

AMBIDENT REACTIVITY OF PROTONATED FUCHSONES*

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The reaction of *p*-benzofuchson (II), *p*-naphthofuchson (III), and *p*-anthrafuchson (IV) with primary and secondary alcohols in acidic media affords products of 1,6- and 1,2-addition and substituted triarylmethanes. The initial stage of the reaction is the formation of protonated species, the stability and charge distribution of which determines the ratio of the 1,6- and 1,2-addition products. The analysis of products is in agreement with quantum chemical calculations on the basis of HMO. Yields of triarylmethanes produced from carbocations by an intermolecular hydride transfer depend on the starting alcohol and decrease in the order 2-propanol > ethanol > methanol.

It may be inferred from several investigations^{1,2} that *p*-quinone methides *I* exhibit two highly reactive centers. The carbonyl oxygen atom is basic enough for reactions with electrophiles while the electron-deficient exocyclic carbon atom may be readily attacked by nucleophilic reagents. As indicated by analysis of calculated electron densities in the basic *p*-quinone methide skeleton (Fig. 1), the exocyclic carbon atom is not the only electron-deficient site; the molecule of *p*-quinone methide (*I*) may be

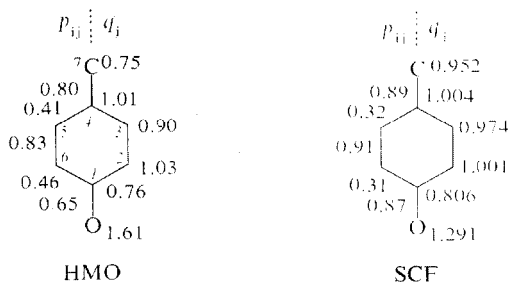
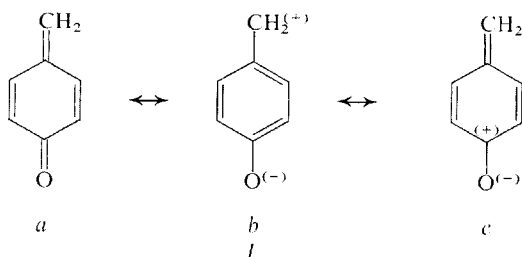


FIG. 1

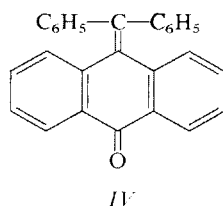
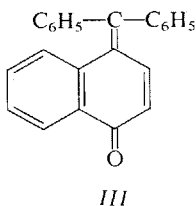
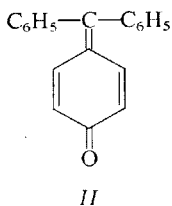
HMO and SCF Molecular Diagrams of *p*-Quinone Methide (*I*)

* Part XII in the series Quinone Methides and Fuchsones; Part XI: Syn. Commun. 6, 305 (1976).

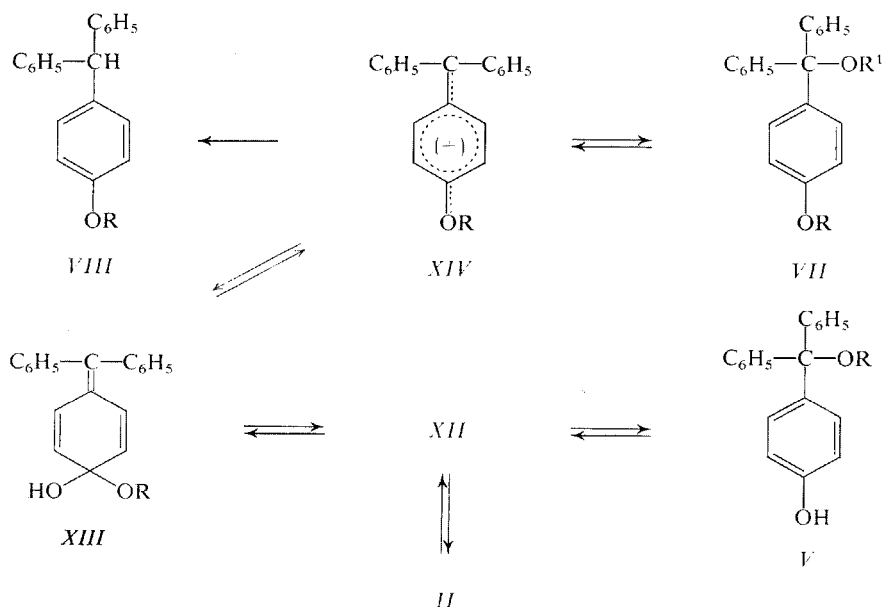
illustrated by mesomeric formulae *Ia–Ic*. Noteworthy, almost identical results were obtained in the independent electron approximation by means of the HMO method³ as well as by the manyelectron method in the SCF PPP approximation⁴. The HMO-calculated electron densities are lowest on $C_{(7)}$ and $C_{(1)}$ centres (position 7 being slightly preferred) whereas the analogous SCF quantity is lowest on the $C_{(1)}$ centre. The much lower differences between the SCF electron densities when compared with the HMO data are generally due to the properties of this method as a self-consistent procedure. It may be thus expected that *p*-quinone methides can add the nucleophiles by both 1,6- and 1,2-mechanism. However, the 1,2-additions have been reported only in reactions of some fuchsones with organometallic agents^{5–9} and bisulfite¹⁰. As it might be predicted on the basis of a few reported data, the regio-specificity of additions to the conjugated system of *p*-quinone methides will be controlled both by the methide structure and the character of the attacking reagent. The solvent effects should also be of some importance.



In order to determine scope and limitations of the occurrence of 1,2-additions in the case of *p*-quinone methide skeletons, the reactivity of fuchsones *II–IV* towards primary alcohols (methanol and ethanol) was examined under conditions of an acidic catalysis. The following points were born in mind. 1) The ambident character of *p*-quinone methides (and also fuchsones) resulting from the competition of the $C_{(1)}$ and $C_{(7)}$ electrophilic centres in the initial stage is retained after protonation. 2) Substitution of the methide carbon atom by two phenyl groups guarantees the stability of both the starting compounds and the protonated species. 3) Annulation of one or two aromatic rings in the naphtofuchsones (*III*) and anthrafuchsones (*IV*) affects the ratio of 1,6- and 1,2-addition.



Contrary to *p*-quinone methides, the addition of primary alcohols to *p*-benzofuchsones (*II*) requires the presence of a catalytic amount of hydrogen chloride or *p*-toluenesulfonic acid. As the reaction product, the 4-hydroxybenzyl ether *V* is obtained in an almost quantitative yield. If the reaction is conducted at the boiling point of the alcohol, the composition of reaction mixture depends on the reaction time. When the reaction was stopped immediately after the disappearance of benzofuchsones, the 4-alkoxytriarylmethane *VI* and the diether *VII* were also present in addition to the 4-hydroxybenzyl ether *V*. The carbinol *VI* is formed in a small amount during the work-up of the reaction mixture. The prolonged time of heating results in disappearance of ether *V* and then the diether *VII* and a simultaneous appearance of a new compound, namely, the 4-alkoxyphenyldiphenylmethane *VIII* which remains as the only reaction product after a sufficiently long refluxing time. The same results may be obtained under analogous conditions when the primary alcohol is allowed to react with ethers *V* or *VI*, or, with the diether *VII*. The cation *XII* is undoubtedly the key intermediate of reactions affording the above products (Scheme 1). Its existence is supported by an additional markedly bathochromically shifted maximum (465 nm) appearing in the alcoholic solution of the benzofuchsones *II*



SCHEME 1

In formulae *V*, *VI* and *VIII*: *a* R = CH₃; *b* R = C₂H₅.

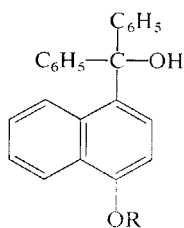
In *VII*: *a* R = R¹ = CH₃; *b* R = R¹ = C₂H₅; *c* R = CH₃, R¹ = C₂H₅.

In *VIII*: *c* R = *i*-C₃H₇.

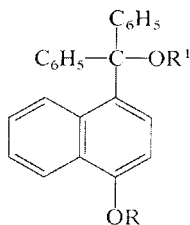
(358 nm) after the addition of *p*-toluenesulfonic acid. Addition of the alcohol to this carbonium ion affords in a kinetically controlled step the 4-hydroxybenzyl ether *V* which is transformed into the thermodynamically more stable diether *VII* by a series of equilibrium reactions *via* the intermediates *XIII* and *XIV*. The formation of the 4-alkoxytriarylmethane *VIII* is the only irreversible reaction. Participation of the carbonium ion *XIV* on the formation of the diether *VII* and the reduction product *VIII* was established spectrophotometrically in a separate reaction. The dimethyl ether *VIIa* in an ethanolic solution of *p*-toluenesulfonic acid exhibited a maximum at 477 nm (reported¹¹, 476 nm), the extinction of which decreased with increasing time. By chromatography, the triarylmethane *VIIIa* and ethyl methyl ether *VIIIc* were isolated from this reaction.

It has been observed in reductions of benzofuchson (II) with alcohols that the rate of the hydride transfer from the alcohol to the carbonium ion *XIV* increases in the order methanol < ethanol < 2-propanol; the rate is thus more likely dependent of the alcohol basicity than of the steric requirements of O-substituents¹². Reduction of the protonated fuchson *XII* has not been observed in any case. The difference in reactivities of both ions towards the hydride anion might be ascribed to the higher thermodynamic stability of the ion *XII* (by extrapolation from the dependence of σ^+ on ΔF^0 , this difference may be estimated as 1–2 kcal mol⁻¹).

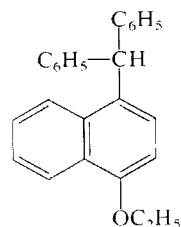
Neither naphthofuchson (*III*) nor anthrafuchson (*IV*) react with alcohols and hydrogen chloride (or *p*-toluenesulfonic acid) at room temperature. A prolonged heating is required to obtain the ether *IX*, the diethers *Xa*, *Xb* and the triarylmethane *XI* from the naphthofuchson (*II*). Anthrafuchson (*IV*) does not undergo the reaction even under these conditions. To our opinion, the differences in reactivities of fuchsons *II–IV* are due to the increasing basicity of the carbonyl oxygen atom in the order *IV* < *III* < *II*. This explanation is supported by the values of stretching vibrations of the carbonyl group that increase in the same sequence (1620, 1635, and 1662 cm⁻¹) and the values of bond orders for the same group (Table I).



IXa: R = CH₃
IXb: R = C₂H₅



Xa: R = R¹ = CH₃
Xb: R = R¹ = C₂H₅
Xc: R = H, R¹ = CH₃



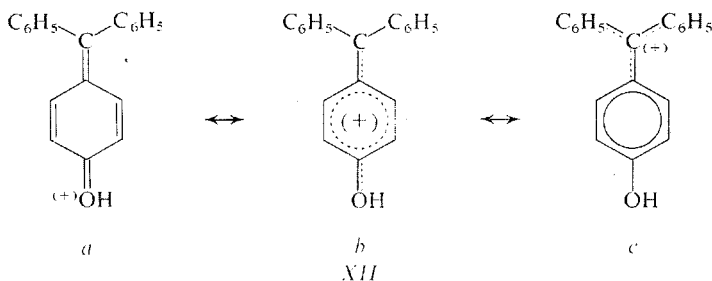
XI

TABLE I
Quantum-Chemical Indices of Compounds *II–IV* and the Corresponding Protonated Forms *XII, XV, and XVI*

Model ^a	Q (a.u.)			S_n (β^{-1})			S_e (β^{-1})			$P_{C=O}$ (a.u.)
	O	C ₍₁₎	C ₍₇₎	O	C ₍₁₎	C ₍₇₎	O	C ₍₁₎	C ₍₇₎	
<i>II</i>	-0.645	0.208	0.184	1.530	2.495	4.174	1.530	0.495	0.588	0.611
<i>III</i>	-0.611	0.241	0.129	1.420	2.459	2.872	1.420	0.458	0.718	0.650
<i>IV</i>	-0.580	0.274	0.074	1.307	2.414	1.945	1.307	0.414	0.861	0.687
<i>XIIa</i>	0.071	0.218	0.262	0.800	8.451	14.433	0.800	0.637	0.425	0.287
<i>XVa</i>	0.079	0.276	0.203	0.790	8.410	8.952	0.790	0.595	0.538	0.310
<i>XVIa</i>	0.089	0.348	0.130	0.774	8.326	4.943	0.774	0.511	0.705	0.337

^a HMO parameters: $h_C = 0$, $h_{C+\delta} = 0$, $h_{O^+} = 2.5$, $h_{O^+\delta} = 1.8$, $h_{O^+}^* = 2.0$, $k_{C=O} = 1.0$, $k_{C=C} = 1.1$, $k_{C-C} = 0.9$, $k_{C=C} = 1.0$, $k_{C-O^+} = k_{C-O^+} = 0.8$ (in β units).

As shown by product analysis of the acid-catalysed reaction of methanol with compounds *II* and *III*, the molar ratio of products was *Va* : *VIIa* : *VIIIa* = 1 : 2 : 13 in the case of benzofuchsones (*II*) and *Xc* : *IXa* : *Xa* = 0 : 1 : 8 in the case of naphthofuchsones (*III*). The greater occurrence of the 1,2-addition in the case of the naphtho derivative *III* is in agreement with calculated data of nucleophilic superdelocalisabilities S_n on C₍₁₎ and C₍₇₎ centres (Table I).



The protonation of fuchsones *II–IV* increases their affinity towards nucleophiles and simultaneously increases the differences between reactivities of the skeletons under investigation. The positive charge on the carbonyl oxygen atom formed by protonation in the first stage may be assumed as distributed to a high extent over the whole skeleton. This assumption is reflected by our parametrisation of HMO

models that would be most likely in accordance with the canonic structures *XIIa* to *XIIc*. The model with parameters commonly used for the positively charged oxygen atom of the carbonyl group would be in the best correspondence with the canonic structure *XIIa*. Models analogous to structures *XIIa*–*XIIc* derived from benzofuchson were also taken into consideration in the case of protonated forms of naphthofuchson (*XVa*–*XVc*) and anthrafuchson (*XVIa*–*XVIc*).

It may be concluded from the computed results that the reactivity order of compounds *II*–*IV* and their protonated forms is the same (Fig. 2). Structure *XII* is most readily attacked by nucleophiles on the $C_{(7)}$ methide carbon atom while in the case of the protonated naphthofuchson (*XV*) the $C_{(1)}$ centre must also be taken into consideration. In the case of the protonated form of anthrafuchson (*XVI*), a reactivity reversal may be observed, the carbon atom of the carbonyl group being now the most reactive centre. Noteworthy, the reactivity proportions remain almost the same also in the case of structures *c* (i.e., with models representing cations of the triphenylmethane type) as it may be seen from data of nucleophilic superdelocalisabilities: *XIIc* S_n^7 25.4, S_n^1 12.3; *XVc* S_n^7 14.5, S_n^1 6.9; *XVIc* S_n^7 6.9, S_n^1 6.84 (in β units).

As shown by comparison of reactivity indices of compounds *II* and *IV*, the reactivity of anthrafuchson (*IV*) is very low. Furthermore, the steric hindrance must be

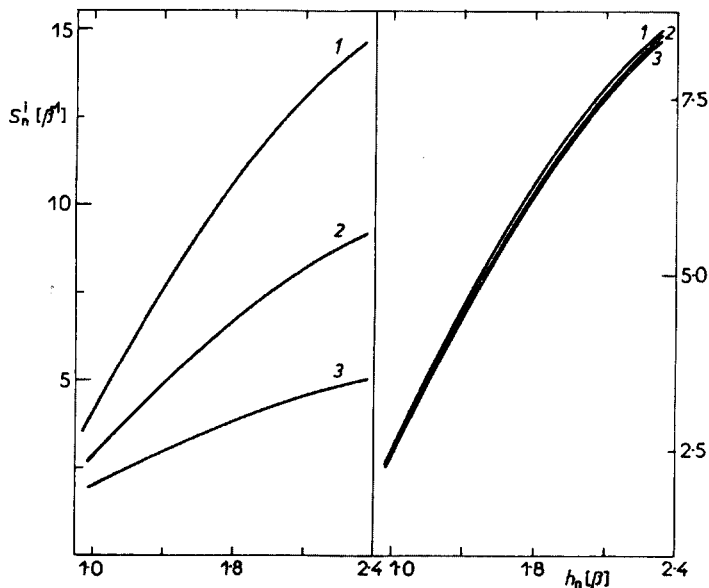


FIG. 2

Dependence of Nucleophilic Superdelocalisabilities S_n at Positions 7 and 1 on the Values of the Carbonyl Oxygen Coulomb Integral

1 *p*-Benzofuchson (*II*), 2 *p*-naphthofuchson (*III*), 3 *p*-anthrafuchson (*IV*).

taken into account though it cannot be reflected by the present level of approximation. The observed relative stability of the skeleton *IV* does not therefore surprise.

In connection with future investigations on reactions of fuchsones, we intend to examine the reactivity of these systems on the level of a general perturbation theory and semiempirical methods taking into account all valence electrons (EHT and CNDO/2) with the aim to elucidate the contradictory conclusions arising from comparison of the static reactivity index $Q_{(1)}$ and the analogous dynamic quantity S_n^1 of fuchsones *II* and *III*.

EXPERIMENTAL

Melting points (uncorrected) were taken on a heated microscope stage (Kofler block). Analytical samples were dried at room temperature and under 0.01 Torr for 8 h. The purity of substances was checked by thin-layer chromatography on silica gel. Mass spectra were measured on an A.E.I. HS 902 apparatus. The IR spectra were recorded on a UR-20 (Carl Zeiss, Jena) apparatus.

Preparation of fuchsones II–IV. Benzofuchson (II), m.p. 166–168°C (benzene–ether) (reported¹³, m.p. 167–169°C) was prepared from 4-hydroxytriphenylmethanol by the usual procedure¹⁴. Naphthofuchson (III), m.p. 182°C (acetone) (reported¹⁵, m.p. 179°C) and anthrafuchson (IV), m.p. 204°C (acetone) (reported¹⁶, m.p. 208°C) were prepared by reaction of phenyldichloromethane with α -naphthol¹⁵ and anthrone¹⁷, respectively.

Acid-Catalysed Reaction of Benzofuchson (II) with Alcohols

A. A solution of benzofuchson (II; 150 mg) in alcohol (anhydrous methanol or anhydrous ethanol, 30 ml each) and a catalytic amount of *p*-toluenesulfonic acid or gaseous hydrogen chloride was stirred at room temperature until the colour disappeared and then neutralised with saturated aqueous sodium hydrogen carbonate. The alcohol was evaporated under diminished pressure and the residue extracted with two 30 ml portions of dichloromethane. The extract was processed as usual to afford the ethers *V*. Methyl (4-hydroxyphenyl)diphenylmethyl ether (*Va*), yield 140 mg, m.p. 105–107°C (benzene–light petroleum). For $C_{20}H_{18}O_2$ (290.3) calculated: 82.73% C, 6.25% H, found: 82.95% C, 6.28% H. Mass spectrum: M^+ 290. Ethyl (4-hydroxyphenyl)diphenylmethyl ether (*Vb*), yield 130 mg, oil. For $C_{21}H_{20}O_2$ (304.4) calculated: 82.87% C, 6.62% H; found: 82.53% C, 6.71% H. Mass spectrum: M^+ 304.

B. The reaction mixture described in paragraph *A* was refluxed under stirring until the colour disappeared and then processed as usual. Chromatography on silica gel in 9 : 1 light petroleum–ether afforded the following substances. (4-Methoxyphenyl)diphenylmethanol (*Via*), 20 mg, m.p. 58–59°C (ether–light petroleum) (reported¹⁸, m.p. 58–61°C); identical physical constants were exhibited by product of the reaction of 4-methoxybenzophenone with phenylmagnesium bromide. Methyl (4-methoxyphenyl)diphenylmethyl ether (*VIIa*), 120 mg, m.p. 70–72°C (light petroleum) (reported¹⁹, m.p. 74°C). (4-Methoxyphenyl)diphenylmethane (*VIIIa*), 10 mg, m.p. 62°C (light petroleum) (reported¹⁹, m.p. 64–65°C). Methyl (4-hydroxyphenyl)diphenylmethyl ether (*Va*), 10 mg. (4-Ethoxyphenyl)diphenylmethanol (*Vib*), 10 mg, m.p. 54–55°C (ether–light petroleum) (reported²⁰, m.p. 54°C). Ethyl (4-ethoxyphenyl)diphenylmethyl ether (*VIIb*), 40 mg, m.p. 85–86°C (ethanol) (reported¹⁹, m.p. 87°C). (4-Ethoxyphenyl)diphenylmethane (*VIIIb*), 100 mg, m.p. 67°C (light petroleum) (reported¹⁹, m.p. 70–71°C). With the use of 2-propanol, (4-isopropoxyphenyl)diphenylmethane (*VIIIc*) was obtained as the only pro-

duct, m.p. 111–112°C (benzene–light petroleum). For $C_{22}H_{22}O$ (302.4) calculated: 87.37% C, 7.33% H; found: 87.28% C, 7.38% H. Mass spectrum: M^+ 302.

Acid-Catalysed Reaction of Naphthofuchson (III) with Alcohols

This reaction was performed under analogous reaction and isolation conditions as in the case of benzofuchson (II), procedure B. The following substances were isolated. (4-Methoxynaphthyl)diphenylmethanol (IXa), 15 mg, m.p. 157–159°C (ether–light petroleum). For $C_{24}H_{20}O_2$ (340.4) calculated: 84.68% C, 5.92% H; found: 84.32% C, 6.04% H. Identical physical constants were observed with the substance obtained by the reaction of 4-methoxynaphthyl phenyl ketone with phenylmagnesium bromide. Methyl (4-methoxynaphthyl)diphenylmethyl ether (IXa), 130 mg, m.p. 144–145°C (light petroleum). For $C_{25}H_{22}O_2$ (354.4) calculated: 84.71% C, 6.25% H; found: 84.32% C, 6.31% H. Mass spectrum: M^+ 354. (4-Ethoxynaphthyl)diphenylmethanol (IXb), 10 mg, m.p. 169–171°C (ether–light petroleum). For $C_{25}H_{22}O_2$ (354.4) calculated: 84.71% C, 6.25% H; found: 84.42% C, 6.31% H. Mass spectrum: M^+ 354. Ethyl (4-ethoxynaphthyl)diphenylmethyl ether (Xb), 120 mg, m.p. 147–149°C (light petroleum). For $C_{27}H_{26}O_2$ (382.5) calculated: 84.78% C, 6.85% H; found: 84.55% C, 6.87% H. (4-Ethoxynaphthyl)diphenylmethane (XIIb), 20 mg, m.p. 160–162°C. For $C_{25}H_{22}O$ (338.4) calculated: 88.80% C, 6.56% H; found: 88.28% C, 6.72% H. Mass spectrum: M^+ 338.

Reaction of methyl (4-methoxyphenyl)diphenylmethyl ether (VIIa) with ethanol in the presence of p-toluenesulfonic acid. The ether VIIa (100 mg) was dissolved in ethanol (20 ml) and a catalytic amount of p-toluenesulfonic acid was added. The mixture was stirred at room temperature for 2 h and processed as usual. Thin-layer chromatography in 10:1 light petroleum–ether yielded 80 mg of the oily ethyl (4-methoxyphenyl)diphenylmethyl ether (VIIc) and 10 mg of (4-methoxyphenyl)diphenylmethane (VIIIa). Compound VIIc: for $C_{22}H_{22}O_2$ (318.4) calculated: 82.99% C, 6.96% H; found: 82.78% C, 6.95% H. Mass spectrum: M^+ 318.

Elemental analyses were performed in the Analytical Department (Dr J. Horáček, Head) of this Institute. Thanks are due to Dr L. Dolejš for measurement of mass spectra.

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