

ULTRAVIOLET SPECTRA OF 4-ALKYLIDENE-2,5-CYCLOHEXADIENONES

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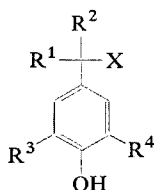
Dehydrohalogenation of 4-substituted benzyl halogenides or oxidation of substituted 4-alkylphenols gave 4-alkylidene-2,5-cyclohexadienones *XXIII–XLIV*. From the comparison of their ultraviolet spectra it follows that in the region of $\pi-\pi^*$ transitions the wave length of the absorption maximum is given by the sum of the wave lengths of unsubstituted 4-methylene-2,5-cyclohexadienone and the increments characteristic of each substituent.

4-Alkylidene-2,5-cyclohexadienones (quinonemethides) represent a group of compounds with a conjugated system of double bonds, which may be classified as quinoid. The relatedness of quinones with quinonemethides also follows from the similarity of their infrared ($\nu_{\text{C=O}}$ 1660–1670 cm^{-1}) and ultraviolet spectra. Quinones display three distinct absorption maxima¹ about 250, 290 and 440 nm, while in alkylidene-cyclohexadienones only the absorption in the 290 nm region has been described². The parallelity of the absorption at 290 nm is only formal. That is, in benzoquinones the absorption was assigned³ to the forbidden $\pi-\pi^*$ transition ($\log \epsilon < 3$), while in quinonemethides the high extinction coefficient value ($\log \epsilon > 4$) suggests that it is evidently due to a permitted $\pi-\pi^*$ transition. As there is not sufficient data in literature, which could serve as a basis for quantum chemical calculations of the quinonemethide system, we decided to prepare a larger number of these compounds and to study mainly their spectral properties.

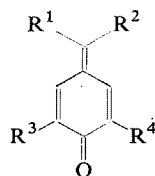
In the first stages of this study we prepared quinonemethides from substituted 4-alkylphenols by oxidation with potassium ferricyanide⁴ or silver oxide⁵. As a phenoxyl radical is a reaction intermediate and the reaction itself was carried out in alkaline medium, we did not obtain good yields of alkylidene-cyclohexadienones in those cases when the starting phenol was substituted in the position 2 only, or when it contained a group easily undergoing nucleophilic reactions. Therefore we later prepared quinonemethides by dehydrohalogenation of substituted 4-hydroxybenzyl chlorides obtained *in situ* from corresponding alcohols under the effect of gaseous hydrogen chloride. For the preparation of quinonemethides *XXXV* and *XLIV* we used the more easily accessible bromides instead of chlorides. As dehydrohalogenating reagent anhydrous potassium carbonate was found suitable. Triethylamine, used alternatively, gave quaternary salts with some benzyl chlorides; in other instances,

in the presence of excess reagent, isomerizations of alkylidenecyclohexadienone to corresponding vinylphenol took place. The majority of the prepared quinone-methides could not be prepared in crystalline state, due to their instability. Therefore we used as a criterion of purity a symmetrical shape of the curve representing the dependence of the absorption on wave-number in the ultraviolet part of the spectrum. The measured extinction coefficients, which ranged in the $1.2-1.8 \cdot 10^4$ interval, only serve for orientation because during the preparation of the starting 4-hydroxybenzyl chlorides unreproducible losses of the compounds took place under the effect of the drying agent.

All substituted 4-alkylidene-2,5-cyclohexadienones (XXIII–XLIV) measured by us displayed a single absorption maximum in the ultraviolet spectrum. In the case of 4-methylene-2,5-cyclohexadienone (XXIII) which we may consider as the funda-



I—XXII

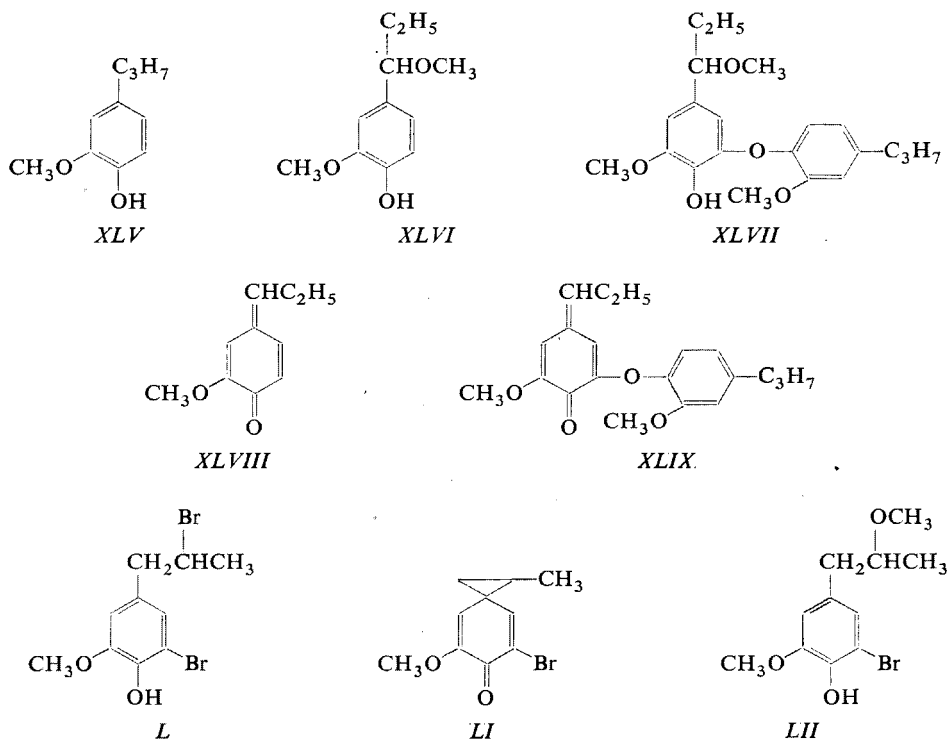


XXIII—XLIV

	X	R ¹	R ²	R ³	R ⁴
I, XXIII	OH	H	H	H	H
II, XXIV	OH	H	CH ₃	H	H
III, XXV	OH	CH ₃	CH ₃	H	H
IV, XXVI	OH	H	H	CH ₃	CH ₃
V, XXVII	OH	H	CH ₃	CH ₃	CH ₃
VI, XXVIII	OH	CH ₃	CH ₃	CH ₃	CH ₃
VII, XXIX	OH	H	H	C(CH ₃) ₃	C(CH ₃) ₃
VIII, XXX	H	H	CH ₃	C(CH ₃) ₃	C(CH ₃) ₃
IX, XXXI	H	CH ₃	CH ₃	C(CH ₃) ₃	C(CH ₃) ₃
X, XXXII	OH	H	H	OCH ₃	OCH ₃
XI, XXXIII	OH	H	CH ₃	OCH ₃	OCH ₃
XII, XXXIV	OH	CH ₃	CH ₃	OCH ₃	OCH ₃
XIII, XXXV	Br	H	H	Br	Br
XIV, XXXVI	OH	H	CH ₃	Br	Br
XV, XXXVII	OH	CH ₃	CH ₃	Br	Br
XVI, XXXVIII	OH	H	H	Br	OCH ₃
XVII, XXXIX	OH	H	CH ₃	Br	OCH ₃
XVIII, XL	OH	CH ₃	CH ₃	Br	OCH ₃
XIX, XLI	OH	H	H	H	OCH ₃
XX, XLII	OH	H	CH ₃	H	OCH ₃
XXI, XLIII	OH	CH ₃	CH ₃	H	OCH ₃
XXII, XLIV	Br	H	CHBrCH ₃	Br	OCH ₃

mental member of this group of substances this maximum lies at 282 nm (35400 cm^{-1}), which is in excellent agreement with the HMO calculation (35300 cm^{-1}) for the lowest $\pi\text{-}\pi^*$ transition⁶. On comparison of the spectra of 4-methylene, 4-ethylidene and 4-isopropylidene-2,5-cyclohexadienones with the spectra of the same compounds substituted in the positions 2 or 6, by methyl, tert-butyl, methoxy or bromine groups we found that any substitution carried out in the fundamental quinonemethide skeleton causes a shift of the absorption maximum to higher wave-lengths (Table I). The magnitude of this shift is dependent on the type, the position and the number of substituents (Table II). The relationship between the absolute value of the shift and the number of substituents is additive, so that the position of the absorption maximum of 4-alkylidene-2,5-cyclohexadienones may be easily computed. The accuracy of this calculation is $\pm 2\text{ nm}$.

A red shift is also observed in absorption maxima of substituted quinones. The magnitude of this shift is not linearly dependent on the number of identical substituents, but it may be derived using the perturbation theory⁷. We have not found an analogous relationship for quinonemethides as yet. Woodward's⁸ empirical rules were found equally unsuitable for the calculation of the position of the absorption



maxima of $\pi\text{-}\pi^*$ transitions in quinonemethides. A calculation, carried out on their basis, was thus so speculative that the agreement between the measured and the calculated value for the basic skeleton may be considered rather as accidental.

The utility of an independent calculation of the absorption maximum of 4-alkylidene-2,5-cyclohexadienones may be demonstrated on the following examples. During the oxidation of 2-methoxy-4-propylphenol (*XLV*) with silver oxide we obtained a yellow solution the absorption maximum of which was at 325 nm (an asymmetrical peak). After addition of methanol we isolated methoxy derivatives *XLVI* and *XLVII* from the reaction mixture derived from quinonemethides *XLVIII* and

TABLE I
Absorption Maxima (λ_{max} , nm) of Quinonemethides *XXIII*–*XLIV*

Compound	Found	Calculated	Compound	Found	Calculated
<i>XXIII</i>	282	282	<i>XXXIV</i>	345	348
<i>XXIV</i>	300	300	<i>XXXV</i>	306	306
<i>XXV</i>	318	318	<i>XXXVI</i>	323	324
<i>XXVI</i>	290	290	<i>XXXVII</i>	342	344
<i>XXVII</i>	303	308	<i>XXXVIII</i>	308	309
<i>XXVIII</i>	326	326	<i>XXXIX</i>	325	327
<i>XXIX</i>	291	290	<i>XL</i>	345	345
<i>XXX</i>	305	308	<i>XLI</i>	292	297
<i>XXXI</i>	326	326	<i>XLII</i>	313	315
<i>XXXII</i>	317	312	<i>XLIII</i>	334	333
<i>XXXIII</i>	330	330	<i>XLIV</i>	330	327

TABLE II
Increments for the Calculation of λ_{max} of the $\pi\text{-}\pi^*$ Transition for 2- or 2,6-Substituted 4-Alkylidene-2,5-cyclohexadienones

Substituent	Position	$\Delta\nu$, nm ^a	Substituent	Position	$\Delta\nu$, nm ^a
CH ₃ —	2 (6)	4	CH ₃ CH ₂ CH=	4	18
t-C ₄ H ₉ —	2 (6)	4	(CH ₃) ₂ C=	4	36
Br—	2 (6)	12	CH ₃ OCH=	4	40 ^b
CH ₃ O—	2 (6)	15	(CH ₃) ₂ NCH=	4	95 ^b
CH ₃ CH=	4	18	NCCH=	4	28 ^b

^a $\lambda_{\text{max}} = 282 + \sum \Delta\nu$; ^b the increments were calculated on the basis of literature data¹⁹.

XLIX. The observed absorption curve was evidently formed by superposition of the maxima of both components. Similarly, on oxidation of bromophenol *L* no product was formed which would absorb at the expected wave-length (325 nm), but its maximum was shifted to shorter wave-lengths (309 nm). The structure of this intermediate follows from the analysis of the NMR spectrum of methoxy derivative *LII* formed from the *spiro* compound *LI* on reaction with methanol.

EXPERIMENTAL

The melting points are uncorrected and they were measured on a Koffler block. Samples for analysis were dried at 0.01 Torr for 8 hours. The purity of the substances and the reaction course was followed by thin-layer chromatography on silica gel. The ultraviolet spectra were measured in dichloromethane, the NMR spectra at 80 MHz in deuteriochloroform using tetramethylsilane as internal standard. The chemical shifts are expressed in δ -units and the coupling constants in Hz.

Preparation of Alcohols *I—VII*, *X—XII* and *XIV—XXI*

4-Hydroxybenzyl alcohols substituted in positions 2 and 2,6 were prepared in 80–90% yields from corresponding 4-hydroxybenzaldehydes by reduction⁹ with sodium borohydride in 2M-NaOH. Analogously substituted 1-(4-hydroxyphenyl)-1-ethanols or 2-(4-hydroxyphenyl)-2-propanols were prepared in 75–80% yields on reaction with methylmagnesium iodide¹⁰ with corresponding 4-hydroxybenzaldehydes or methyl esters of 4-hydroxybenzoic acids. 4-Hydroxybenzyl alcohol (*I*), m.p. 121–123°C (benzene), lit.¹¹ m.p. 124.5–125.5°C. 1-(4-Hydroxyphenyl)-1-ethanol (*II*), m.p. 135–136°C (ether–light petroleum), lit.¹² m.p. 137–138°C. 2-(4-Hydroxyphenyl)-2-propanol (*III*), m.p. 105–107°C (benzene). For C₉H₁₂O₂ (152.2) calculated: 71.03% C, 7.95% H; found: 71.04% C, 8.00% H. 4-Hydroxy-3,5-dimethylbenzyl alcohol (*IV*), m.p. 104–105°C (benzene), lit.¹³ m.p. 104.5–105°C. 1-(4-Hydroxy-3,5-dimethylphenyl)-1-ethanol (*V*), m.p. 94–96°C (benzene–light petroleum). For C₁₀H₁₄O₂ (166.2) calculated: 72.26% C, 8.49% H; found: 72.31% C, 8.52% H. 2-(4-Hydroxy-3,5-dimethyl)-2-propanol (*VI*), identified as dibenzoate of m.p. 113–115°C (ether–light petroleum). For C₂₅H₂₄O₄ (388.5) calculated: 77.30% C, 6.23% H; found: 77.32% C, 6.21% H. 4-Hydroxy-3,5-ditert-butylbenzyl alcohol (*VII*), m.p. 139–140°C (benzene), lit.¹⁴ m.p. 139–140°C. 4-Hydroxy-3,5-dimethoxybenzyl alcohol (*X*), m.p. 127–132°C (ethyl acetate), lit.¹⁵ m.p. 131–132°C. 1-(4-Hydroxy-3,5-dimethoxyphenyl)-1-ethanol (*XI*), m.p. 91–93°C (benzene). For C₁₀H₁₄O₄ (198.2) calculated: 60.59% C, 7.12% H; found: 60.62% C, 7.09% H. 2-(4-Hydroxy-3,5-dimethoxyphenyl)-2-propanol (*XII*), m.p. 105–107°C (benzene–light petroleum). For C₁₁H₁₆O₄ (212.2) calculated: 62.25% C, 7.60% H; found: 62.10% C, 7.60% H. 1-(3,5-Dibromo-4-hydroxyphenyl)-1-ethanol (*XIV*), m.p. 150–152°C (benzene). For C₈H₈Br₂O₂ (296.0) calculated: 32.62% C, 2.71% H; found: 32.46% C, 2.72% H. 2-(3,5-Dibromo-4-hydroxyphenyl)-2-propanol (*XV*), m.p. 163–166°C (benzene). For C₉H₁₀Br₂O₂ (310.0) calculated: 34.87% C, 3.20% H; found: 35.00% C, 3.41% H. 3-Bromo-4-hydroxy-5-methoxybenzyl alcohol (*XVI*), m.p. 132–133°C (ethanol–water), lit.⁹ m.p. 132–133°C. 1-(3-Bromo-4-hydroxy-5-methoxyphenyl)-1-ethanol (*XVII*), m.p. 144–146°C (benzene). For C₉H₁₁BrO₃ (247.1) calculated: 43.75% C, 4.49% H, 32.34% Br; found: 43.94% C, 4.42% H, 32.46% Br. 2-(3-Bromo-4-hydroxy-5-methoxyphenyl)-2-propanol (*XVIII*), m.p. 134–136°C (benzene). For C₁₀H₁₆BrO₃ (261.1) calculated: 46.00% C, 5.02% H, 30.60% Br; found: 46.29% C, 4.88% H, 30.55% Br. 4-Hydroxy-3-methoxybenzyl alcohol (*XIX*) m.p. 113–115°C (benzene), lit.¹⁶ m.p. 113°C. 1-(4-Hydroxy-3-methoxyphenyl)-1-ethanol (*XX*), m.p. 100–102°C (benzene), lit.¹⁰ m.p. 100 to 102°C. 2-(4-Hydroxy-3-methoxyphenyl)-2-propanol (*XXI*), m.p. 89–91°C (ether–light petroleum). For C₁₀H₁₄O₃ (182.2) calculated: 65.91% C, 7.74% H; found: 66.16% C, 7.61% H.

Preparation of Chlorides

Anhydrous magnesium sulfate (0.80 g) was added to a solution of alcohol (1 mmol) in dichloromethane (50 ml) and dry hydrogen chloride was passed into the mixture cooled at -80°C under stirring for 3–5 minutes. The drying agent was filtered off and washed with dichloromethane (3 · 20 ml). The solution was concentrated on a rotatory evaporator to about 20 ml and made up to 50 ml with dichloromethane.

Preparation of Bromides *XIII* and *XXII*

3,5-Dibromo-4-hydroxybenzyl bromide (*XIII*) was prepared by bromination of 4-hydroxybenzyl alcohol in acetic acid in a 75% yield, m.p. $150-151^{\circ}\text{C}$ (benzene), lit.¹¹ m.p. $149-150^{\circ}\text{C}$. 2-Bromo-4-(1,2-dibromo-1-propyl)-6-methoxyphenol (*XXII*) was prepared from 1-(4-hydroxy-3-methoxyphenyl)-1-propane on bromination in ether in a 61% yield, m.p. $137-140^{\circ}\text{C}$, lit.¹⁷ m.p. 138°C .

Preparation of Quinonemethides *XXIII-XXIV*

A. A solution of crude chloride or bromide ($2 \cdot 10^{-2}\text{M}$, 5 ml) was shaken with anhydrous potassium carbonate (1 g) for 5 minutes. The solid phase was filtered off, washed with dichloromethane (2 · 2 ml) and the combined filtrates were diluted to 10 ml. For spectral measurement this stock solution was diluted 50 times. By this procedure quinonemethides *XXIII*, *XXVI*, *XXIX*, *XXXII*, *XXXV*, *XXXVIII*, *XLI*, and *XLIV* were prepared.

B. Freshly distilled triethylamine (0.015 ml) was added to a solution of crude chloride ($2 \cdot 10^{-2}\text{M}$, 5 ml) and the solution so prepared was diluted one hundred times for spectral measurements. By this procedure the following quinonemethides were prepared: *XXIV*, *XXV*, *XXVII*, *XXVIII*, *XXXIII*, *XXXIV*, *XXXVI*, *XXXVII*, *XXXIX*, *XL*, *XLII* and *XLIII*.

C. On oxidation of 4-alkylphenols *VIII* and *IX* with potassium ferricyanide in potassium hydroxide⁴ the quinonemethide *XXX*, m.p. $90-91^{\circ}\text{C}$, lit.¹⁸ m.p. 91°C , and *XXXI*, m.p. 103 to 105°C , lit.⁴ m.p. $101-103^{\circ}\text{C}$ were obtained.

Oxidation of 2-Methoxy-4-propylphenol (*XLV*)

A solution of 2-methoxy-4-propylphenol (40 mg) in dichloromethane (10 ml) was stirred under nitrogen and at room temperature for 1 hour with silver oxide (100 mg). In the UV region the reaction mixture had an absorption maximum at 325 nm (indistinct inflexion about 310 nm). After filtration off of the oxidant the filtrate was added with methanol (2 ml). After 12 hours' standing at room temperature the solvent was distilled off and the residue chromatographed on silica gel. Elution gave the following compounds: 1-(4-hydroxy-3-methoxyphenyl)-1-methoxypropane (*XLVI*) (20 mg), identified by NMR spectrum: 0.825 (t, $J = 7$, 3 H, CH_3), 1.705 (bm, $J = 7 + 6$, 2 H, CH_2), 3.18 (s, 3 H, alif. OCH_3), 3.83 (s, 3 H, arom. OCH_3), 3.915 (t, $J = 6 + 6$, 1 H, CHO), 5.65 (bs, 1 H, OH), 6.815 (cm, 3 H, arom. H). 2-Hydroxy-2',3'-dimethoxy-4'-propyl-4-(1-methoxypropyl)diphenyl ether (*XLVII*) (12 mg), identified by NMR spectrum: 0.79 (t, $J = 7$, CH_3), 0.925 (t, $J = 7$, CH_3), 1.635 (bm, $2 \times \text{CH}_2$), 2.55 (t, CH_2), 3.15 (s, alif. OCH_3), 3.84 (s, arom. OCH_3), 3.85 (m, CHO), 3.89 (s, arom. OCH_3), 6.015 (bs, OH), 6.475 + 6.60 d + d, $J = 1.7$, arom. H), 6.82 (cm, arom. H).

Oxidation of 2-Bromo-4-(2-bromo-1-propyl)-6-methoxyphenol (*L*)

Using the procedure described in the preceding section phenol *L* (20 mg) gave a solution of spirocyclohexadienone *LI* (λ_{max} 309 nm) which after reaction with methanol afforded phenol

LII (14 mg). The structure of the product was confirmed by NMR spectra: 1·10 + 1·215 (d + d, $J = 6\cdot5$, 3 H, CH₃), 2·64 (cm, 2 H, CH₂), 3·30 (s, 3 H, alif. OCH₃), 3·43 (m, 1 H, CHO), 3·87 (s, 3 H, arom. OCH₃), 5·80 (bs, 1 H, OH), 6·65 + 6·92 (d + d, $J = 2$, 2 H, arom. H).

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