Mechanism of the Gibbs Reaction. 3.[1] Indophenol Formation *via* Radical Electrophilic Aromatic Substitution ($S_{RE}Ar$) on Phenols

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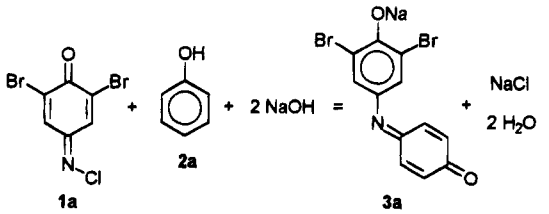
Different products are formed, depending on the *para* substituent (R) when 2,6-dichlorobenzoquinone *N*-chloroimine (**1b**) reacts with the anion of the 4-substituted phenol (**2**). If the group R can leave as a cation (i.e., R is an electrofugal leaving group) such as H, CH_2NMe_2, CH_2OH, etc., then the reaction yields indophenol (**3**), the normal Gibbs product. If the group R cannot leave as a cation such as CH_3, the final product of the reaction will be type **10**, 1,1-disubstituted 2,5-cyclohexadienone. If the group R is OH or NH_2, then the reaction gives the corresponding benzoquinone **4** or benzoquinone imine **1** and 2,6-dichlorobenzoquinone imine (**1d**). In all these cases the reaction proceeds at a 1:1 stoichiometry. If, however, the group R can leave as an anion (i.e., R is a nucleofugal leaving group) such as halogen, alkoxy, or OCH_2Ph, then the reaction proceeds at a 1:2 stoichiometry. In this case the reaction of a second mole of phenolate with type **26** intermediate yields the indophenol product **3** and the oxidized product of the phenol. If the two *ortho* positions of the phenolate are substituted then the oxidized product of the phenol will be the corresponding benzoquinone. The mechanism of the reaction has been studied by kinetic and nonkinetic (NMR) methods. It has been concluded that the first step of the mechanism is a single electron transfer (SET) from the phenolate to the benzoquinone *N*-chloroimine **1b** which is the rate-determining process in most of the cases. In some of the nucleofugal cases the final oxidation, involving the second mole of phenolate, is the rate-determining step. For the radical reaction three different alternatives are suggested: a combination of radicals in a solvent cage (direct reaction) and two different chain reactions (chain A and chain B). Quantum chemical calculations revealed that the direct reaction and the chain A mechanisms were energetically more favored than chain B. The reaction shows an extremely large *para* selectivity although the substitution does follow a radical mechanism.

Introduction

In 1927 H. D. Gibbs suggested the use of 2,6-dibromobenzoquinone *N*-chloroimine (**1a**) as a phenol assay reagent[2] (Scheme 1). According to his method, phenol (**2a**) reacts quantitatively with **1a** in alkaline solution to give the blue[3,4] anion of indophenol **3a**, the concentration of which is established by colorimetric methods.

Since then the Gibbs reaction has been generally used,[5–19] but **1a**[5–8] is replaced in most cases by the corresponding 2,6-dichloro compound **1b**.[8–15] The assay is usually positive even in the case when the phenol measured carries a substituent other than hydrogen at the *para* position, e.g., CH_2NH_2,[6] $CH_2N(CH_3)_2$,[6] CH_2OH,[17] COOH,[18] OCH_2Ph,[6] alkoxy,[6,10–12] Cl,[6,10] Br,[10] and I,[10,12] or even F.[12] It is remarkable that among these *para* substituents there are several which can be eliminated exclusively as a nucleofugal leaving group.

Scheme 1



A mechanism of this reaction was suggested by D. Svobodova et al.[8] as well as by P. D. Josephy and A. van Damme.[12] Accordingly, in an alkaline solution, **1a** or **1b** is converted into 2,6-dihalobenzoquinone imine **1c** or **1d** and hypochlorite, where the former are the active reagents being responsible for the reaction. This hypothesis seems to be rather convincing since it is well known that **1d** and its analogues give indophenol **3** with phenol if it is replaced with nucleofugal leaving groups at C-4.[20–23]

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(1) (a) Part 1: Pallagi, I.; Dvortsák, P. *J. Chem. Soc., Perkin Trans. 2* **1986**, 105–110. (b) Part 2: Pallagi, I.; Toró, A.; Müller, J. *Tetrahedron* **1994**, *50*, 8809–8814.
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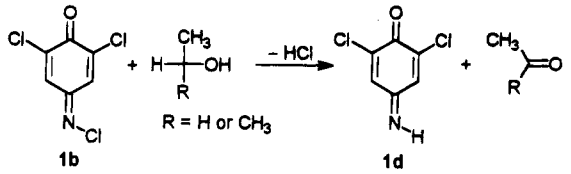
Scheme 2



In our previous paper,[1a] we showed that, in an aqueous alkaline solution **1b** is not transformed into **1d**. This conversion takes place only if an alcohol is present. It was proven that **1b** is reduced by the alcohol to **1d**, while the alcohol is oxidized simultaneously into the corresponding aldehyde or ketone (Scheme 2).

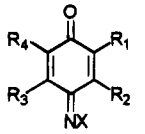
As the aforementioned authors[6,8-10,12,18,19] carried out their experiments in the presence of an alcohol, they actually studied the reaction of **1d** and not that of **1b** with varying phenols.[24] It is well known that phenols are more sensitive to oxidation than alcohols; we have supposed that the reaction of phenols with benzoquinone *N*-chloroimines (Gibbs reaction) may involve an oxidative step. Nevertheless, there are some other controversial mechanistic considerations[2,18] and a review,[25] which have prompted us to reinvestigate this reaction in detail. Especially, the stoichiometry, the kinetics, the mechanism as well as the *para* specificity were studied.

Results and Discussion

The Reaction of Phenols Carrying a Nucleofugal Leaving Group at C-4. At first the stoichiometry of the Gibbs reaction was determined by applying the method of continuous variations,[26] to compare that of phenols carrying electrofugal- and nucleofugal leaving groups at C-4. The Job plot[26] (see the supplementary material) maximum of 2,6-dimethylphenol (**2b**) is at the mole fraction of 0.5, indicating that one molecule of **1b** reacts with one molecule of phenol **2b** to yield one anion of indophenol **3b** (see Scheme 1). The anion of a similar product was formed when 2,6-dimethyl-4-chlorophenol (**2c**) was used instead of **2b**, but in this case the maximum appears at 0.67 (see the supplementary material), i.e., the stoichiometry of the reaction of **1b** and **2c** is 1:2.[27] This discrepancy urged us to investigate the role of the second molecule of **2c** in the reaction. According to spectroscopic data (UV, ^{1}H- and ^{13}C-NMR) besides **3b**, 1 equiv of 2,6-dimethylbenzoquinone (**4a**) was also formed in the latter reaction. This must originate from the second molecule of chlorophenol **2c** which undergoes oxidation and a subsequent hydrolysis to yield the corresponding quinone **4a**. 2,5-Diisopropyl-4-chlorophenol (**2d**), 2,6-diisopropyl-4-chlorophenol (**2e**), 2,6-di-*tert*-butyl-4-chlorophenol (**2f**), and 2,6-di-*tert*-butyl-4-methoxyphenol (**2g**) behaved similarly giving the corresponding quinones **4b**, **4c**, **4d**, and **4d**, respectively (Table 3). In the Gibbs reaction of **2f** with **1b**, the tertiary amine **5** (Scheme 3) was formed too.[28] When replacing Cl in **2f** to OCH_3 (**2g**), the reaction will lead to the quinol intermediate **6a** which is converted into **4d**.

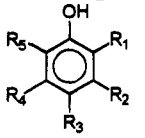
In the Gibbs reaction of 4-methoxyphenol (**2h**) and 2-*tert*-butyl-4-methoxyphenol (**2i**), the oxidation of the

Table 1. Benzoquinone Imines and *N*-Chloroimines Investigated in This Article



	R_1	R_2	X	R_3	R_4
1a	Br	H	Cl	H	Br
1b	Cl	H	Cl	H	Cl
1c	Br	H	H	H	Br
1d	Cl	H	H	H	Cl
1e	H	H	Cl	H	H
1f	*t*-Bu	H	H	H	*t*-Bu
1g	H	Cl	Cl	Cl	H
1h	Cl	H	Cl	H	H
1i	Cl	Cl	Cl	H	H
1j	Cl	Cl	Cl	H	Cl
1k	H	H	H	H	H

Table 2. Phenols Investigated in This Article



	R_1	R_2	R_3	R_4	R_5
2a	H	H	H	H	H
2b	Me	H	H	H	Me
2c	Me	H	Cl	H	Me
2d	*i*-Pr	H	Cl	*i*-Pr	H
2e	*i*-Pr	H	Cl	H	*i*-Pr
2f	*t*-Bu	H	Cl	H	*t*-Bu
2g	*t*-Bu	H	OMe	H	*t*-Bu
2h	H	H	OMe	H	H
2i	*t*-Bu	H	OMe	H	H
2j	H	H	$OCH_2C_6H_4$-4′-OMe	H	H
2k	OMe	H	$CH_2N(Me)_2$	H	OMe
2l	H	H	Me	H	H
2m	Me	H	Me	H	H
2n	*t*-Bu	H	Me	H	*t*-Bu
2o	H	Me	Me	H	H
2p	Me	H	Me	H	Me
2q	*t*-Bu	H	*t*-Bu	H	*t*-Bu
2r	H	H	*t*-Bu	H	H
2s	Me	H	*t*-Bu	H	Me
2t	H	*t*-Bu	H	*t*-Bu	H
2u	*t*-Bu	H	H	H	*t*-Bu
2v	*t*-Bu	H	NH_2	H	*t*-Bu
2w	Cl	H	H	H	Cl
2x	Cl	H	H	Cl	H
2y	H	Me	H	H	H
2z	H	Me	H	Me	H
2aa	Me	H	H	H	H
2ab	*i*-Pr	H	H	Me	H
2ac	H	H	Cl	H	H
2ad	Me	H	Cl	H	H
2ae	H	H	F	H	H
2af	*i*-Pr	H	H	H	*i*-Pr
2ag	Cl	H	Cl	Cl	H
2ah	Me	H	OMe	H	Me
2ai	H	H	OH	H	H
2aj	*t*-Bu	H	OH	H	*t*-Bu
2ak	Cl	H	NH_2	H	Cl
2al	*t*-Bu	H	*t*-Bu	H	H

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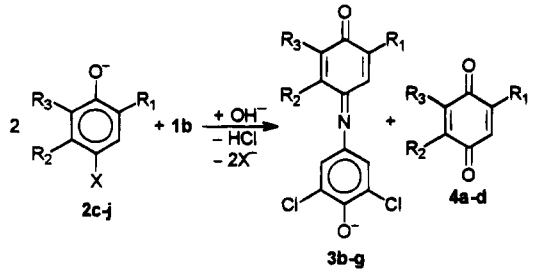
(24) We have checked that these substituents can be eliminated by benzoquinone *N*-chloroimines alone.
(25) Badaire, B.; Lacroix, J.; Lacroix, R.; Viel, C. *Bull. Soc. Pharm. Bordeaux* **1990**, *129*, 137–164.
(26) Job, P. *Ann. Chim. Ser. 10* **1928**, *9*, 113–134.
(27) These established stoichiometries exclude benzoquinone imines as intermediates in the Gibbs reaction (see ref 4, 22).
(28) The *ortho*→*ortho* cyclohexadienone rearrangement of **5**: see part 2 (see ref 1b).

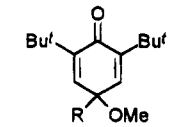
Table 3. Indophenols and Quinones Formed in the Reaction of 4-Nucleofugal Phenols 2c–j with 1b

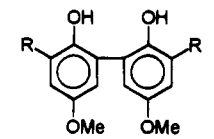


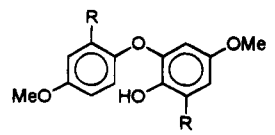
2	X	3	R_1	R_2	R_3	4
c	Cl	b	Me	H	Me	a
d	Cl	c	*i*-Pr	*i*-Pr	H	b
e	Cl	d	*i*-Pr	H	*i*-Pr	c
f	Cl	e	*t*-Bu	H	*t*-Bu	d
g	OMe	e	*t*-Bu	H	*t*-Bu	d
h	OMe	f	H	H	H	no quinone[a]
i	OMe	g	*t*-Bu	H	H	no quinone[a]
j	OCH_2Ph-4-OMe	f	H	H	H	no quinone[a]

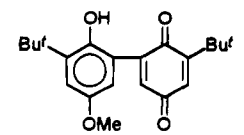
[a] See text.

second phenol molecule did not furnish benzoquinone (**4e**) and 2-*tert*-butylbenzoquinone (**4f**), respectively. In the reaction of 4-methoxyphenol (**2h**) with **1b** in a molar ratio of 2:1, besides indophenol **3f**, the dimeric product **7a** was formed.[29] The dimeric **7b**, **8a**, and **9** oxidation products were formed besides the indophenol **3g** when the compound **1b** and *ortho tert*-butyl analogue **2i** were applied in a molar ratio 2.5:1. Only **7b** and **8a** were formed, however, when this ratio was increased to 4:1.[30] In the cases of **2i**, **2g**, and hydroquinone 4-methoxybenzyl ether (**2j**), applying a 1:1 molar ratio with **1b**, beside indophenols (**3g**, **3e**, and **3f**) and the oxidation products of the phenols (**2i**, **2g**, and **2j**), a considerable amount of compounds **10a**, **10b**, and **10c**, respectively, was formed too. The rate of the formation of the compounds **10a**, **10b**, and **10c**, respectively, relative to the corresponding indophenols increased with the reactivity of their parent phenols. When compounds **10a**, **10b**, and **10c**, respectively (produced separately in solution), are reacted with their parent phenols (**2i**, **2g**, and **2j**) besides the appropriate indophenols (**3g**, **3e**, and **3f**), the formation of equivalent amount of the oxidation products (**7b**, **8a**, and **4a**, respectively) are also observed in the case of **10a** and **10b**. That means that in these cases, the slowest process in the indophenol formation is the reaction of intermediates **10a**, **10b**, and **10c**, respectively, with a second molecule of the corresponding phenol derivatives.



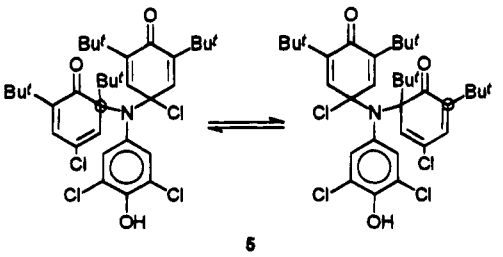


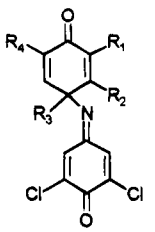




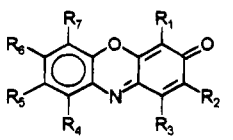
The Reaction of Phenols Carrying Electrofugal Leaving Group at C-4. It was reported that **1b** and its derivatives react also with phenols carrying an electrofugal leaving group (e.g., CH_2NH_2,[6] $CH_2N(CH_3)_2$,[6] CH_2OH,[17] COOH[17]) at C-4 instead of H. According to our results, **2b** and **2k** reacted with **1b** at a 1:1 stoichiometry (see supplementary material). Since the elimination of the leaving groups from these phenols is very fast, especially when it is a hydrogen, for obtaining some information about the mechanism, two different types of phenols were investigated. In the first case, phenols **2l–p** carrying a 4-methyl group, which is a poor leaving group, were investigated. The reactions of these phenols **2l–p** with **1b** was also fast and, although the isolation of the products were impossible due to their instability, they were stable enough to record their NMR spectra after extracting them into an organic solvent. According to ^{1}H- and ^{13}C-NMR data, the 4-methylphenols **2l–p** afforded quantitatively the 1,1-disubstituted 2,5-cyclohexadienones **10d–h**, respectively. In the second case,

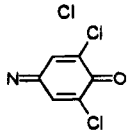
Scheme 3





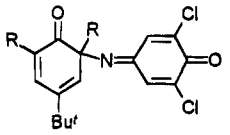
	R_1	R_2	R_3	R_4
10a	Bu^t	H	OMe	H
10b	Bu^t	H	OMe	Bu^t
10c	H	H	OCH_2-C_6H_4-4-OMe	H
10d	H	H	Me	H
10e	Me	H	Me	H
10f	Bu^t	H	Me	Bu^t
10g	H	Me	Me	H
10h	Me	H	Me	Me
10i	Bu^t	H	Bu^t	Bu^t



	R_1	R_2	R_3	R_4	R_5	R_6	R_7
11a	Cl	Cl	H	H	Bu^t	H	H
11b	Cl	Cl	H	H	H	H	H
11c	Cl	Cl	H	H	Bu^t	H	Bu^t
11d		Cl	H	H	Bu^t	H	H
11e	H	H	Cl	Bu^t	H	Bu^t	H
11f	H	H	Cl	H	Bu^t	H	Bu^t

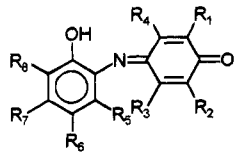
phenols **2q–s** carrying a 4-*tert*-butyl group were investigated. This substituent is also an electron-donating group like the methyl group, but can be eliminated as a *tert*-butyl cation which is stabilized as 2-methylpropene

(13). In these experiments due to the steric hindrance of the 4-*tert*-butyl group along with compounds type **10**, type **3** indophenols and *ortho*-substituted derivatives could also be isolated. Accordingly, in the reaction of 4-*tert*-butylphenol (**2r**) with **1b** besides indophenol **3f**, tricyclic compounds **11a** and **11d** were formed, too. Similarly 2,6-dimethyl-4-*tert*-butylphenol (**2s**) gave **3b** and 1,1-disubstituted 2,4-cyclohexadienone **12a**. In the



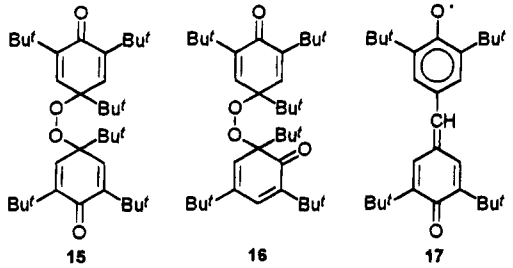
12a R = Me
12b R = Bu^t

13

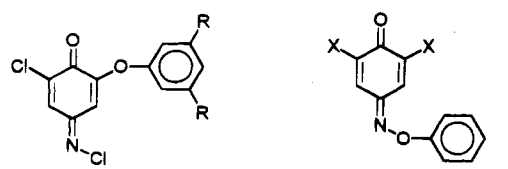


	R_1	R_2	R_3	R_4	R_5	R_6	R_7	R_8
14a	Cl	Cl	H	H	H	Bu^t	H	Bu^t
14b	H	H	Cl	Cl	Bu^t	H	Bu^t	H
14c	H	H	Cl	Cl	H	Bu^t	H	Bu^t

reaction of these phenols (**2r** and **2s**), the type **10** intermediates, leading to indophenols **3f** and **3b**, respectively, could not be observed. However, during the reaction of 2,4,6-tri-*tert*-butylphenol (**2q**), both the intermediates **10i** (*para*) and **12b** (*ortho*), respectively, were formed, and in the case of **12b** even its transformation into *o*-indophenol **14a** and then cyclization into **11c** could be detected by ^{1}H-NMR in 1,1,2,2-tetrachloroethane-d_2 (TCE). Attempts to isolate **14a** failed, since during preparative thin layer chromatography (prep TLC), **14a** cyclized into the tricyclic **11c**. In the Gibbs reaction of phenol **2q**, peroxides **15** and **16** were also formed due to trapping of the 2,4,6-tri-*tert*-butylphenoxy radical[31] by an oxygen molecule.[32] Formation of peroxides **15** and **16** raises the question whether the homolytic reaction occurs only in the case of **2q** or the Gibbs reaction itself is homolytic in general. We found that the formation of the parent indophenol **3h** from **2a** and **1e** could be inhibited[33]



15 **16** **17**



18a R = H
18b R = Bu^t

19a X = Br
19b X = Cl

using radical scavengers such as 2,6-dichloronitrosobenzene (DCNB), 2,2,6,6-tetramethylpyperidine-*N*-oxyl (TEMPO) or galvinoxyl (**17**). The effect of these scavengers clearly demonstrates that the indophenol formation

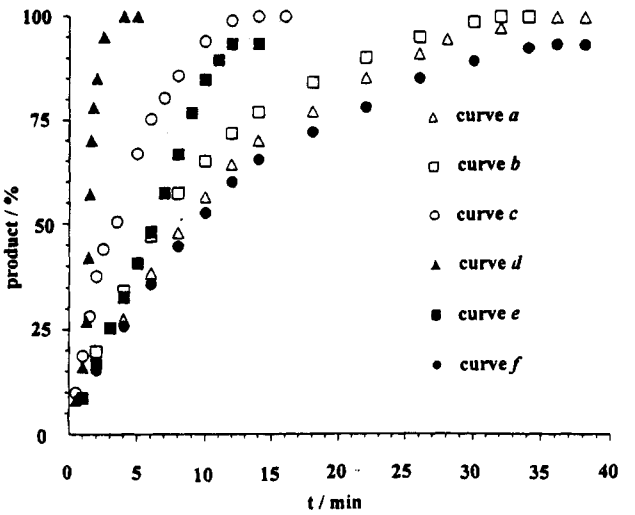


Figure 1. The acceleration effect of acetonitrile on the Gibbs reaction of **1b** with **2a** and the blocking effect of TEMPO on this acceleration, in borate buffer (pH = 9.2) at 295 K with [**1b**] = 6.14×10^{-5} mol dm^{-3} and [**2a**] = 2.98×10^{-3} mol dm^{-3}, where product vs time is plotted. (△) [MeCN] = 0.15 vol %, (□) [MeCN] = 2.65 vol %, (○) [MeCN] = 4.65 vol %, (▲) [MeCN] = 10.15 vol %, (■) [MeCN] = 10.15 vol % and [TEMPO] = 1.23×10^{-5} mol dm^{-3}, (●) [MeCN] = 10.15 vol % and [TEMPO] = 3.68×10^{-5} mol dm^{-3} or 2.45×10^{-4} mol dm^{-3}.

from **2a** and **1e** is a radical reaction, and a consecutive ionic mechanism can be excluded.[34] Furthermore, although radicals could not be detected by ESR study, the fast consumption of the added radical scavenger TEMPO indicated indirectly a radical reaction. Interestingly, the kinetics of the Gibbs reaction of **2a** and **1b** were not affected by scavengers. However, the addition of some acetonitrile to the solvent had a dramatic effect on this reaction.[35] In Figure 1 the dependence of the product vs time curve with increasing acetonitrile concentration is depicted (curves a–d). Even 10% of acetonitrile[36] changed the second-order curve to an *S*-shaped one with a considerable acceleration (curve d). Even more interesting is that the effect of acetonitrile could be blocked by TEMPO (curves e, f), and applying more than 0.6 **1b** equiv of TEMPO, curve a could be recovered.[37] These results suggest that the Gibbs reaction of **2a** and **1e** is a radical chain reaction since it can be inhibited by scavengers, but that of **2a** and **1b** is not. Furthermore, in the presence of acetonitrile, a radical direct and a

(29) This indophenol is a 2:1 mixture of the two tautomers **3fa** and **3fb** in chloroform-*d*.

(30) Further oxidation of the dimer **7b** indicates that when there is not sufficient phenol to be oxidized, the dimers take part in the reaction. Indeed, applying an excess of **1b** (1:4), several unidentified polymers formed, rather than the dimers as phenol oxidation products. In those reactions, when the oxidation of the phenol afforded the corresponding quinone, this latter always formed, independently whether the phenol, or **1b** was in excess.

(31) Cook, C. D.; Woodworth, R. C. *J. Am. Chem. Soc.* **1953**, *75*, 6242–6244.

(32) When the reaction is carried out under argon atmosphere, only **10i** and **12b** formed.

(33) The indophenol formation could be prevented with DCNB and TEMPO, but could not with galvinoxyl, because of its low solubility to reach this stage.

(34) Zhang, X.-M.; Yang, D.-L.; Liu, Y.-C. *J. Org. Chem.* **1993**, *58*, 224–227.

(35) Moderate acceleration has been also observed in the presence of 10% of DMSO or *tert*-butyl alcohol, but their effect could not be offset by TEMPO (the second-order kinetic remained in these solvents).

(36) Propionitrile has the same effect.

(37) In the presence of 10% of acetonitrile 30% hyperchromic effect was observed on the UV spectra of indophenol **3f**. DMSO and *tert*-butyl alcohol did not show this effect.

Table 4. Effect of Metal Ions on the Kinetics of the Gibbs Reaction of 2a with 1b[a]

metal ion	concentration × 10^{-5} mol dm^{-3}	$t_{1/2}$, s
	2.45	50
Mn^{2+}	6.13	40
	12.10	38
	30.70	110
Ag^{+}	61.30	95
	92.00	95
Cu^{2+}	6.13	200
	24.60	200
none		480

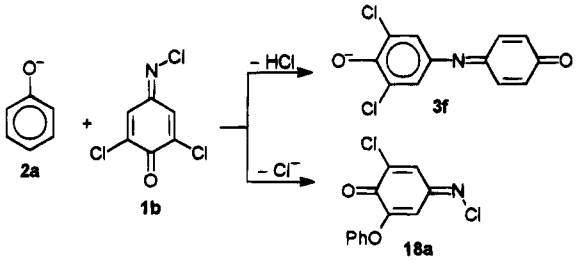
[a] **1b** (6.13×10^{-5} mol dm^{-3}) and **2a** (2.93×10^{-3} mol dm^{-3}) in borate buffer (pH = 9.2) at 22 °C.

radical chain reaction proceeds simultaneously, since the radicals, having escaped from the reaction cage by the assistance of acetonitrile, could start a parallel chain reaction,[38] the chain carriers of which could be scavenged again.

Similarly to acetonitrile, Mn^{2+} had the same dramatic effect which could be blocked by TEMPO. Ag^{+} and Cu^{2+} showed similar but less pronounced effects (Table 4). However, these ions, similarly to acetonitrile, did not affect the reaction of **2a** and **1e**. These results suggest that these ions facilitate merely the electron transfer from phenolate **2a** to *N*-chloroimine **1b**, but do not afford further chain initiators (over the ones escaped from the solvent cage) with either reactant alone.[39]

Reactions in Nonaqueous Medium. The reaction of the sodium salt of **2a** and **1b** in several dipolar aprotic and apolar aprotic solvents, monitored by ^{1}H-NMR, was very fast compared to that in aqueous solution (pH = 9.2). In dipolar aprotic solvents, e.g., in DMSO-d_6, DMF-d_7, and acetonitrile-d_3, the main product was the phenol ether **18a**, the carbon-substituted product, whereas in apolar aprotic solvents, e.g., in pyridine-d_5, chloroform-*d*, benzene-d_6, and carbon tetrachloride, indophenol **3f** was formed, similarly to the aqueous medium, along with traces of **18a** (Table 5).[40] The formation of **3f** both in water as well as in apolar aprotic solvents, despite the difference between their dielectric constants, i.e., their polarity, is probably due to the fact that, in both types of solvent the oxygen atom of the phenolate anion is blocked either by solvation with a hydrogen bond in water or by ion aggregation in apolar aprotic solvents. When tetraethylammonium phenolate was used instead of the sodium salt in chloroform-*d* as solvent, the amount of **18a** increased considerably, demonstrating the higher reactivity of the phenolate oxygen when a softer and bulkier cation, forming a less compact aggregate, was applied. In dipolar aprotic solvents when only the cation is solvated, the naked phenolate anion is extremely active at the oxygen site, which explains the formation of **18a**. This hypothesis was backed by the fact that unlike the sodium salt of 3,5-di-*tert*-butylphenol (**2t**), which does not react in aqueous solution with **1b** and forms phenol ether

Table 5. Solvent Dependence of the Gibbs Reaction of Phenolate 2a with *N*-Chloroimine 1b



solvent	$\epsilon_{25\,°C}$	**18a**, %	**3f**, %
water	78	<1	>99
DMSO-d_6 + 27% D_2O		38	62
DMSO-d_6 + 11% D_2O		85	15
DMSO-d_6	46.6	96	4
DMF-d_7	37.0	97	3
acetonitrile-d_3	36.2	87	13
pyridine-d_5	12.3	20	80
chloroform-d[a]	4.6	<1	>99
chloroform-*d*/pyridine-d_5 9/1		<1	>99
chloroform-d[b]		24	76
benzene-d_6[a]	2.3	2	98
carbon tetrachloride[a]	2.2	25	75

[a] Sodium phenolate dissolved by 18-crown-6. [b] Tetraethylammonium phenolate applied instead of sodium phenolate.

18b in DMSO-d_6 immediately, the sodium salt of 2,6-di-*tert*-butylphenol (**2u**) forms indophenol **3e** with **1b** in both solvents.

Mechanistic Considerations. In his pioneering paper, Gibbs[2] suggested that the most likely nucleophilic centrum would be the negatively charged phenolic oxygen in the reaction of *N*-chloroimine **1a**. Accordingly an intermediate aryl oxime ether **19a** should be formed, the rearrangement of which into the indophenol is fast; therefore, it would not influence the reaction rate. Checking this hypothesis, the dichloro derivative **19b** was synthesized. However, under the conditions of the Gibbs reaction, aryl oxime ether **19b** remained unchanged excluding it as a possible intermediate.[41] The reactions of **1b** with phenol **2u** or with its 4-amino derivative **2v** were very fast (in the latter case **1d** and **1f** were formed), but there was no reaction between phenol **2t** and **1b** or **1d**. Accordingly, any mechanism giving priority to the attack of the phenolic oxygen can be excluded. We suggest that the nitrogen atom of **1b** attacks the *para* position of the phenol directly.[42] Although the prevention of the *para* substitution of phenol **2t** with *N*-chloroimine **1b** can also be rationalized by steric hindrance, that of the *ortho* substitution hardly can.[43]

According to Gibbs,[2] the rate of the formation of indophenol **3a** depends on the pH, but it does not when the phenolate anion (PhO^-) is considered as a reactive partner. Our experiments were in full agreement with this statement in the case of phenol **2a**, as the rate constant $v = k[\mathbf{1b}][PhO^-]$ did not change when the molar

(38) The hyperchromic effect of acetonitrile on the UV spectra of the indophenol **3f** indicates a characteristic solvating effect on the product **3f**. On this base, a similar solvent effect might be supposed during the reaction, i.e., on the chain initiation.

(39) We think that the acceleration effect of these metal ions is that they assist the electron transfer from increased distance, making possible the escape of chain initiators from the cage by solvation, and start a chain reaction, being concurrent with the in-cage direct reaction.

(40) In **18a** the *anti*-arrangement of the *N*-chloro atom was determined by the assignment of the analogous **1b**: Saito, H.; Nukada, K. *J. Can. Chem.* **1968**, *46*, 2989–3000.

(41) Nevertheless, it should be noted that **19b** could rearrange by a photochemical reaction into indophenol **3f** and tricyclic **11b**. As Gibbs reaction of **2a** with **1b** is not influenced by light and does not afford tricyclic product deriving from *o*-indophenol, this hypothesis can be rejected.

(42) The fact that *ortho*-substituted derivatives are also formed from 4-*tert*-butylphenols is due to the steric hindrance of the *tert*-butyl group.

(43) There is some evidence that the chloro and hydrogen substitutions on benzoquinone *N*-chloroimines have a special effect on the regioselectivity, since 3,5-dichloro **1g** did afford *ortho* products with **2t**. Accordingly, in the reaction of **2t** and **1g**, the two tricyclic isomers **11e** and **11f** were formed *via* interconversion of the *o*-indophenol intermediates **14b, c**.

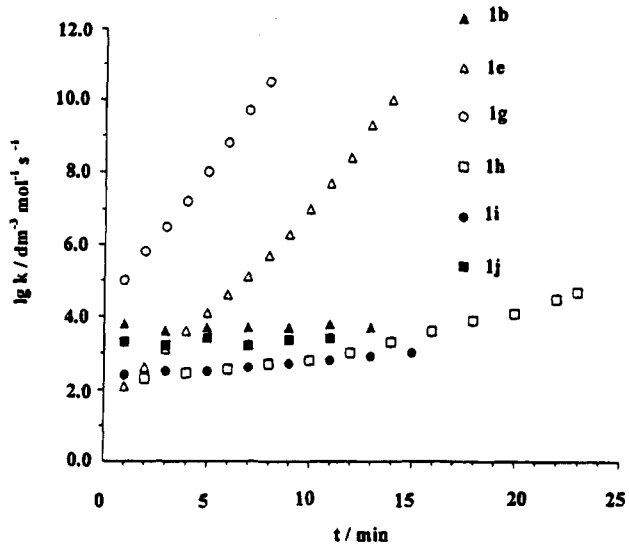


Figure 2. Hypothetical second-order rate constants vs time plot of the Gibbs reaction of several benzoquinone *N*-chloroimines with **2a** in borate buffer (pH = 9.2) at 295 K where the concentration of benzoquinone *N*-chloroimines was always 6.14×10^{-5} mol dm^{-3} and f = the rate of the observed and depicted k. (▲) [**2a**] = 4.88×10^{-3} mol dm^{-3}, $f = 1$; (△) [**2a**] = 2.36×10^{-1} mol dm^{-3}, $f = 10^{-2}$; (○) [**2a**] = 2.93×10^{-3} mol dm^{-3}, $f = 1$; (□) [**2a**] = 2.28×10^{-2} mol dm^{-3}, $f = 10^{-1}$; (●) [**2a**] = 5.86×10^{-3} mol dm^{-3}, $f = 1$; (■) [**2a**] = 7.6×10^{-4} mol dm^{-3}, $f = 10$.

concentration of *N*-chloroimine **1b** and that of PhO^- was commensurable, independently of the molar ratio of **2a** and **1b** which could be in the range of 30–530:1. Investigating the kinetics of **2a** with other benzoquinone *N*-chloroimine derivatives **1e** and **1g–j**, we have concluded that the occurrence of the second-order kinetics depends on the reactivity of the benzoquinone *N*-chloroimine derivatives. The validity of the equation applied to calculate the second-order rate constants can be judged from the agreement of these points with the theoretical horizontal straight lines in Figure 2 where the hypothetical second-order rate constants of the reaction of **2a** with several *N*-chloroimines type **1** vs time is plotted. Thus, the second-order rate can be applied on the reactions of **2a** with **1b** and **1j** whereas it cannot on that with the parent **1e**, the monochloro **1h**, and the dichloro **1g** and **1i**.[44] Moreover, when the formation of indophenols are plotted against time (Figure 3) *N*-chloroimines **1b**, **1i**, and **1j** give characteristic curves, while the less active **1e** and **1h** as well as **1g**, being more active than **1b**, deviate from these. The curve of parent *N*-chloroimine **1e** shows well that the formation of the parent indophenol **3h** is slow at the beginning of the reaction and then it accelerates, due to the chain reaction character proved previously.

To summarize these results, a collection of mechanisms shown in Schemes 4–6, is proposed for the Gibbs reaction of phenol **2a** with *N*-chloroimines **1b** or **1e**. These *N*-chloroimines are typical representatives of the nonchain and the chain reaction mechanisms, respectively. These schemes demonstrate these two types of mechanisms and the connection between them.

The first step of the reaction is a reversible single electron transfer (SET) from phenolate **2a** to *N*-chloroimine **1b** or **1e** forming a radical pair (**20a** and **21a** or **21b**) in a solvent cage (Scheme 4). The formation and further transformation of this radical pair will influence the overall rate of the reaction. In the case of the more reactive **1b**, the fast combination of **20a** and **21a** gives **22a** and subsequent fast[45] elimination of hydrochloric acid yields indophenolate **3f**.[46] Since both the combination and HCl elimination are fast, the oxidation of phenolate by SET remains the rate-determining step. Indeed, the second-order kinetics as well as the linear relationship of the logarithm of this second-order rate constant of the Gibbs reaction of **1b** vs the half-wave oxidative potential of the reacting phenols (Figure 4) verify this theory.[47] When the less reactive **1e** is the electron acceptor, the combination of **20a** and **21b** is negligible; therefore, the radicals, once escaped from the solvent cage, can start a chain reaction, which can be stopped completely by TEMPO. However, when the kinetics of the reaction of **1e** and the more reactive phenols **2b** or **2u** were investigated, a second-order kinetics was obtained again, and the reaction could not be scavanged by TEMPO. Thus, the forward direction of the reaction toward combination, i.e., the combination of the radicals in the solvent cage (direct reaction) or the chain reaction *via* competitive escape of the radicals from the cage depends on the reactivity of the radicals forming the radical pair. Moreover, further connection between the nonchain and the chain reaction was demonstrated by the effect of acetonitrile or metal ions, as additives. These additives changed the mechanism from the former to the latter, as described above in the case of the reactions involving **1b**. The radicals once escaped can enter into two alternative chains. In chain A (Scheme 5), the addition of phenoxy radical **20a** to *N*-chloroimine **1e** forms the radical adduct **23b**, another SET to which

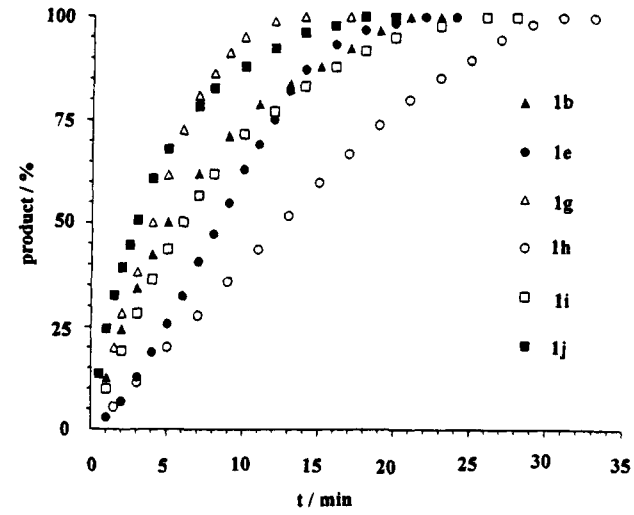


Figure 3. Product vs time plot of the data depicted in Figure 2.

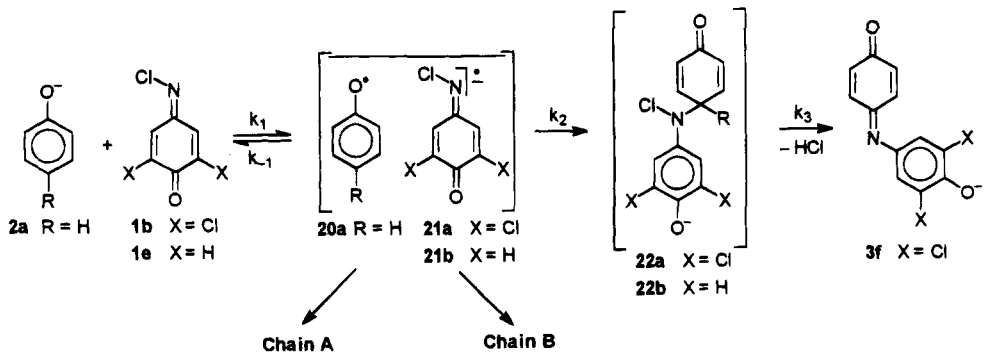
(44) However, the reaction of **1e** with more reactive phenols **2b** and **2u** shows second-order kinetics (see later).

(45) Applying 4-deuteriophenol, a kinetic isotope effect was not observed.

(46) With radical **21a** the loss of chloride ion in the solvent cage is an alternative possibility, followed by the combination of radicals **20a** and **24a** to give **26a**. In the thermodynamic sense this process is not likely (see Table 8; cp. chain b), but a significantly exothermic solvation of the chloride ion can make the process possible.

(47) Above was shown, while *N*-chloroimines **1b** and **1j** gave a unchanged second-order rate constant with phenol in function of time (direct reaction in the solvent cage), the compounds **1e**, **1g**, **1h**, and **1i** gave growing rate constants proceeding with the reaction (chain reaction); therefore, only a qualitative relationship can be established between the reducibility of *N*-chloroimines and the logarithms of the rate constants.

Scheme 4



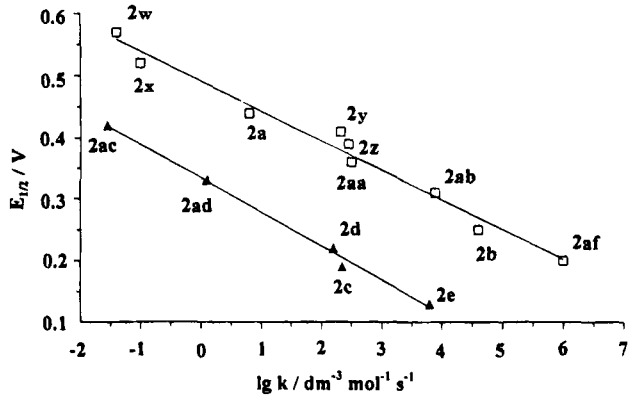


Figure 4. The plot of the oxidative $E_{1/2}$ of several phenols vs the logarithm of the second-order rate constant of the Gibbs reaction of **1b** with these phenols in borate buffer (pH = 9.2) at 295 K.

from phenolate **2a** gives the same type of intermediate **22b** as in the direct reaction with a simultaneous recovery of the phenoxy radical **20a** to complete the chain. Fast dehydrochlorination of **22b**, similarly to that in the direct reaction in Scheme 4, affords the indophenolate **3h**. Consequently, considering the mechanism of chain A, it has the same intermediate **22** as the direct reaction, but the formation of this product is autocatalyzed by phenoxy radicals. In chain B (Scheme 6), a chloride elimination from radical anion **21b** gives imine radical **24b**, the addition of which to phenolate **2a** leads to the radical anion adduct **25b**. To complete the chain, a second SET is accomplished from adduct **25b** to *N*-chloroimine **1e** to recover radical anion **21b** with simultaneous formation of intermediate **26b**, the aromatization of which affords indophenolate **3h**. In this case the formed intermediate **26b** is different from that in chain A since the *N*-chloride has been eliminated already within the chain. Thus in the direct reaction and in chain A, the chloride ion and the proton can be eliminated simultaneously after the addition. This is an essential difference between the first two mechanisms and the third one, in which the chloride ion is eliminated early in the chain and the deprotonation occurs only in the terminating step.

On the other hand, the astonishing high regio- and chemoselectivity of the Gibbs reaction[48] raises other questions. In the reactions of phenolates involving phenoxy radicals, the dimerization or polymerization of the substrate affording a large variety of products are always detectable.[49] As the concentration of the initiating radicals is low when the Gibbs reaction is a chain reaction, which is indicated by the inductive period in the kinetics (S-shaped curve), the homodimerization of these radicals is negligible. This follows that the chemoselectivity of this reaction depends on the reaction rates of the addition of phenoxy radicals to *N*-chloroimine or to phenolate. The former is probably much faster, therefore the regioselectivity of the reaction will be influenced by the radical. Indeed, spin density calculations, based on ESR experiments of phenoxy radicals, predict high *para* selectivity[50] (see Table 7, too). Consequently, any mechanism of the Gibbs reaction can be termed as radical electrophilic aromatic substitution or simply $S_{RE}Ar$. Since both the initiating SET and the combination or the chain reaction is independent on the character of the *para* leaving group, this mechanism can be extended over all phenols reacting with benzoquinone *N*-chlorimines at the aromatic ring. Indeed, a similar straight line was obtained for 4-chlorophenols as for 4-unsubstituted phenols when the logarithm of the second-order rate constant vs $E_{1/2}$ was plotted in Figure 4, and even the scavanger effect could be demonstrated in the reaction of *N*-chloroimine **1e** and phenols **2g**, **2f**, and **2ah** with DCNB. This generalization leads to type **22** intermediate adduct (Schemes 4, 5), further transformation of which depends on the leaving character of the *para* substituent (R). When R represents an electrofugal leaving group, e.g., $CH_2N(CH_3)_2$ or *tert*-butyl, it transforms into type **3** indophenol with elimination of chloride anion and R^+, as described above in the case of R = H. When R has a poor leaving character, after elimination of chloride anion from type **22** adduct, the formed bis-quinoidal compound either remains unchanged, e.g., when R = methyl to afford **10d–h** or, when R = OH, e.g., from hydroquinone (**2ai**) or 2,6-di-*tert*-butyl-4-hydroxyphenol (**2aj**), and NH_2, e.g., from phenol **2v** or 2,6-dichloro-4-aminophenol (**2ak**), it decomposes to afford oxidized products of the phenol, e.g., quinones **4e** or **4d** and imines **1f** or **1d**, respectively, along with imine **1d** deriving from the reduction of *N*-chloroimine **1b**.

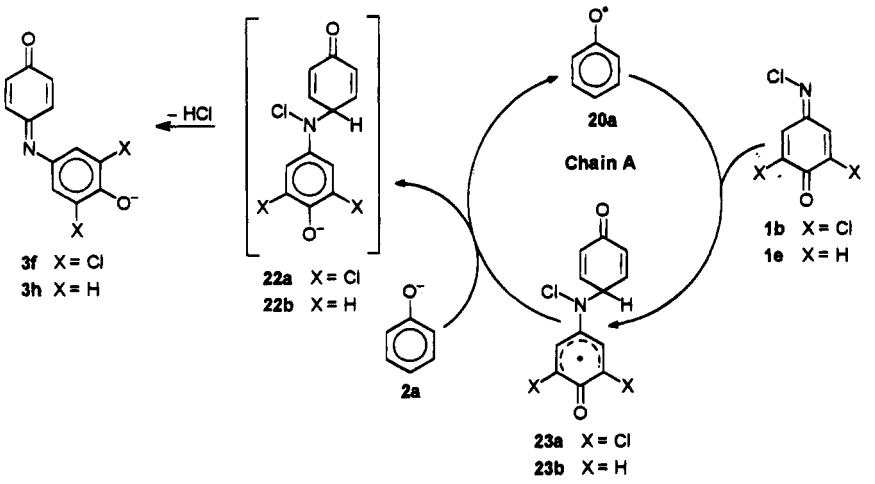
When R represents a nucleofugal leaving group, the further transformation of the type **22** intermediate adduct is demonstrated on the adduct of phenol **2c** and *N*-chloroimine **1b** (**22c** in Scheme 7).

(48) Monitoring the Gibbs reaction of *N*-chloroimines **1b** or **1e** with phenol **2a** by ^1H NMR in D_2O, quantitative formation of indophenols **3f** or **3h** was observed.

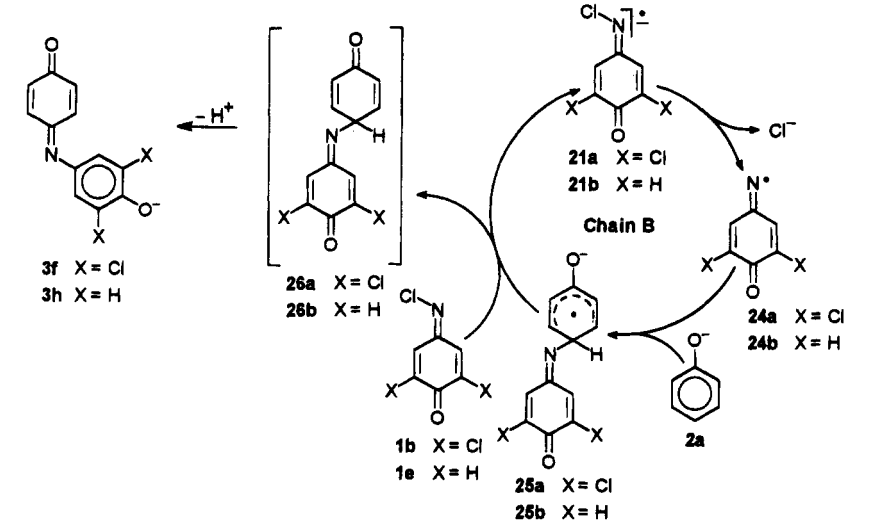
(49) Patai, S. *The Chemistry of the Hydroxyl Group*; John Wiley & Sons: New York, 1971; Part 1, pp 505–592.

(50) (a) Stone, T. J.; Waters, W. A. *J. Chem. Soc.* **1964**, 213–218. (b) Dixon, W. T.; Norman, R. O. C. *J. Chem. Soc.* **1964**, 4857–4860. (c) Potassium nitrosodisulfonate, $ON(SO_3K)_2$, known as Fermy's salt, affords preferentially *p*-quinones with *para*-unsubstituted phenols even when the *ortho* positions are free. This reaction is passing through a phenoxy radical intermediate (see ref 49, pp 568–569.).

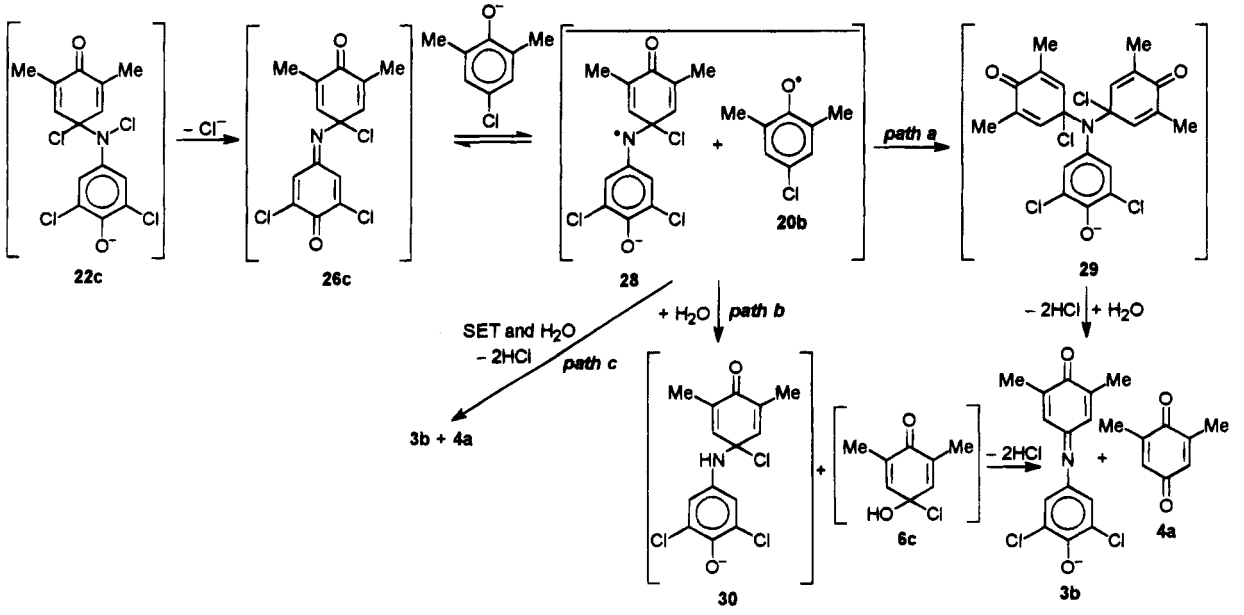
Scheme 5



Scheme 6

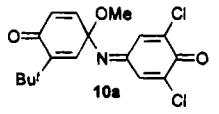
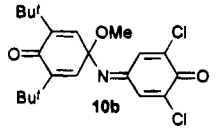
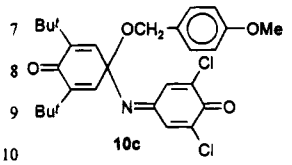


Scheme 7



It is evident that Cl cannot be eliminated as an anion from intermediate **26c**, the chloride-eliminated product of **22c**. Therefore, is oxidizes a second molecule of phenol **2c**, which is in full agreement with the established stoichiometry. The oxidation of the second phenol molecule was investigated as well. If this oxidation is presumed to be a SET with a chain reaction, the formed phenoxy radical can be trapped by oxygen to give hydro-

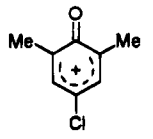
Table 6. Reactions of Intermediates 10a–c with Phenols[a]

entry	intermediate	parent phenol, $E_{1/2}$, (V)[b]		second phenol, $E_{1/2}$, (V)[b]		indophenol			
						intramolecular, %		intermolecular, %	
1	 **10a**			**2c**	0.19		67	**3b**	33
2		**2i**	0.12	**2h**	0.23	**3g**	100	**3f**	0
3				**2ac**	0.42		100	**3f**	0
4	 **10b**			**2c**	0.19		29	**3b**	71
5		**2g**	-0.01	**2h**	0.23	**3e**	75	**3f**	25
6				**2ah**	0.11		99	**3b**[c]	1
7	 **10c**			**2c**	0.19		75	**3b**	25
8		**2j**	0.15	**2f**	0.03	**3f**	100	**3e**	0
9				**2u**	0.35		100	**3e**	0
10				**2t**	0.05		no reaction		

[a] For details see experimantal section.
[b] $E_{1/2}$ was determined in borate buffer (pH = 9.2) at 298 K.
[c] In water the rate was the same.

peroxide, which is known to transform into quinol in an alkaline medium.[51] To check this hypothesis hydroperoxide **6b** was synthesized and its stability was examined. However, under the conditions of the Gibbs reaction, it remained unchanged and could not be converted into quinol **6a**. On the other hand, **6a** was formed even in those cases when the reaction was performed under argon. Accordingly, **6a** can be considered as the primary oxidation product of phenol **2g**. The formation of indophenols from *N*-chloroimine **1e** and phenols **2g**, **2f**, or **2ah** could be prevented by scavenger DCNB, but it cannot when intermediate **10b** and a second phenol molecule are applied; these facts suggest a mechanism, in which the first oxidation step, the formation of the intermediate **22**, is a SET with chain reaction, like the reactions of **2a** with **1e** and, in the presence of an additive, with **1b**, whereas the second oxidation step, the formation of the indophenol and the oxidized phenol, is not. This second oxidation step was further investigated by reducing intermediates **10a–c** with phenols being different from that forming the intermediate. In this way, information can be obtained on the role of the second phenol molecule whether it just reduces the intermediate affording intramolecular indophenol or whether it substitutes the nitrogen, which would result in an exchange of the parent and the attacking phenols to afford intermolecular indophenol or the mixture of these two. Determination of the rate of these intra- and intermolecular indophenols can allow these questions to be answered. In these experiments our aim was to compare the redox potentials and the steric effects of the phenols that form the intermediates with the characteristics of the phenols reducing them, in water or in TCE, respectively. In water only intramolecular indophenols were formed. However, in TCE, in several cases both indophenols were formed indicating some exchange reaction. In Table 6, the polarographic half-wave oxidative potentials ($E_{1/2}$) of the parent as well as the reducing phenols and the percentage of the intra- and intermolecular indophenols are summarized. Applying phenol **2c** to reduce intermediates **10a–c**, the lower was the $E_{1/2}$ of the parent phenol, i.e., the more oxidizable it was, the more intermolecular indophenol was formed (entries 1, 4, and 7). The same is true for **2h** (entries 2 and 5).

In the last two entries, two reducing phenols (**2u** and **2t**) carrying an electrofugal leaving group at C-4 are also depicted. These experiments indicate that the electron transfer proceeds from the *para* position of the reducing phenol; when it is hindered there is no oxidation at all. Previous experiments demonstrated that this step is not a chain reaction. It was attractive to suppose a SET for this redox step also, although the formation of the quinone derivatives implied that a way *via* phenoxenium ion[52] **27** also should be considered. Comparing the heats


27

of formation of the possible intermediates (Table 8), we found that the redox reaction of intermediate **26c** and phenol **2c** probably cannot afford the free phenoxenium ion[53] **27**, but rather a SET from phenol **2c** to **26c** can proceed (Scheme 7). For the further transformation of the radical pair, involving amine radical **28** and phenoxy radical **20b** in the solvent cage, three pathways are proposed: combination of these radicals (path a) affords tertiary amine **29**, which will hydrolyze to quinone **4a** and indophenol **3b**. These products are formed also either *via* hydrogen and hydroxyl abstraction from water by the radical pair (path b), or *via* another SET from phenoxy radical **20b** to amine radical **28** and a concerted water addition (path c) yielding indophenol **3b** and

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(53) A significantly exothermic solvation of this cation can make the process possible.

Table 7. Squares of LCAO Coefficients of the HOMOs for *Para*-Substituted Phenolate Ion and the SHOMOs for Phenoxy Radical Derivatives

	anions			radicals		
atom	R:H	R:F	R:Me	R:H	R:F	R:Me
C_i	0.03	0.03	0.03	0.02	0.02	0.02
C_o	0.23	0.22	0.22	0.22	0.20	0.20
	–	–	–	*0.28*[a]	–	*0.25*[a]
C_m	0.00	0.00	0.00	0.00	0.01	0.01
C_p	0.30	0.30	0.30	0.38	0.40	0.39
	–	–	–	*0.42*[a]	–	*0.44*[a]

[a] Calculated spin densities based on ESR experiments; see ref 50.

Table 8. Computed PM3[60] Energies of Selected Reactants, Potential Reaction Intermediates, and Products of the Gibbs Reaction

comp label	energy, kcal mol^{-1}	comp label	energy, kcal mol^{-1}
1b	+3.3	**24a**	+56.2
2a	−44.1	**24a**$^-$	−3.3
2c	−74.2	**25a**	−55.9
3b	−82.1		(−53.4)[a]
3f	−65.1	**26a**	+8.9
4a	−49.6	**26c**	−13.4
6c	−71.2	**27**	+170.6
20a	+3.3	**28**	−81.4
20b	−23.2	**29**	−108.6
21a	−60.8	**30**	−95.1
22a	−79.2 (−71.5)[a]	**Cl**$^-$	−51.5
		HCl	−20.5
23a	−7.5 (−7.2)[a]	**H_2O**	−53.4

[a] Energy of the *ortho* isomer.

quinone ***4a*** *via* quinamine **30** and quinole **6c** (see ref 52e). It is evident that the decomposition of the tertiary amine **29**, to a given mixture of indophenols will depend on the oxidizability of the phenols involved, i.e., $E_{1/2}$ (see entries 1, 4, and 7 or 2 and 7 in Table 6).

Quantum Chemical Calculations

Methods. A modified hybrid version of MOPAC 5.00 program,[54] labeled as MOPAC 5.50, has been used throughout the computations. The modification included the incorporation of the EF[55] and the GDIIS[56] optimization methods, from MOPAC 6.00 program[57] and TX90 program,[58] respectively. More important was the fact that the routines of Pulay's TX90,[59] necessary for the automatic generation[58] and use of *natural internal coordinates* were also incorporated. The modified hybrid MOPAC 5.50 was found to be reliable and fast during geometry optimization in the natural internal coordinates with the efficient use of the updated Hessian matrix in each successive cycle.

Since some of the molecules had open electron shells, all molecules (even those that had closed electron shells) were studied within the UHF formalism. Full conformational study was carried out wherever the molecular flexibility allowed the formation of different conformers. However, only the global minima are reported in this paper.

Scope. The strong *para* selectivity is a predominant feature of the Gibbs reaction; therefore, the primary question, whether the aromatic substitution took place on the anion of **2a** or on the phenoxy radical (**20a**), had to be dealt with. This made the analysis of the electronic structures of the reactants necessary. In particular, the electron or spin density of the HOMO of the reacting ion or single highest occupied molecular orbital (SHOMO) of radical **20a**, respectively, was of particular importance. Since the primary reactant is the phenolate ion, for the free radical mechanism the radical **20a** had to be formed by SET which opened up the realms of possibilities for chain reaction mechanisms.

The main purpose of the computation was to compare the energetics of the intermediates of potential reaction mechanisms. The energetics of the reactions are presented as relative values with respect to the reactant state.

Results. The squares of the LCAO coefficients of the HOMO for the phenolate and radical **20a** are summarized in Table 7 for a number of substituents. This table clearly indicates that the squares of the LCAO coefficients of HOMO are changing proportionally with the *para* substituent. Consequently, a given substituent (e.g., F) in the *para* position will not redirect the Gibbs reaction to the *ortho* position but rather it departs during the substitution and the *para* isomer is formed. From the data presented in Table 7 it is clear that the partial electron density difference in the *para* position is greater in the case of the radical **20a** than in the case of the phenolate ion favoring the *para* position. Consequently, if the reaction is occurring from the radical **20a** formed *via* SET the *para* selectivity of the subsequent reaction is practically guaranteed. The question whether the reaction is indeed occurring from the radical **20a** can only be answered from the knowledge of the energetics associated with the potential reaction mechanism. If we take the SHOMO electron density of the radical **20a** to be equal to the spin density then the squares of the LCAO coefficients of SHOMO may be compared to the calculated spin densities[50] based on ESR experiments. The comparison is favorable (Table 7). The computed total energies of selected compounds can be found in Table 8. The energetics for a selected pair of reactants, their possible reaction intermediates associated with potential reaction mechanisms, and final products are summarized in Table 9. These energies were combined for the SET process as well for the three potential reaction mechanisms: I, direct; II, chain A; III, chain B. The energetics are presented graphically in Figure 5. These results clearly support the previous conclusion that mechanism I and II are similar and III is completely different. However this energy level diagram also suggests that mechanisms I and II are favored, at least in the thermodynamic sense, over mechanism III. Although it may be conceivable that solvation might modify the computed energy differences, nevertheless, the qualitative nature of the conclusion, in general, is predicted to be valid.

Summary and Conclusions

The stoichiometry of the Gibbs reaction, indophenol **3** formation from phenol **2** with *N*-chlorobenzoquinone imines **1**, is 1:1 when the *para* substituent (R) of the phenol is an electrofugal leaving group, while it is 2:1 when R is a nucleofugal leaving group. The first step of the reaction, which is rate-determining in several cases,

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Table 9. Computed and Relative Energetics (kcal mol^{-1}) of Potential Reaction Mechanisms

	Initial state						Final state
a.	**2a,1b**	⟶	**20a,21a**				
	-40.8		-57.6				
	0.0		*-16.8*				
b.	**2a,1b**	⟶	**20a,21a**	⟶	**22a**	⟶	**3f (HCl)**
	-40.8		-57.6		-72.9		-85.6
	0.0		*-16.8*		*-32.2*		*-44.8*
c.	**20a,1b (2a)**	⟶		**23a,2a**	⟶ **22 a (20a)**	⟶	**3f (20a,HCl)**
	-37.5			-51.6	-69.7		-82.4
	0.0			*-14.1*	*-32.2*		*-44.8*
d.	**21a (2a,1b)**	⟶	**24a,2a (1b,Cl⁻)**	⟶ **25a,1b (Cl⁻)**	⟶ **26a (21a,Cl⁻)**	⟶	**3f (21a,HCl)**
	-101.6		-36.1	-104.1	-103.5		-146.4
	0.0		*+65.5*	*-2.5*	*-1.9*		*-44.8*

a. SET reaction.
b. *Direct reaction*
c. *Chain A*
d. *Chain B*

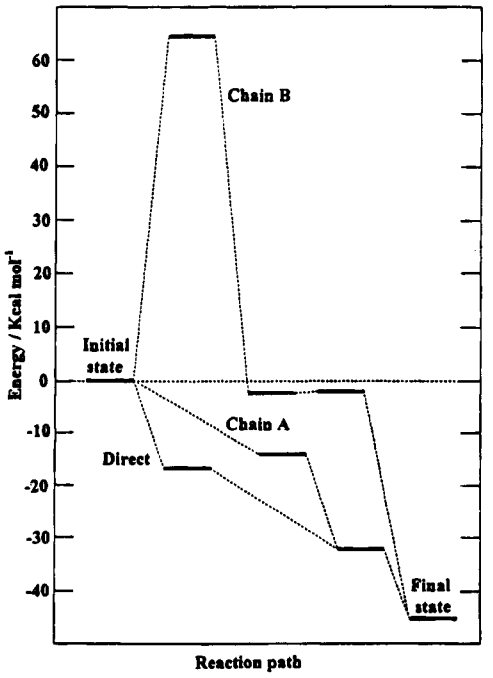

Figure 5. PM3 energy level diagrams for potential reaction mechanisms. For more details see Table 9.

is a SET from phenolate to *N*-chloroimine **1**. When R is a nucleofugal leaving group, the reaction goes through an intermediate. In these cases the slow step is another SET from phenolate to this intermediate; several of them could be isolated due to the large difference between the rates of these SETs. In these cases, if we want to obtain the indophenol **3**, it is practical to convert *N*-chloroimine **1** (with alcohol or 2,6-dichloro-4-aminophenol) to benzoquinone imine.[1a] For these radical reactions two different alternatives are suggested: either a combination of the radicals, formed by a SET, in the solvent cage or, if they can escape from this, a chain reaction. The particular pathway depends on the reactivity of the radical and the character of the solvent. When these pathways ran parallel, in some cases, they could be separated or transformed one to the other. The reaction shows an extremely high *para* selectivity even if the substitution does follow radical mechanism. Spin density data calculated by semiempirical quantum chemical methods and from ESR measurement[50] are in good agreement with the observed *para* selectivity.

Experimental Section

Reaction kinetics were measured UV spectrophotometrically by assaying the concentration of indophenols **3** in an aqueous solution containing 1% (7% in the assay of **2d**, **2e**, and **2ai**) acetonitrile, at 25 °C, and the pH was adjusted to 9.2 by borate buffer. If required, the pH was decreased by adding hydrochloric acid (0.1 M), besides maintaining the ionic strength with NaCl solution. The ^{1}H and ^{13}C NMR spectra were recorded by a Bruker AC 250 spectrometer equipped with an ASPECT 3000 computer, at frequencies of 250.1 and 62.9 MHz, respectively. Unless otherwise noted, all NMR spectra were recorded in acid free 1,1,2,2-tetrachloroethane-d_2 (TCE) with tetramethylsilane (TMS) and TCE (73.8 ppm) as reference standards. In the experiments, ^{1}H, ^{1}H–^{1}H COSY, ^{1}H NOE, ^{13}C, DEPT, selective INEPT,[61] proton-coupled ^{13}C (gated), selective proton-decoupled ^{13}C, ^{13}C–^{1}H COSY, measurements were applied.[62] In many cases unstable structures, detectable only in solution, were elucidated. These compounds were assigned as part of multicomponent systems in which the signals of the known compounds were confirmed by adding them prepared in a different route into the solution recorded. ESR measurements were carried out on JES-ME-3X spectrometer at ambient temperature. Polarographic measurements were carried out with a PAR 174-A Polarographic Analyser (glassy carbon PT and SCE electrodes) in the aqueous, 1.224×10^{-4} mol dm^{-3} solution of the test compound buffered by $Na_2B_4O_7$, at dc operation. 4-Deuteriophenol was prepared from Grignard compound by D_2O. **1b** was purchased from Merck, further benzoquinone *N*-chloroimines were prepared by the known method,[63] and preparation of **1g** was carried out in a two-phase system of hexane–water with a fast extraction of **1g** into hexane. Computations were carried out on an IBM RISC 6000/320 and 560 workstation in the

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Department of Theoretical Chemistry of the L. Eötvös University Budapest.

Reaction of 2,6-Di-*tert*-butyl-4-chlorophenol (2f) with 1b. To a solution of **1b** (31 mg, 0.15 mmol) in *tert*-butyl alcohol (10 mL) was poured a solution of $Na_2B_4O_7$ (225 mL, 6×10^{-3} M), and then a solution of **2f** (90 mg, 0.37 mmol) in *tert*-butyl alcohol (30 mL) was added. The mixture was kept at ambient temperature (25 °C) for 20–25 min and then the solution was shaken with hexane (100 mL), the pH was adjusted to 6.5–7.0 (6.5 mL, 0.5 M HCl), and after repeated shaking, the two layers were separated. The extraction was repeated with 100 mL of solvent. The organic extracts were combined, washed with water (2 × 100 mL), dried over anhydrous sodium sulfate, and concentrated to 4–5 mL at reduced pressure (water bath temperature 30–35 °C). After addition of TCE (0.5 mL) the rest of the hexane was removed. The molar ratio of the products **3e**:**4d**:**5** was 1:1:2 by ^{1}H NMR. (Spectroscopic data of **5** are listed in part 2 of this series). **4d**: ^{1}H NMR δ 6.49 (s, 2H), 1.26 (s, 18H); ^{13}C NMR δ 188.4 (s), 187.5 (s), 157.7 (s), 129.9 (d), 35.4 (s), 29.3 (q). The stability of **5** (see part 2) was markedly affected by the acidity of the solvent, but in water and acid-free TCE the rate of conversion to indophenol **3e** could be significantly suppressed (no significant transformation was detected at 250 K during 3 days). ^{1}H NMR spectra of the indophenol **3e** is sensitive to both acid and alteration of temperature. Since the transformation of compound **5** to **4d** and indophenol **3e** is an acid-producing step, the δ_H values of **3e** depend on time. ^{1}H NMR spectra of **3e** were recorded within 20 min at 298 K: δ 7.25 (s, br, 1H), 7.05 (s, br, 2H), 6.85 (d, J = 2.5 Hz, 1H). After compound **5** was converted to indophenol **3e**, dichloromethane (30 mL) was added to the solution, it was washed first with $Na_2B_4O_7$ (0.05 M, 2 × 10 mL) and subsequently with water (10 mL) and dried, and the dichloromethane was removed by evaporation under reduced pressure. **2,6-Bis(1,1-dimethylethyl)-4-[(3,5-dichloro-4-hydroxyphenyl)imino]-2,5-cyclohexadien-1-one (3e)**: ^{1}H NMR δ 6.97 (d, J = 2.5 Hz, 1H), 6.89 (s, 2H), 6.77 (d, J = 2.5 Hz, 1H), 1.31 (s, 9H), 1.22 (s, 9H); ^{13}C NMR δ 187.3 (s), 159.5 (s), 154.4 (s), 153.4 (s), 145.5 (s), 142.6 (s), 134.1 (d), 121.5 (s), 121.3 (d), 120.8 (d), 35.7 (s), 35.2 (s), 29.3 (q).

Reaction of 2,6-Dimethyl-4-chlorophenol (2c) with 1b. The same procedure as described for the reaction of **2f** and **1b** was applied using a solution of **1b** (21 mg, 0.1 mmol) in acetonitrile (10 mL), a solution of $Na_2B_4O_7$ (225 mL, 6×10^{-3} M), and a solution of **2c** (40 mg, 0.25 mmol) in acetonitrile (10 mL) with 20 min reaction time. The molar ratio of the products **3b**:**4a** was 1:1 by ^{1}H NMR. **2,6-Dimethyl-4-[(3,5-dichloro-4-hydroxyphenyl)imino]-2,5-cyclohexadien-1-one (3b)**: ^{1}H NMR δ 7.03 and 6.81 (sextet, J = 2.7, 1.4 Hz, 2H), 6.86 (s, 2H), 2.08 (d, J = 1.4 Hz, 3H), 2.01 (d, J = 1.4 Hz, 3H). **4a**: ^{1}H NMR δ 6.55 (q, J = 0.5 Hz, 2H), 2.04 (d, J = 0.5 Hz, 6H); ^{13}C NMR δ 188.1 (s), 187.7 (s), 145.7 (s), 133.1 (d), 15.9 (q).

Reaction of 2,6-Di-*tert*-butyl-4-methoxyphenol (2g) with 1b. Method a: The same procedure as described for the reaction of **2f** and **1b** was applied using a solution of **1b** (17 mg, 0.08 mmol) in acetonitrile (10 mL), a solution of $Na_2B_4O_7$ (225 mL, 6×10^{-3} M), and a solution of **2g** (47 mg, 0.2 mmol) in acetonitrile (20 mL) with 10 min reaction time. The molar ratio of the products **3e**:**6**:**4d** was 2:1:1 by ^{1}H NMR. The ^{1}H and ^{13}C NMR data of **3e** and **4d** are listed at the reactions of **2f** and **1b**. The NMR spectra should be immediately recorded after processing since quinol **6a** rapidly transforms into quinone **4d**. **2,6-Bis(1,1-dimethylethyl)-4-hydroxy-4-methoxy-2,5-cyclohexadien-1-one (6)**: ^{1}H NMR δ 6.56 (s, 2H), 6.0–6.4 (OH, 1H), 3.40 (s, 3H), 1.21 (s, 18H); ^{13}C NMR δ 186.4 (s), 149.4 (s), 131.4 (d), 97.3 (s), 50.7 (q), 35.0 (s), 29.3 (q). **Method b**: The same procedure as described for method a was applied using a solution of **1b** (21 mg, 0.1 mmol) in acetonitrile (10 mL), a solution of $Na_2B_4O_7$ (225 mL, 6×10^{-3} M), and a solution of **2g** (24 mg, 0.1 mmol) in acetonitrile (20 mL). After 3–4 min the reaction mixture was processed as described above without giving TCE, with evaporation to dryness (water bath temperature 25 °C) at reduced pressure. The molar ratio of the products **10b**:**1b**:**3e**:**6**:**4d** was 20:6:3:1:2 by ^{1}H NMR. At ambient temperature compound **10b** decomposes within minutes; thus, the dry residue obtained after evaporation should be immediately dissolved in cold, acid-free $CDCl_3$ and the NMR spectra should be recorded immediately.

2,6-Bis(1,1-dimethylethyl)-4-methoxy-4-[(3,5-dichloro-4-oxo-2,5-cyclohexadienyl)imino]-2,5-cyclohexadien-1-one (10b): ^{1}H NMR ($CDCl_3$, T = 264 K) δ 7.69 (d, J = 2.5 Hz, 1H), 7.36 (d, J = 2.5 Hz, 1H), 6.39 (s, 2H), 3.29 (s, 3H), 1.27 (s, 18H); ^{13}C NMR (T = 263 K) δ 185.1 (s), 172.9 (s), 154.4 (s), 149.3 (s), 140.1(d), 139.2 (s), 137.0 (s), 136.0 (d), 125.7(d), 88.0 (s), 50.8 (q), 35.2 (s), 29.2 (q). After recording the NMR spectra, either phenol **2ah**, **2i**, or **2c** was added. After 15 min, in the first two cases, only indophenol **3e** was obtained, but the reaction of **2c** and **10b** gave a mixture of indophenols **3e** and **3b** (1:2.5). The reaction of **10b** with **2ah** and **2c** was carried out in water, too: the dry residue, obtained on evaporation of the hexane solution, was dissolved in tetrahydrofuran (60 mL), water (400 mL) and $Na_2B_4O_7$ (0.05 M, 50 mL) were added, this solution was halved, and either **2ah** or **2c** (10 mg) in THF (2 mL) was added. After 15 or 50 min, the reaction mixture was processed the known way to record the ^{1}H NMR spectra. In both cases only indophenol **3e** was formed, and **3b** could not be detected.

Reaction of 2-*tert*-Butyl-4-methoxyphenol (2i) with 1b. Method a: The same procedure as described for the reaction of **2f** and **1b** was applied using a solution of **1b** (42 mg, 0.2 mmol) in acetonitrile (10 mL), a solution of $Na_2B_4O_7$ (225 mL, 6×10^{-3} M), and a solution of **2i** (144 mg, 0.8 mmol) in acetonitrile (20 mL) with 10 min reaction time. The molar ratio of the products **3g**:**7b**:**8a** was 4:3:1 by ^{1}H NMR. Subsequently, the TCE solution was diluted with dichloromethane (50 mL), washed with NaOH (0.1 M, 2 × 70 mL) and water (2 × 60 mL), dried, and evaporated at reduced pressure to dryness. **7b** and **8a** were separated by column chromatography (1:1 benzene/hexane). **3g** was isolated from the alkaline solution after neutralization and subsequent extraction with dichloromethane. **7b**: ^{1}H NMR ($CDCl_3$) δ 6.96 (d, J = 3.0 Hz, 2H), 6.62 (d, J = 3.0 Hz, 2H), 5.02 (s, OH, 2H), 3.77 (s, 6H), 1.43 (s, 18H); ^{13}C NMR δ 153.2 (s), 145.9 (s), 138.9 (s), 123.2 (s), 115.3 (d), 111.8 (d), 55.8 (q), 35.2 (s), 29.5 (q). **8a**: ^{1}H NMR ($CDCl_3$) δ 6.96 (d, J = 2,9 Hz, 1H), 6.75 (d, J = 8,8 Hz, 1H), 6.66 (dd, J = 8.8, 2.9 Hz, 1H), 6.59 (d, J = 2,9 Hz, 1H), 6.18 (d, J = 2.9 Hz, 1H), 5.60 (s, OH), 3.80 (s, 3H), 3.64 (s, 3H), 1.44 (s, 9H), 1.42 (s, 9H); ^{13}C NMR δ 155.5 (s), 152.1 (s), 148.9 (s), 145.2 (s), 142.2 (s), 140.1 (s), 137.3 (s), 120.6 (d), 113.9 (d), 110.9 (d), 107.2 (d), 101.0 (d), 55.7 (q), 55.6 (q), 35.0 (s), 34.9 (s), 30.3 (q), 29.4 (q). **3g**: ^{1}H NMR ($CDCl_3$, mixture of Z and E isomers) δ 7.08 (6.92) (d, J = 2.8 Hz, 1H), 6.98 (7.12) (dd, J = 9.9, 2.8 Hz, 1H), 6.87 (6.90) (s, 2H), 6.49 (6.58) (d, J = 9.9 Hz, 1H), 1.32 (1.23) (s, 9H). If the molar ratio of **2i** and **1b** was not 4:1 but 2.5:1 in the reaction mixture, **9** was also formed besides **7b** and **8a** (**7b**:**8a**:**9** ≈ 5:1:2). **9**: ^{1}H NMR ($CDCl_3$) δ 6.99 (d, J = 3.0 Hz, 1H), 6.72 (d, J = 2.5 Hz, 1H), 6.67 (d, J = 2.5 Hz, 1H), 6.50 (d, J = 3.0 Hz, 1H), 6.26 (s, OH), 3.77 (s, 3H), 1.44 (s, 9H), 1.34 (s, 9H); ^{13}C NMR δ 189.7 (s), 187.9 (s), 157.0 (s), 153.5 (s), 149.3 (s), 146.1 (s), 141.1 (s), 135.0 (d), 131.7 (d), 124.8 (s), 116.7 (d), 112.3 (d), 55.7 (q), 35.7 (s). 35.2 (s), 29.8 (q), 29.3 (q). **Method b**: The same procedure as described for the reaction of **2f** and **1b** was applied using a solution of **1b** (42 mg, 0.2 mmol) in acetonitrile (10 mL), a solution of $Na_2B_4O_7$ (225 mL, 6×10^{-3} M), and a solution of **2i** (36 mg, 0.2 mmol) in acetonitrile (20 mL) with 2–3 min reaction time. The hexane layer was washed with Na_2CO_3 solution (0.1 M, 2 × 100 mL) and water (2 × 50 mL). After drying, the organic layer was concentrated to 4–5 mL at reduced pressure, TCE was added, and the residual hexane was removed by evaporation. **3g** was isolated from the carbonate solution after neutralization and subsequent extraction with dichloromethane. (Assignment: see under method a). Without washing the solution with Na_2CO_3, the molar ratio of the products **1b**:**3g**:**10a** was 2:5:4 by ^{1}H NMR, in TCE. **2-(1,1-Dimethylethyl)-4-methoxy-4-[(3,5-dichloro-4-oxo-2,5-cyclohexadienyl)-imino]-2,5-cyclohexadien-1-one (10a)**: ^{1}H NMR δ 7.82 (d, J = 2.5 Hz, 1H), 7.38 (d, J = 2.5 Hz, 1H), 6.63 (dd, J = 9.9, 3.0 Hz, 1H), 6.42 (d, J = 3.0 Hz, 1H), 6.35 (d, J = 9.9 Hz, 1H), 3.32 (s, 3H), 1.26 (s, 9H); ^{13}C NMR (T = 268 K) δ 184.7 (s),

173.0 (s), 154.8 (s), 148.0 (s), 142.3 (d), 140.4 (d), 139.2 (s), 138.7 (d), 136.8 (s), 131.8 (d), 126.2 (d), 88.1 (s), 51.2 (q), 34.8 (s), 28.8 (q). An experiment was also performed without working up the aqueous solution after standing for 2–3 min, but **2i** (40 mg, 0.22 mmol) in acetonitrile (20 mL) was added instead. Then the reaction mixture was processed in the usual way after 10 min. The recorded ^{1}H NMR spectra indicated the presence of **3g**, **7b**, and **8a**, suggesting that the redox reaction of **10a** and **2i** also yielded **7b** and **8a** in addition to **3g**. (When **2i** was added to the solution containing compound **10a**, and monitored by ^{1}H NMR, only **10a** reacted with the phenol derivative added, while **1b** did not. In TCE solution, compounds **3g**, **7b**, and **8a** formed).

Reaction of 4-Methoxyphenol (2h) with 1b. To a solution of **1b** (21 mg, 0.1 mmol) in acetonitrile (10 mL) were added a solution of $Na_2B_4O_7$ (225 mL, 6×10^{-3} M) and then a solution of **2h** (25 mg, 0.2 mmol) in acetonitrile (10 mL). After 20 min the reaction mixture was extracted with hexane (100 mL) and, after neutralization with HCl (3.3 mL, 1 M), with dichloromethane (2×80 mL). The dichloromethane layer was dried and evaporated. **3f** and **7a** were separated from this residue by prep TLC (silica, diisopropyl ether). **7a**: ^{1}H NMR ($CDCl_3$) δ 6.96 (d, J = 8.8 Hz, 2H), 6.86 (dd, J = 8.8, 2.9 Hz, 2H), 6.81 (d, J = 2.9 Hz, 2H) 5.7–5.2 (OH, 2H), 3.80 (s, 6H); ^{13}C NMR δ 154.2 (s), 146.6 (s), 124.9 (s), 117.7 (d), 115.9 (d), 115.5 (d), 55.8 (q).

Reaction of Hydroquinone 4-Methoxybenzyl Ether (2j) with 1b. To a solution of **1b** (53 mg, 0.25 mmol) in *tert*-butyl alcohol (15 mL) were added a solution of $Na_2B_4O_7$ (225 mL, 6×10^{-3} M) and then a solution of **2j** (58 mg, 0.25 mmol) in *tert*-butyl alcohol (15 mL). After 50 min the reaction mixture was extracted with dichloromethane as described for the preparation of **5** then the organic layer was washed with Na_2CO_3 (0.1 M, 100 mL) and water (2×60 mL), dried, and then processed as described for **5**. **3f** was isolated from the carbonate solution by neutralization and extraction with dichloromethane. In this case, 4-methoxybenzyl alcohol (**31**) deriving from the *para* leaving group could be detected. Before washing the solution with Na_2CO_3, the molar ratio of the products **3f**:**31**:**10c**:**1b** was 1:1.1:0.5:0.5 by ^{1}H NMR, in TCE. **31**: ^{1}H NMR δ 7.27 (d, J = 9.5 Hz, 2H), 6.90 (d, J = 9.50 Hz, 2H), 4.58 (s, 2H), 3.78 (s, 3H); ^{13}C NMR δ 158.7 (s), 132.8 (s), 128.8 (d), 113.7 (d), 64.7 (t), 55.3 (q). **3f**: ^{1}H NMR (2:1 mixture of tautomers **3fa** and **3fb**) **4-[(3,5-dichloro-4-hydroxyphenyl)imino]-2,5-cyclohexadien-1-one (3fa)**: δ 7.27 (dd, J = 10.0, 2.6 Hz, 1H), 7.11 (dd, J = 10.3, 2.6 Hz, 1H), 6.92 (s, 2H), 6.70 (dd, J = 10.0, 2.6 Hz, 1H), 6.60 (dd, J = 10.3, 2.6 Hz, 1H); **2,6-dichloro-4-[(4-hydroxyphenyl)imino]-2,5-cyclohexadien-1-one (3fb)**: δ 7.57 (d, J = 2.4 Hz, 1H), 7.42 (d, J = 2.4 Hz, 1H), 6.95 (s, 4H); **4-[(4-methoxybenzyl)oxy]-4-[(3,5-dichloro-4-oxo-2,5-cyclohexadienyl)imino]-2,5-cyclohexadien-1-one (10c)**: ^{1}H NMR δ 8.00 (d, J = 2.5 Hz, 1H), 7.34 (d, J = 2.5 Hz, 1H), 7.23 (d, J = 9.5 Hz, 2H), 6.87 (d, J = 9.5 Hz, 2H), 6.79 (d, J = 10.0 Hz, 2H), 6.42 (d, J = 10.0 Hz, 2H), 4.50 (s, 2H), 3.79 (s, 3H); ^{13}C NMR (T = 265 K) δ 184.6 (s), 173.1 (s), 159.2 (s), 155.7 (s), 145.2 (d), 140.4 (s), 139.4 (d), 137.0 (d), 129.8 (d), 129.7 (d), 128.6 (s), 126.6 (s), 113.8 (d), 87.0 (s), 66.3 (t), 55.4 (q). If phenol **2j** was added to the solution containing compound **10c**, according to ^{1}H NMR, in addition to **3f** and **31**, several unidentified compounds giving methylene signals were formed, resulting probably from the reactions of the oxidized phenols formed in the TCE solution. (Only **10c** reacts with the phenol derivative added to the solution under these circumstances; **1b** does not). The finding that **3f** and **31** were formed in a molar ratio of 1:1, similarly to the reaction carried out in aqueous solution, suggested that the oxidized phenol failed to yield **31**.

Reaction of 4-Methylphenol (2l) with 1b. The same procedure as described for the reaction of **2f** and **1b** was applied using a solution of **1b** (126 mg, 0.6 mmol) in acetonitrile (20 mL), a solution of $Na_2B_4O_7$ (225 mL, 6×10^{-3} M), and a solution of **2l** (22 mg, 0.2 mmol) in acetonitrile (5 mL) with 5 min reaction time. **2,6-Dichloro-4-[(1-methyl-4-oxo-2,5-cyclohexadienyl)imino]-2,5-cyclohexadien-1-one (10d)**: ^{1}H NMR δ 7.34 (d, J = 2.5 Hz, 1H), 7.24 (d, J = 2.5 Hz, 1H), 7.05 (d, J = 10.0 Hz, 2H), 6.37 (d, J = 10.0 Hz, 2H), 1.80 (s, 3H); ^{13}C NMR δ 184.4 (s), 172.8 (s), 157.8 (s), 152.3 (d), 140.4 (d), 139.8 (s), 136.7 (s), 127.1 (d), 123.7 (d), 62.8 (s), 31.5 (q). **1b**: ^{1}H NMR δ 7.99 (d, J = 2.5 Hz, 1H), 7.51 (d, J = 2.5 Hz, 1H); ^{13}C NMR δ 172.8 (s), 165.1 (s), 141.5 (s), 136.1 (s), 134.5 (d), 124.4 (d). Signals of **1b** were verified by adding more **1b** to the solution recorded.

Reaction of 2,4-Dimethylphenol (2m) with 1b. The same procedure as described for the reaction of **2f** and **1b** was applied using a solution of **1b** (126 mg, 0.6 mmol) in acetonitrile (20 mL), a solution of $Na_2B_4O_7$ (225 mL, 6×10^{-3} M), and a solution of **2m** (24 mg, 0.2 mmol) in acetonitrile (5 mL) with 5 min reaction time. **2,6-Dichloro-4-[(1,3-dimethyl-4-oxo-2,5-cyclohexadienyl)imino]-2,5-cyclohexadien-1-one (10e)**: ^{1}H NMR δ 7.34 (d, J = 2.5 Hz, 1H), 7.24 (d, J = 2.5 Hz, 1H), 7.02 (dd, J = 9.9, 3.3 Hz, 1H), 6.80 (sextet, J = 3.3, 1.5 Hz, 1H), 6.35 (d, J = 9.9 Hz, 1H), 1.95 (d, J = 1.5 Hz, 3H), 1.78 (s, 3H); ^{13}C NMR δ 185.0 (s), 172.8 (s), 157.4 (s), 152.1 (d), 147.6 (d), 140.5 (d), 139.5 (s), 136.5 (s), 133.8 (s), 126.8 (d), 123.9 (d), 63.1 (s), 31.6 (q), 15.7 (q).

Reaction of 2,6-Di-*tert*-butyl-4-methylphenol (2n) with 1b. The same procedure as described for the reaction of **2f** and **1b** was applied using a solution of **1b** (63 mg, 0.3 mmol) in acetonitrile (10 mL), a solution of $Na_2B_4O_7$ (225 mL, 6×10^{-3} M), and a solution of **2n** (24 mg, 0.1 mmol) in acetonitrile (5 mL) with 5 min reaction time. **2,6-Dichloro-4-[(3,5-bis(1,1-dimethylethyl)-1-methyl-4-oxo-2,5-cyclohexadienyl)imino]-2,5-cyclohexadien-1-one (10f)**: ^{1}H NMR δ 7.32 (d, J = 2.5 Hz, 1H), 7.26 (d, J = 2.5 Hz, 1H), 6.64 (s, 2H), 1.72 (s, 3H), 1.23 (s, 18H); ^{13}C NMR δ 185.3 (s), 172.9 (s), 157.4 (s), 144.6 (d), 143.6 (d), 140.4 (d), 138.6 (s), 136.4 (s), 124.3 (d), 62.4 (s), 34.6 (s), 31.7 (q), 29.0 (q).

Reaction of 3,4-Dimethylphenol (2o) with 1b. The same procedure as described for the reaction of **2f** and **1b** was applied using a solution of **1b** (126 mg, 0.6 mmol) in acetonitrile (20 mL), a solution of $Na_2B_4O_7$ (225 mL, 6×10^{-3} M), and a solution of **2o** (24 mg, 0.2 mmol) in acetonitrile (5 mL) with 5 min reaction time. **2,6-Dichloro-4-[(1,2-dimethyl-4-oxo-2,5-cyclohexadienyl)imino]-2,5-cyclohexadien-1-one (10g)**: ^{1}H NMR δ 7.37 (d, J = 2.5 Hz, 1H), 7.11 (d, J = 2.5 Hz, 1H), 6.99 (d, J = 10.0 Hz, 1H), 6.32 (dd, J = 10.0, 1.7 Hz, 1H), 6.21 (quintet, J = 1.7, 1.4 Hz, 1H), 1.92 (d, J = 1.4 Hz, 3H), 1.83 (s, 3H); ^{13}C NMR δ 184.8 (s), 172.7 (s), 163.4 (s), 158.0 (s), 152.6 (d), 140.2 (s), 140.1 (d), 136.6 (s), 126.7 (d), 126.2 (d), 123.0 (d), 65.1 (s), 31.2 (q), 19.2 (q).

Reaction of 2,4,6-Trimethylphenol (2p) with 1b. The same procedure as described for the reaction of **2f** and **1b** was applied using a solution of **1b** (126 mg, 0.6 mmol) in acetonitrile (20 mL), a solution of $Na_2B_4O_7$ (225 mL, 6×10^{-3} M), and a solution of **2p** (26 mg, 0.2 mmol) in acetonitrile (5 mL) with 5 min reaction time. **2,6-Dichloro-4-[(1,3,5-trimethyl-4-oxo-2,5-cyclohexadienyl)imino]-2,5-cyclohexadien-1-one (10h)**: ^{1}H NMR δ 7.27 (d, J = 2.5 Hz, 1H), 7.18 (d, J = 2.5 Hz, 1H), 6.75 (s, 2H), 1.89 (s, 6H), 1.70 (s, 3H); ^{13}C NMR δ 185.6 (s), 172.8 (s), 156.9 (s), 147.4 (d), 140.5 (d), 139.1(s), 136.2 (s), 133.2 (s), 124.0 (d), 62.8 (s), 31.6 (q), 15.8 (q).

Reaction of 2,4,6-Tri-*tert*-butylphenol (2q) with 1b. The same procedure, but under argon atmosphere as described for the reaction of **2f** and **1b** was applied using solutions being kept under argon gas flow for 30 min before the reaction, of **1b** (106 mg, 0.5 mmol) in acetonitrile (15 mL), $Na_2B_4O_7$ (225 mL, 6×10^{-3} M) and **2q** (39 mg, 0.15 mmol) in acetonitrile (25 mL) with 25 min reaction time (**1b**:**10i**:**12b** $\approx$ 1:0.22:0.18 by ^{1}H NMR). **2,6-Dichloro-4-{[1,3,5-tris(1,1-dimethylethyl)-4-oxo-2,5-cyclohexadienyl]imino}-2,5-cylohexadien-1-one (10i)**: ^{1}H NMR (T = 278 K) δ 7.40 (d, J = 2.5 Hz, 1H), 7.25 (d, J = 2.5 Hz, 1H), 6.53 (s, 2H), 1.21 (s, 18H), 1.00 (s, 9H); ^{13}C NMR (T = 278 K) δ 185.7 (s), 173.2 (s), 157.8 (s), 146.6 (s), 141.8 (d), 140.9 (d), 138.2 (s), 136.0 (s, overlapping a signal of **1b**), 124.7 (d), 70.0 (s), 42.5 (s), 35.0 (s), 29.1 (q), 25.6 (q). **2,6-Dichloro-4-{[1,3,5-tris(1,1-dimethylethyl)-6-oxo-2,4-cyclohexadienyl]imino}-2,5-cyclohexadien-1-one (12b)**: ^{1}H NMR (T = 278 K) δ 7.43 (d, J = 2.5 Hz, 1H), 7.04 (d, J = 2.4 Hz, 1H), 6.34 (d, J = 2.5 Hz, 1H), 5.93 (d, J = 2.4 Hz, 1H), 1.23 (s, 9H), 1.13 (s, 9H), 0.98 (s, 9H); ^{13}C NMR (T = 278 K) δ 203.8 (s), 173.3 (s), 157.3 (s), 144.4 (s), 141.5 (s, overlapping a signal of **1b**), 140.4 (d), 138.1 (s), 135.9 (d), 135.8 (s), 132.7

(d), 126.6 (d), 79.3 (s), 42.4 (s), 34.8 (s), 34.3 (s), 29.1 (q, overlapping a signal of **10i**), 28.5 (q), 24.8 (q). During overnight standing of the solution monitored by NMR on ambient temperature, besides 10% decomposition of **10i**, *ortho* adduct **12b** transformed into *o*-indophenol **14a** with formation of 2-methylpropene (**13**), confirmed by adding it to the recorded solution. **2,6-Dichloro-4-{[3,5-bis(1,1-dimethylethyl)-2-hydroxyphenyl]imino}-2,5-cyclohexadien-1-one (14a)**: ^{1}H NMR δ 7.71 (d, J = 2.5 Hz, 1H), 7.57 (d, J = 2.5 Hz, 1H), 7.40 (d, J = 2.2 Hz, 1H, overlapping a signal of **10i**), 6.71 (d, J = 2.2 Hz, 1H), 1.42 (s, 9H), 1.31 (s, 9H); ^{13}C NMR (T = 278 K) δ 173.4 (s), 151.2 (s), 150.3 (s), 142.4 (s), 139.3 (s), 138.9 (d), 136.2 (s), 136.1 (s), 135.2 (s), 128.2 (d), 126.8 (d), 116.5 (d), 34.9 (s), 34.3 (s), 31.6 (q), 29.1 (q, overlapping a signal of **10i**). **13**: ^{1}H NMR (T = 278 K) δ 4.65 (septet, J = 1.1 Hz, 2H), 1.72 (t, J = 1.1 Hz, 6H); ^{13}C NMR (T = 278 K) δ 142.7 (s), 110.6 (t), 24.2-(q). *o*-Indophenol **14a** cyclized into **11c** during PTLC (silica, chloroform). After PTLC, red **11c** was eluted from the silica with chloroform, dissolved in hexane (40 mL), washed with NaOH (1 M, 4 × 40 mL) and water (2 × 40 mL), and then evaporated. **11c**: ^{1}H ($CDCl_3$) δ 7.75 (d, J = 2.4 Hz, 1H), 7.73 (s, 1H), 7.71 (d, J = 2.4 Hz, 1H), 1.58 (s, 9H), 1.40 (s, 9H); ^{13}C NMR (relaxation delay* was 15 s) δ 172.4 (s), 149.1 (s), 144.9 (s), 144.6 (s), 140.1 (s), 139.9 (s), 137.6 (s), 133.6 (s), 130.6 (d), 129.6 (d), 125.5 (d), 112.2* (s), 35.2 (s), 35.0 (s), 31.3 (q), 29.6 (q). If oxygen was not removed from the solvents applied in the reaction, **15** and **16** were also formed besides **10i** and **12b** (**10i**:**12b**:**15**:**16** ≈ 5:3:2:1 by ^{1}H NMR). **15**: ^{1}H NMR δ 6.72 (s, 4H). **16**: ^{1}H NMR δ 6.86 (d, J = 2.7 Hz, 1H), 6.84 (d, J = 2.5 Hz, 1H), 6.68 (d, J = 2.7 Hz, 1H), 6.11 (d, J = 2.5 Hz, 1H). (Compounds **15** and **16** were also prepared by a different route[64]).

Reaction of 2,6-Dimethyl-4-*tert*-butylphenol (2s) with 1b. The same procedure as described for the reaction of **2f** and **1b** was applied using a solution of **1b** (32 mg, 0.15 mmol) in acetonitrile (15 mL), a solution of $Na_2B_4O_7$ (225 mL, 6 × 10^{-3} M), and a solution of **2s** (9 mg, 0.05 mmol) in acetonitrile (5 mL) with 15 min reaction time. **12a** rapidly decomposes; thus, the ^{1}H NMR measurement has to be carried out immediately after processing. Assignment of **3b**: see under the reaction of **2c** and **1b** (**3b**:**12a** ≈ 1:2 by ^{1}H NMR). **2,6-Dichloro-4-{[1,5-dimethyl-3-(1,1-dimethylethyl)-6-oxo-2,4-cyclohexadienyl]imino}-2,5-cyclohexadien-1-one (12a)**: ^{1}H NMR δ 7.42 (d, J = 2.5 Hz, 1H), 7.14 (sextet, J = 2.4, 1.4 Hz, 1H), 6.37 (d, J = 2.5 Hz, 1H), 6.02 (d, J = 2.4 Hz, 1H), 1.99 (d, J = 1.4 Hz, 3H), 1.72 (s, 3H), 1.16 (s, 9H).

Reaction of 4-*tert*-Butylphenol (2r) with 1b. The same procedure as described for the reaction of **2j** and **1b** was applied using a solution of **1b** (63 mg, 0.3 mmol) in acetonitrile (15 mL), a solution of $Na_2B_4O_7$ (225 mL, 6 × 10^{-3} M), and a solution of **2r** (340 mg, 2.25 mmol) in acetonitrile (15 mL) with 60 min reaction time but without adding TCE. The residue obtained on evaporation was dissolved in hexane (40 mL) and extracted first with NaOH (1 M, 2 × 30 mL) and then with water (2 × 20 mL). Compounds **11a** and **11d** were separated by column chromatography (silica, benzene). The fraction containing **11a** was rechromatographed (1:1 benzene/chloroform to remove the residual **2r**). **3f** was isolated from the carbonate solution by neutralization and extraction with dichloromethane and then purification by column chromatography applying first benzene and then 9:1 benzene/ethanol as eluant to remove **2r** (**3f**:**11a**:**11d** ≈ 10:1:1). **11a**: ^{1}H NMR ($CDCl_3$) δ 7.87 (d, J = 2.3 Hz, 1H), 7.72 (s, 1H), 7.72 (dd, J = 8.7, 2.3 Hz, 1H), 7.47 (d, J = 8.7 Hz, 1H), 1.41 (s, 9H); ^{13}C NMR δ 172.5 (s), 150.2 (s), 145.7 (s), 145.1 (s), 141.4 (s), 139.9 (s), 133.1 (s), 131.7 (d), 131.0 (d), 127.1 (d), 116.0 (d), 112.9 (s), 34.8 (s), 31.3 (q). **11d**: ^{1}H NMR ($CDCl_3$) δ 7.89 (d, J = 2.4 Hz, 1H), 7.77 (s, 1H), 7.70 (dd, J = 8.7, 2.4 Hz, 1H), 7.67 (d, J = 2.5 Hz, 1H), 7.38 (d, J = 8.7 Hz, 1H), 6.89 (d, J = 2.5 Hz, 1H), 1.40 (s, 9H); ^{13}C NMR δ 173.3 (s), 170.2 (s), 159.0 (s), 150.2 (s), 146.0 (s), 141.6 (s), 139.3 (s), 138.6 (d), 138.5 (s), 138.2 (s), 137.4 (s), 133.6 (s), 131.9 (d), 131.1 (d), 127.4 (d), 127.2 (d), 126.0 (s), 116.0 (d), 34.8 (s), 31.2 (q).

Reaction of 1b with Sodium Phenolate. Method a: After adding a solution of sodium salt of **2a** (24 mg, 0.21 mmol), dissolved by warming and cooling, in DMSO-d_6 (1.2 mL) to a solution of **1b** (52 mg, 0.25 mmol) in DMSO-d_6 (0.3 mL), the ^{1}H-NMR spectra of this mixture was recorded immediately. **18a**: ^{1}H NMR δ 7.77 (d, J = 2.5 Hz, 1H), 7.56 (t, J = 8.1 Hz, 2H), 7.38 (t, J = 8.1 Hz, 1H), 7.29 (d, J = 8.1 Hz, 2H), 6.50 (d, J = 2.5 Hz, 1H). Besides **18a**, indophenol **3f** was also formed but their ratio was determined by chromatography because signals of **3f** were broad and flat. After recording the ^{1}H NMR spectra, to this solution was added HCl solution (30 mL, 10^{-4} M) and then extracted with dichloromethane (50 mL, 20 mL). The organic solution was washed with water (2 × 30 mL), dried, and evaporated. **18a** and **3f** were separated by column chromatography. Firstly **18a** was obtained (3:2 dichloromethane/hexane, R_f 0.55) and then **3f** was eluted (dichloromethane, R_f 0.25). The ratio of **18a**:**3f** was 96:4. **Method b**: To a solution of the sodium salt of **2a** (6 mg, 0.05 mmol) and 18-crown-6 (28 mg, 0.1 mmol) in acid-free chloroform-*d* (0.3 mL) was poured a solution of **1b** (13 mg, 0.06 mmol) in chloroform-*d* (0.3 mL), and the ^{1}H NMR spectra of this solution was recorded immediately. **3f**: ^{1}H NMR δ 7.33 (d, J = 9.9 Hz, 2H), 7.27 (s, 2H) 6.57 (d, J = 9.9 Hz, 2H).

Preparation of *O*-Phenyl-2,6-dichloroquinone 4-Oxime (19b). *O*-Phenylhydroxylamine hydrochloride[65] (1240 mg, 8.5 mmol) was added to a solution of sodium ethoxide (0.04 M, 21.3 mL) at −30 °C. Sodium chloride was filtered off and washed with cold ethanol (5 mL). This solution was added to a hot solution of 2,6-dichloroquinone (1504 mg, 8.5 mmol in ethanol (20 mL). Thereafter, HCl−ethanol (1 mL, 10%) was added dropwise to the solution, which initiated the precipitation of the product. The mixture was cooled and filtered and the product was recrystallized from ethanol (320 mg yellow needles, sensitive to light, mp 167−168 °C). **19b**: ^{1}H NMR ($CDCl_3$) δ 8.07 (d, J = 2.5 Hz, 1H), 7.53 (d, J = 2.5 Hz, 1H), 7.39 (t, J = 7.8 Hz, 2H), 7.30 (d, J = 7.8 Hz, 2H), 7.18 (t, J = 7.8 Hz, 1H); ^{13}C NMR δ 173.2 (s), 158.3 (s), 148.3 (s), 139.0 (s), 135.1 (s), 133.6 (d), 129.6 (d), 124.8 (d), 122.1 (d), 114.9 (d). Anal. Calcd for $C_{12}H_7NO_2Cl_2$: C, 53.76; H, 2.63; N, 5.22; Cl, 26.45. Found: C, 53.67; H, 2.56; N, 5.11; Cl, 26.39.

Photoizomerization of 19b. A mixture of a solution of **19b** (15 mg, 0.06 mmol) in acetonitrile (70 mL) and $Na_2B_4O_7$ (125 mL, 0.01 M) was irradiated for 20 min using a 125 W Philips HPK BA 15D immersion lamp with an S-shaped vessel. To this mixture was added water (100 mL) and then neutralized with HCl (3.3 mL, 1 M) and extracted with dichloromethane (100 mL + 50 mL). The organic layer was washed with water, dried, and evaporated at reduced pressure. According to the ^{1}H NMR spectra of this residue in $CDCl_3$, only **2a**, **3f**, and **11b** were observed. The ratio of **2a**:**3f**:**11b** was 1.6:2:1. After recording the NMR spectra, dichloromethane (25 mL) was added, washed with NaOH (3 × 25 mL, 0.1 M) and water (2 × 20 mL), dried, and then evaporated. **11b**: ^{1}H NMR ($CDCl_3$) δ 7.89 (dd, J = 7.9, 1.5 Hz, 1H), 7.73 (s, 1H), 7.66 (ddd, J = 8.6, 8.4, 1.5 Hz, 1H), 7.54 (dd, J = 8.4, 1.4 Hz, 1H), 7.47 (ddd, J = 8.6, 7.9, 1.4 Hz, 1H).

Reaction of 3,5-Di-*tert*-butylphenol (2t) with 1g. The same procedure as described for the reaction of **2j** and **1b** was applied using a solution of **1g**[66] (42 mg, 0.16 mmol) in acetonitrile (25 mL), a solution of $Na_2B_4O_7$ (225 mL, 6 × 10^{-3} M), and a solution of **2t** (124 mg, 0.6 mmol) in acetonitrile (10 mL) with 70 min reaction time, but the hexane layer was washed with NaOH (0.1 M, 3 × 100 mL) before washing with water. The mixture of **11e** and **11f** (their ratio was 3:5) was purified by column chromatography (95:5 benzene/acetone, silica). **11e**: ^{1}H NMR ($CDCl_3$) δ 7.42 (d, J = 2.0 Hz, 1H), 7.22 (d, J = 2.0 Hz, 1H), 7.06 (d, J = 2.0 Hz, 1H), 6.26 (d, J = 2.0 Hz, 1H), 1.61 (s, 9H), 1.38 (s, 9H). **11f**: ^{1}H NMR ($CDCl_3$) δ 7.80 (d, J = 2.4 Hz, 1H), 7.64 (d, J = 2.4 Hz, 1H), 7.10 (d, J = 2.0 Hz, 1H), 6.35 (d, J = 2.0 Hz, 1H), 1.49 (s, 9H), 1.39 (s, 9H). The presence of **11f** prepared by a different way, by the reaction of **2al** and **1g**, was verified by adding it to the measured solution.

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(66) **1g** was contaminated by 10% of 2,6-dichlorobenzoquinone.

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Supplementary Material Available: Copies of ^{1}H and/or ^{13}C NMR spectra of all compounds and the Job plots of the Gibbs reaction of **1b** with **2b**, **2c** and **2k**. (72 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.