PREPARATION AND REACTIONS OF 7-PHENYLSULFONYL- AND 7-ARYLTHIOQUINONE METHIDES*

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The manganese dioxide oxidation of the sulfone *I* afforded 2,6-di-tert-butyl-7-phenyl-7-phenylsulfonylquinone methide (*II*) which was converted to the 7-arylthio-7-phenyl-2,6-ditert-butylquinone methides *IVa—IVf* by reaction with the appropriate thiophenoxide anions. By reaction with piperidine, the quinone methide *II* was transformed to the 7-piperidinoquinone methide *IVg*. The ethoxide and cyanide anions react with transient 7-ethoxy- or 7-cyanoquinone methides *IVh* and *IVi* to afford the bis derivatives *VIh* and *VIi*, resp. The structure of the product of the reaction between the quinone methide *II* with nucleophiles is controlled by the thermodynamic stability of the anion *V*.

The quinone methides substituted on the $C_{(7)}$ methide carbon atom by a heteroatom are rather rare. The substituted 7-aminoquinone methides were prepared by reaction of the corresponding 4-hydroxybenzylidene chloride with secondary amines[1] or by the ferricyanide oxidation of N,N-dialkyl-4-hydroxybenzylamines[2]. 7-Methoxy- and 7-ethoxyquinone methides were obtained by oxidation of the corresponding 4-hydroxybenzyl ether with 2,4,6-tri-tert-butylphenoxyl[3]. 7,7-Bis(alkylthio)quinone methides are formed by alkylation of the 4-hydroxydithiobenzoic acid dianion[4] or by oxidation of 4-hydroxybenzaldehyde thioacetal with dichlorodicyanobenzoquinone[5]. However, the theoretically interesting 7-monoarylthioquinone methides have not been so far prepared.

Since phenyl 4-hydroxybenzyl sulfides are readily accessible from Mannich bases[6], dehydrogenation was believed as the method of choice. However, none of the attempted reagents afforded the required product. The ferricyanide oxidation[7] of 3,5-di-tert-butyl-4-hydroxybenzyl phenyl sulfide yielded a mixture of 2,6-di-tert-butyl-4-hydroxybenzaldehyde and 2,6-di-tert-butyl-4-hydroxybenzoic acid. By the action of activated manganese dioxide[8], the same sulfide was degraded in a low yield to 2,6-di-tert-butylbenzoquinone whereas the reaction with dichlorodicyanobenzoquinone[9] did not take place at all. In some recent cases[10–12], quinone methides have been prepared by the base-catalysed elimination of the phenylsulfonyl group from substitut-

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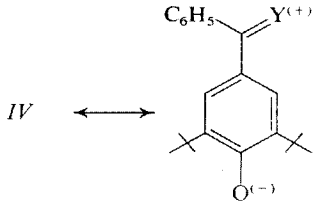
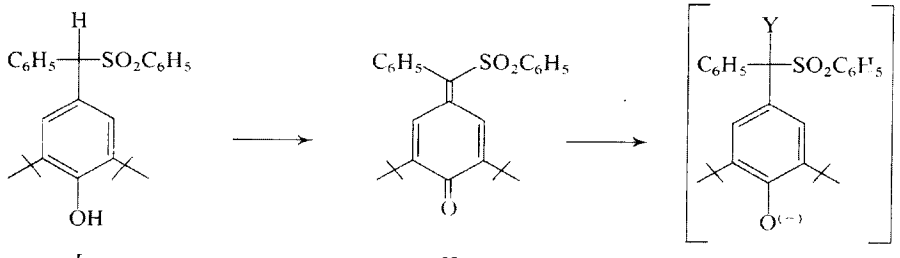
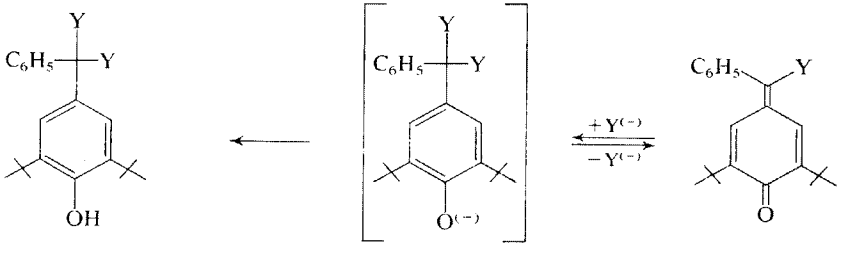
ed 4-hydroxybenzyl sulfones. Since phenylsulfonyl proved to be an equally good leaving group as chloride, it was of interest to attempt this reaction in the preparation of 7-arylthioquinone methides.



VII



I *II* *III*



VI *V* *IV*

In formulae *III* and *IV*: *a* Y = 4-$CH_3OC_6H_4S$
b Y = 4-$CH_3C_6H_4S$
c Y = C_6H_5S
d Y = 4-FC_6H_4S
e Y = 4-ClC_6H_4S
f Y = 4-BrC_6H_4S
g Y = $C_5H_{10}N$
In formulae *III*–*VI*: *h* Y = CN
i Y = C_2H_5O

SCHEME 1

As the starting material of the synthesis, the 7-phenylsulfonylquinone methide *II* was used. Compound *II* was obtained in a fair yield from the phenylsulfonyldiarylmethane *I* with activated maganese dioxide[13] (Scheme 1). The quinone methide *II* is a stable crystalline substance which is almost colourless in contrast to other quinone methides. However, the proposed structure is supported by infrared spectrum (C=O, 1 629 cm^{-1}) and mass spectrum (M^+ 434 and the corresponding fragments). The base- as well as acid-catalysed hydrolysis of the quinone methide *II* affords the known 3,5-di-tert-butyl-4-hydroxybenzophenone[14]. The further step of the synthesis consisted in addition of thiophenoxide to the phenylsulfonylquinone methide *II*. The reaction was performed in 2-propanol and led to the labile anion *III* which was stabilised by extrusion of the phenylsulfonyl group. The intensively yellow to orange 7-arylthioquinone methides *IV* were obtained in excellent yields. A similar reaction may be observed between the sulfonylquinone methide *II* and piperidine. All 7-arylthioquinone methides as well as the 7-piperidinoquinone methide are readily hydrolysed with the formation of the corresponding benzophenone. When dissolved in piperidine, the 7-phenylthioquinone methide *IVc* is quantitatively converted to the 7-piperidinoquinone methide *IVg*. By the action of one equivalent of thiophenoxide on a solution of the 7-methoxyphenylthioquinone methide *IVa* in 2-propanol, a mixture is obtained containing approximately equal amounts of the starting 7-methoxyphenylthioquinone methide *IVa* and 7-phenylthioquinone methide *IVc*. The formation of the quinone methide *IV* thus depends more likely on the low thermodynamical stability of the anion *V* ($k_r \gg k_f$) than on the decreased reactivity of the quinone methide *IV* due to participation of the mesomeric structure *VII*. The course of the reaction between the phenylsulfonylquinone methide *II* and cyanide ions is in accord with this proposal. The 7-cyanoquinone methide *IVh* produced in the first addition-elimination steps is merely a transient intermediate which is converted by repeated addition of the cyanide ion to the anion *Vh*. Owing to the firm C—CN bond, the anion *Vh* is so stable that the dicyano derivative *VIh* may be isolated in an almost quantitative yield. In the reaction between equimolar amounts of the quinone methide *II* and cyanide, the dicyano derivative is formed in about 50% yield. As suggested by this result, the reaction rate of the *II* → *III* step is at least one order of magnitude lower than that of the *IV* → *V* step. A similar observation was made in the reaction of the phenylsulfonylquinone methide *II* with ethanolic sodium ethoxide since only the ketal *VIi* was encountered but not the quinone methide *IVi*.

EXPERIMENTAL

Melting points were taken on a heated microscope stage (Kofler block) and were not corrected. Analytical samples were dried at room temperature and 0·1 Torr for 8 h. The UV spectra were

measured on a Specord UV VIS spectrophotometer (Carl Zeiss, Jena). Mass spectra were recorded on an A.E.I. MS 902 spectrometer (70 eV, 110—230°C).

2,6-*Di-tert-butyl-7-phenyl-7-phenylsulfonylquinone methide* (II). Activated manganese dioxide[13] (45 g) was added to a solution of the 4-hydroxybenzyl sulfone *I* (4·36 g) in benzene (100 ml) and the suspension was stirred at room temperature until the sulfone *I* disappeared (as determined by thin-layer chromatography). The reaction mixture was filtered, the filtrate evaporated at 30°C on a rotatory evaporator, and the residue crystallised from chloroform–hexane to afford a 73% yield of the sulfone *II*.

2,6-*Di-tert-butyl-7-phenyl-7-arylthioquinone methides* IVa—IVf. A solution of the appropriate thiophenol (1·1 mmol) and sodium hydride (27 mg; 1·1 mmol) in 2-propanol (3 ml) was added portionwise with stirring to a suspension of the quinone methide *II* (435 mg; 1·0 mmol) in 2-propanol (10 ml). After 10 min, the mixture was poured into saturated aqueous citric acid (50 ml). The precipitate of the arylthioquinone methide was crystallised from hexane to afford compounds *IVa—IVf* in 91—97% yields. For the physical constants see Table I.

TABLE I
Quinone Methides *II* and *IV*

Compound	M.p., °C	λ_{max}, nm (log ε)[a]	Formula (m.w.)	Calculated/Found		
				% C	% H	% S
II	188—189	322 (4·41)	$C_{27}H_{31}O_3S$ (434·6)	74·62 74·26	7·19 7·02	7·37 7·60
IVa	154—155	387 (4·43)	$C_{28}H_{32}O_2S$ (432·6)	77·74 77·39	7·45 7·30	7·41 7·52
IVb	135—136	390 (4·43)	$C_{28}H_{32}OS$ (416·6)	80·72 79·96	7·74 7·70	7·69 7·75
IVc	150—151	387 (4·43)	$C_{27}H_{30}OS$ (402·6)	80·55 81·00	7·51 7·43	7·96 7·86
IVd	155—157	383 (4·44)	$C_{27}H_{29}FOS$ (420·6)	77·11 77·08	6·95 6·86	7·62 7·45
IVe	176—177	384 (4·44)	$C_{27}H_{29}OSCl$ (437·1)	74·20 74·06	6·69 7·02	7·34 7·18
IVf	181—182	387 (4·44)	$C_{27}H_{29}BrOS$ (481·5)	67·35 67·19	6·07 5·93	6·66 6·53
IVg	193—194	430 (4·51)	$C_{26}H_{35}NO$ (377·6)	82·71 82·62	9·34 9·28	[b] [b]

[a] n-Hexane; [b] calculated: 3·71% N; found: 3·69% N.

2,6-*Di-tert-butyl-7-phenyl-7-piperidinoquinone methide* (IVg). The sulfone *II* (435 mg; 1·0 mmol) was dissolved in piperidine (10 ml). After 30 min, the excess piperidine was removed on a rotatory evaporator at 40°C. The residue was crystallised from chloroform–hexane to afford the red quinone methide *IVg* in 95% yield.

(3,5-*Di-tert-butyl-4-hydroxyphenyl*)*phenylmalononitrile* (VIh). A solution of the sulfone *II* (435 mg; 1·0 mmol) and sodium cyanide (145 mg; 3·0 mmol) in dimethyl sulfoxide (5 ml) was heated at 50°C for 10 min, cooled down, poured into ice-cold water (25 ml), and extracted with three 15 ml portions of ether. The extracts were combined, washed with five 10 ml portions of water, and evaporated. Crystallisation of the residue from hexane yielded 85% of the nitrile *VIh*, m.p. 124–125°C. For $C_{23}H_{26}N_2O$ (346·4) calculated: 79·73% C, 7·56% H, 8·08% N; found: 79·55% C, 7·82% H, 7·95% N. Mass spectrum: M^+ 346.

Diethoxy(*phenyl*)(3,5-*di-tert-butyl-4-hydroxyphenyl*)*methane* (VIi). The sulfone *II* (435 mg; 1·0 mmol) was dissolved at room temperature in 10 ml of ethanol containing 1·1 mmol of sodium ethoxide. The ethanol was evaporated and the residue extracted with ether. Compound *VIi* m.p. 86–88°C (hexane), was obtained in 80% yield. For $C_{25}H_{36}O_3$ (384·5) calculated: 78·08% C, 9·43% H; found: 78·20% C, 9·40% H. Mass spectrum: M^+ 384.

Reaction of the methoxyphenylthioquinone methide IVa with thiophenoxide. Sodium hydride (7 mg; 0·25 mmol) was added to a solution of the quinone methide *IVa* (110 mg; 0·25 mmol) and thiophenol (27 mg; 0·25 mmol) in 2-propanol (5 ml). After 10 min, the mixture was poured into saturated aqueous citric acid (20 ml) to deposit crystals which were chromatographed on silica gel (10 g) in 7 : 3 light petroleum–benzene. The front fractions yielded 35 mg of compound *IVc* and the posterior fractions afforded 41 mg of the quinone methide *IVa*.

Aminolysis of the quinone methide IVc *with piperidine.* Compound *IVc* (100 mg; 0·25 mmol) was dissolved at room temperature in piperidine (3 ml). After 40 min, the piperidine was removed on a rotatory evaporator at 40°C and the residue was crystallised from chloroform–hexane. Yield, 82% of the quinone methide *IVg*, m.p. 192–194°C.

Hydrolysis of the quinone methide II. A solution of the quinone methide *II* (50 mg) in 2-propanol (5 ml) was treated with 0·1M-NaOH (1 ml). After 10 min, the mixture was acidified with citric acid, evaporated, and the residue extracted with ether to afford 3,5-di-tert-butyl-4-hydroxyphenyl phenyl ketone (29 mg), m.p. 123–126°C (reported[14], m.p. 123–124°C). In another experiment a mixture of the quinone methide *II* (50 mg), 2-propanol (5 ml), and 1M-HCl (1 ml) was kept at room temperature for 4 h, evaporated, and the residue crystallised from hexane to afford 32 mg of 3,5-di-tert-butyl-4-hydroxyphenyl phenyl ketone, m.p. 124–125°C.

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