₆S₃: C, H, S.

(3,5-Di-tert-butyl-4-hydroxyphenyl)(dimethylamino)(methylthio)carbenium iodide, (*10a*) was prepared from 3,5-di-*tert*-butyl-4-hydroxy-*N,N*-dimethylthiobenzamide⁵ (3.0 g, 10.2 mmol) and methyl iodide (1.7 g, 12 mmol) in refluxing acetone (25 ml). The solution was allowed to stand at room temperature overnight. A precipitate was formed which was filtered off and washed with dry acetone. Yield: 4.1 g (94 %) of white prisms, m.p. 212–214 °C. Anal. C₁₈H₃₀NOSI: C, H, N, S.

2,6-Di-tert-butyl-4-[(dimethylamino)(methylthio)methylene]-2,5-cyclohexadien-1-one, (*10*) was prepared by the reaction between *10a* (5.0 g, 11.5 mmol) and triethylamine (1.2 g, 11.8 mmol) in carbon disulfide (50 ml). An intensely orange solution was immediately formed. The solution was allowed to stand for 1 h at room temperature and the white precipitate (triethylammonium iodide) was filtered off. The solution was evaporated and the remainder recrystallized from ligroin giving 3.1 g (88 %) of orange needles, m.p. 136–137 °C. Anal. C₁₈H₂₈NOS: C, H, N, S. IR (KBr): C=O: 1 600 cm⁻¹, C=C: 1508 cm⁻¹.

UV [cyclohexane (log ϵ): 413 (4.47), 273 (3.79) nm.

RESULTS AND DISCUSSION

The ¹H NMR spectra of compounds *6*–*10* were recorded on carbon disulfide solutions and the ambient temperature data are given in Table 1. At this temperature the spectra of *6*–*9* show one singlet for the *S*-methyls, although somewhat broadened in the case of *6*. On lowering the temperature decoalescence was observed, for *6* at 22 °C and for *8* and *9* at –113 and –103 °C, respectively. The results are collected in Table 1. For *7* no splitting of the *S*-methyl signal was observed down to –120 °C in any of the solvents CS₂, CHCl₂F or CH₂Cl₂/C₆H₆F (1:1).

In *10*, two potential barriers may be imagined, to rotation around the C=C bond, which at slow exchange should give rise to anisochronous ring protons (3 and 5), and to rotation around the C–N bond, which should cause non-equivalence of the *N*-CH₃ methyls. At probe temperature, both of these types of protons give sharp singlets and show no effect of slow rotation down to –120 °C in CS₂ or in CHCl₂F. Instead, a non-selective broadening of all signals started at –80 °C, and below –110 °C only extremely broad bands remained.

Table 1. ¹H NMR parameters for 6–10 in carbon disulfide solution.

Compound	Chemical shift/ δ	Coupling constants/Hz	$\Delta\nu$ /Hz	T_c /K	ΔG^\ddagger /kJ mol ⁻¹	
6	CH ₃ S	2.52 ^a		6.3	259.3	65.8
	CH ₃ O	3.73				
	H ³	7.42	$J_{3,4} = 9.5$			
	H ⁴	5.93	$J_{4,6} = 2.5$			
	H ⁶	5.53	$J_{3,6} \approx 0$			
7	CH ₃ S	2.53			(50–55)	
	CH ₃ O	3.79				
	H ³	5.65	$J_{5,6} = 10.1$			
	H ⁵	7.73	$J_{2,6} = 1.8$			
	H ⁶	6.02	$J_{3,5} \approx 0$			
8	CH ₃ S	2.30		29.4	160	32.8
	H ³	6.36	$J_{3,4} = 9.8$			
	H ⁴	7.22 ^b				
	H ⁶ -H ⁸	6.88–7.33 ^c				
9 ^d	CH ₃ S	2.47		42.0	170	34.4
	H ³	8.07 ^d	$J_{2,3} = 10.0$			
	H ²	6.45				
	H ⁵ -H ⁸	7.30–8.80 ^c				
10	(CH ₃) ₂ C	1.25				
	CH ₃ S	2.34				
	(CH ₃) ₂ N	3.33				
	H ^{3,5}	7.04				

^a Broadened. ^b Partly hidden in H (arom.). ^c Multiplet. ^d In CS₂+10% CH₂Cl₂ for solubility reasons.

Since an interpretation in terms of accidental chemical shift equivalence could not be ruled out in the cases of 7 and 10, ¹³C NMR studies were also carried out for these compounds (Table 2). The *S*-methyl signal of 7 showed selective broadening below -30°C but re-

mained a broad, unresolved singlet down to -100°C, and thus a very small chemical shift difference is likely. A value of 50–55 kJ mol⁻¹ can be estimated for the barrier.

In 10 the *ortho* ring carbons and the *N*-methyl carbons both appear as sharp singlets at probe temperature and decoalesce to symmetrical doublets at low temperature (Table 3).

In general terms, the low barriers to rotation around the exocyclic C=C bond in the *bis*-(methylthio)quinone methides demonstrate the ease of polarization of these compounds and that the power of the ring to stabilize the negative charge is at least as important as the most powerful combinations of electron-attracting groups (*e.g.* NO₂, CN and COR).⁸

The importance of the stabilization of the transition state by resonance is instructively shown by comparison of the rotational barriers in 8 and 11. The activation energy for the rotation of 11 is 97.5 kJ mol⁻¹,¹⁴ which is 64.7 kJ mol⁻¹ higher than the barrier in 8. The effects of steric interactions in 8 and 11

Table 2. ¹³C NMR for 7 and 10.^a

Compound 7	δ /ppm ^b	Compound 10	δ /ppm ^c
CH ₃ S	20.8	CH ₃ S	19.0
CH ₃ O	54.5	CH ₂ C	29.7
C(2)	104.0	C(quart.)	35.1
C(4)	109.2	CH ₂ N	45.1
C(6)	124.4	C(4)	109.7
C(5)	135.7	C(3; 5)	129.7
C(3)	156.5	C(2; 6)	141.7
C(7)	163.4	C(7)	170.6
C(1)	186.3	C(1)	182.8

^a Numbering according to Scheme 1. ^b In benzene-*d*₆. ^c In CS₂+20% (CD₃)₂CO.

Table 3. Coalescence data for 10 from ^{13}C NMR in $(\text{CD}_3)_2\text{CO}/\text{CS}_2$ (2:1).

	$\Delta\nu/\text{Hz}$	T_c/K	$\Delta G^\ddagger/\text{kJ mol}^{-1}$
C=C	60	176	35.0
C-N	51	193	39.0

should be of about the same magnitude, so that the main part of the difference in the barrier of 64.7 kJ mol^{-1} comes from a π -electron stabilization of the transition state of 8.

A comparison within the series 6–9 is harder to rationalize. The height of the barrier in these compounds is determined essentially by two effects: (1) The difference in π -electron stabilization between the planar ground state and the 90° twisted transition state. (2) The magnitude of the steric strain in the ground state.

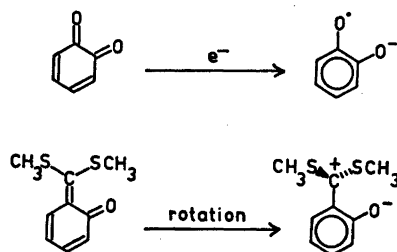
SCF-MO calculations^{15–17} on quinones and quinodimethides do not unequivocally answer the question as to the stability of the *ortho* quinonoid structure compared to *para* quinonoid structure. Such calculations give higher resonance energy but lower heat of atomization for the *ortho* isomer.

The activation process represents a change from the quinonoid structure in the ground state to a phenolate anionic system in the transition state. The formal similarity between this process and the reduction of the corresponding quinones, shown in Scheme 3, encouraged a comparison between the barrier heights and the reduction potentials (Table 4).

Taking the nonbonding interaction into account (*vide infra*), the same order is obtained within the two series. If these values reflect ground state properties, the *ortho* quinone methides should be considered more stable than the *para* isomers.

Table 4. Rotational barriers for 6–9 and polarographic reduction potentials for the corresponding quinones.

	$\Delta G^\ddagger/\text{kJ mol}^{-1}$	$E_{1/2}/\text{V}$	Ref.
6	65.8	0.783	18
7	50–55	0.715	19
8	32.8	0.576	19
9	34.4	0.482	20



Scheme 3.

Turning to the steric effects, the destabilizations of the ground state by an *ortho* carbonyl oxygen atom and an *ortho* methoxy group are of the same magnitude as judged from conformational analysis of appropriate compounds.²¹ Thus, the difference in barrier between 6 and 7 essentially reflects effects of type (1), since both barriers are sterically lowered to about the same extent. In the naphthoquinone methides 8 and 9 the *peri* effect has an important lowering influence on the barrier. A logical step to test the importance of *peri* interactions would be to determine the barrier in 12. Unfortunately, synthesis of this compound has proved elusive. The *ortho* carbonyl oxygen of 8 further destabilizes the planar state of this molecule compared to 9. A compensation for this effect would probably lead to reversed order of barrier between 8 and 9.

The combination of one dimethylamino and one methylthio group, as in 10, is effectively stabilizing the zwitterionic transition state. Only few C=C barriers in compounds with these donor substituents have actually been measured and they are lower than in the corresponding compounds with two methylthio groups as donors.^{22,23}

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