One-electron oxidation of enol phosphates, enol phosphites and enol phosphinates. Evidence for an unprecedented P–O bond cleavage in phosphoenol radical cations in solution[1]

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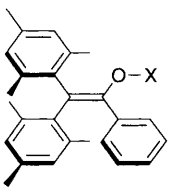
For the first time phosphoenol radical cations are generated in solution and monitored by cyclic voltammetry and EPR; the sterically congested radical cations undergo an unprecedented P–O bond cleavage, the kinetics of which are determined.

In the context of one-electron oxidation chemistry[2,3] enol type radical cations C=C–OX$^{\bullet+}$ have received ample attention.[4] With various groups X (X = H, alkyl, COMe, SiR_3, SnR_3 *etc.*)[4] they constitute important intermediates in the α-umpolung of ketones and aldehydes,[5] in synthetically useful cyclisations[6] and dimerisations[7] and in redox-triggered protection group chemistry.[8] In addition, they are considered to play an important role in the ribonucleotide reductase mechanism.[9] For all the transformations cited above the bond cleavage of C=C–O–X$^{\bullet+}$ into fragments C=C–O$^{\bullet}$ and X$^+$ or C=C–O$^+$ and X$^{\bullet}$, the so-called mesolytic cleavage,[10] is a process of paramount importance since it often limits the lifetime of the odd-electron species.

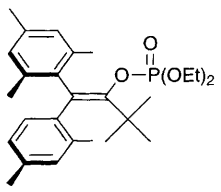
Intriguingly, even for such seemingly simple radical cations there is little direct study of their reactivity in solution. The kinetics of O–H,[11] O–C(O)R[12] and O–SiR_3[13] bond cleavage in the corresponding enol radical cations (X = H, COMe, SiR_3) in solution have only recently been investigated, the last of which has been recognised to constitute a case of a nucleophile-induced bond cleavage process. As a consequence, the bond scission rate constant could be readily fine tuned over more than five orders of magnitude.[13]

Herein, we present our results on the mesolytic O–P bond cleavage in phosphoenol radical cations, constituting the first examples of such a process. As model compounds we have chosen the sterically congested enol derivatives **1–5**. Due to the steric hindrance about the β-carbon exerted by the mesityl groups, side reactions of the radical cations, in particular dimerisation and attack by nucleophiles, are completely excluded, which should allow the study of the P–O bond cleavage.

The phosphoenols were synthesised by functionalising the enols using a strong base and the appropriate phosphochloride.† 2,2-Dimesityl-1-phenylethenol[14] served as starting material for the preparation of model compounds **1–4**, whereas the synthesis of enol phosphate **5** commenced from 1-*tert*-butyl-2,2-dimesitylethenol.[14] The crude enol derivatives were purified by column chromatography‡ to afford the pure compounds in yields of 29–44%.



1 X = $PO(OEt)_2$
2 X = $PO(OPh)_2$
3 X = P(O)MePh
4 X = $P(OEt)_2$



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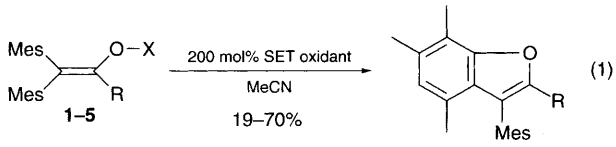
All the phosphoenols exhibited irreversible oxidation potentials in acetonitrile at v = 100 mV s^{-1} indicative of a rapid follow-up reaction. The corresponding anodic peak potentials E_{pa}, as obtained by cyclic voltammetry (CV), are given in Table 1. Characteristically, with all model compounds a decrease of $i_{pa}v^{-1/2}$ with increasing v was observed (i_{pa} = anodic current, v = sweep rate) indicative of an EC- or ECE-mechanism.[15] Analysis of the peak currents i_{pa} of the model compounds reveals that the irreversible oxidation waves contain two electrons, thus an ECE mechanism seems to be operative. In contrast, partially reversible waves were monitored for **1–3**, **5** at v = 100 mV s^{-1} in the less nucleophilic and less polar solvent dichloromethane.

In comparison with 2,2-dimesityl-1-phenylethenol (E_{pa} = 0.61 V *vs.* Fc)[16] and the trimethylsilyl substituted derivative thereof (E_{pa} = 0.65 V *vs.* Fc),[13] the oxidation peak potentials of **1–3**, **5** are significantly higher by 350–600 mV. This indicates a substantial electron-withdrawing effect exerted by the various $P(=O)X_2$ groups, present even in the corresponding phosphinate derivative. In contrast, the oxidation potential of enol phosphite **4** is at E_{pa} = 0.74 V *vs.* Fc, only 130 mV above that of the parent enol.

To understand the follow-up reactions, model compounds **1–5** were oxidised with an appropriately strong one-electron oxidant, *i.e.* with either $Fe(phen)_3(PF_6)_3$ [**Fephen**, phen = 1,10-phenanthroline, $E_{1/2}$ = 0.70 V *vs.* Fc (ferrocene/ferricenium)] or tris(*p*-nitrophenyl)aminium hexafluoroantimonate (**TNPA**, $E_{1/2}$ = 1.17 V *vs.* Fc). In all cases, the 4,6,7-trimethyl-3-mesitylbenzofuran derivatives **6** or **7**[17] were afforded as the main products in up to 70% yield, [eqn. (1)]. The conversion of



(1)

R = Ph, Bu^t Mes = mesityl **6** R = Ph **7** R = Bu^t

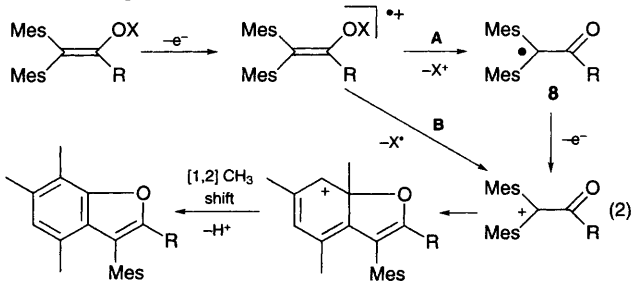
the oxidation reactions was kept low, in order to avoid follow-up oxidations of the benzofurans formed.

Table 1 Oxidation yields and oxidation potentials (*vs.* Fc) of compounds **1–5**

	Oxidations		Oxidation potentials	
Comp.	Oxidant	Yield (%) of benzofuran (conversion)	E_{pa}[a]/V	$E_{1/2}$[b]/V
1	**TNPA**	41 (46)	1.01	0.90
2	**TNPA**	19 (26)	1.10	0.87
3	**Fephen**	70 (69)	0.97	0.86
4	**Fephen**	46 (100)	0.74	0.66[c]
5	**TNPA**	64 (66)	1.22	1.00[c]

[a] Acetonitrile, 100 mV s^{-1}. [b] Dichloromethane, 100 mV s^{-1}. [c] E_{pa}.

Notably, the benzofurans **6** or **7** could be detected in the CV studies on the phosphoenols. In multiple sweep experiments, the oxidation waves of the benzofurans **6** (partially reversible; $E_{1/2}$ = 0.87 V) and **7** (reversible, $E_{1/2}$ = 0.93 V) showed up during the oxidation of compounds **1**, **2**, **3** and **5**, respectively. Benzofuran formation in the chemical and anodic oxidation of **1**–**5** is indicative of a P–O bond cleavage in the overall reaction. Hence, by analogy with mesolytic bond cleavage reactions in other enol radical cations,[11–13] we propose that P–O bond cleavage takes place at the stage of **1**$^{\bullet+}$–**5**$^{\bullet+}$ thereby generating the α-carbonyl cation **9** by two possible cleavage modes [paths **A** and **B** in eqn. (2)]. Formation of benzofurans from **9** can then



6 R = Ph
7 R = Bu^t

easily be rationalised.[12,13] In contrast, direct cyclisation at the stage of **1**$^{\bullet+}$–**5**$^{\bullet+}$ to finally yield **6** and **7**, respectively, is highly unlikely for steric reasons.

EPR measurements at −100 °C allowed the direct monitoring of radical cations **1**$^{\bullet+}$–**3**$^{\bullet+}$ generated from the phosphoenols by oxidation with O_2AsF_6 in $CHClF_2$. Unfortunately, only unresolved spectra (for *g* values see Table 2) were obtained precluding any structural information from being obtained. To probe directly the kinetic reactivity of **1**$^{\bullet+}$–**5**$^{\bullet+}$ we have recorded the cyclic voltammograms at scan rates up to 10000 V s^{-1}. Notably, the stability of the enol phosphite **4**$^{\bullet+}$ in acetonitrile is completely different from the four other model compounds. In acetonitrile only irreversible anodic waves were obtained at $v \leqslant$ 10000 V s^{-1} indicating a fast chemical step following the electrochemical oxidation, whereas the enol phosphates **1**, **2** and **5** display reduction waves beginning at v > 1.0 V s^{-1}. From the kinetic analysis[13] of the partially reversible oxidation waves, the rate of fragmentation of all radical cations was determined assuming an ECE mechanism. In dichloromethane, the same order of kinetic stability can be observed with all systems being more stable in dichloromethane. In this solvent, the enol phosphite radical cation **4**$^{\bullet+}$ actually displayed a reduction wave at high scan rates allowing for an estimation of the rate constant.

Altogether the kinetic results reveal a clear trend in the O–P bond cleavage rate constants: k (enol phosphate$^{\bullet+}$) < k (enol phosphinate$^{\bullet+}$) < k (enol phosphite$^{\bullet+}$). While all the enol phosphate radical cations exhibit very similar rate constants around k = 1 s^{-1}, the P–O bond in the enol phosphite **4**$^{\bullet+}$ is cleaved more rapidly by six orders of magnitude. At present, it is not entirely clear why the presence of a P=O group should stabilize the P–O bond against mesolytic fragmentation.

Table 2 Rate constants k_f/s^{-1} for the fragmentation of the phosphoenol radical cations and EPR data (*g* values)

Comp.	k_f^a/s^{-1}	k_f^b/s^{-1}	*g*
1	3.9×10^{-2}	0.9	2.0015
2	5.0×10^{-2}	0.7	2.0012
3	0.5[c]	5.8×10^{2}	2.0019
4	1.0×10^{4}	$>10^{5}$	Rapid decomp.
5	0.2[c]	1.1[c]	—

[a] In dichloromethane. [b] In acetonitrile. [c] In these cases, i_{pc}/i_{pa} is slightly susceptible to concentration indicative of an alternative decomposition pathway *via* the dication formed from disproportionation of two radical cations.

However, AM1 calculations[18] show that the homolytic bond dissociation energy (BDE) of the P–O bond in $PO(OMe)_3$ is higher than the one in $P(OMe)_3$ by about 85 kJ mol^{-1}. Assuming a similar BDE difference in the neutral enol phosphates as compared to the enol phosphite, one can derive from simple thermochemical cycle calculations,[12] using the different enol oxidation potentials in Table 1, that for the mesolytic cleavage of **1**$^{\bullet+}$, **2**$^{\bullet+}$, **5**$^{\bullet+}$ *vs.* **4**$^{\bullet+}$ this difference should be reduced to about 45 kJ mol^{-1}. Hence, thermochemical cycle considerations indeed suggest that the P–O bond in the enol phosphite$^{\bullet+}$ is easier to cleave than the one in the enol phosphate$^{\bullet+}$ in agreement with our kinetic results.

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Footnotes

† *Typical synthesis*: Preparation of **1**. A solution of 2,2-dimesityl-1-phenylethenol (1.1 mmol) in 5 cm^3 of anhydrous THF was slowly added to a suspension of NaH (1.1 mmol) in 4 cm^3 of anhydrous THF. The reaction mixture was stirred for 1 h, then diethyl chlorophosphate (1.4 mmol) was added. After heating to reflux for 19 h, the solvent was evaporated and the product was purified by column chromatography (silica gel, diethyl ether–cyclohexane, 2 : 1, R_f 0.53) yielding a pale yellow oil, which crystallised on standing.

‡ The new compounds **1**–**5** have been fully characterised by C, H elemental analysis, ^{1}H and ^{13}C NMR, IR and mass spectroscopy. *E.g.* for **1**: δ_H(200 MHz, C_6D_6) 7.86–7.95 (2 H, m, Ph-H), 6.99–7.15 (3 H m, Ph-H), 6.86 (2 H, br s, Mes-H), 6.72 (2 H, s, Mes-H), 3.55–4.10 (4 H, m, OCH_2CH_3), 2.23–2.88 (12 H, br s, Mes-*o*-CH_3), 2.22 (3 H, s, Mes-*p*-CH_3), 2.12 (3 H, s, Mes-*p*-CH_3), 1.01 (6 H, br s, OCH_2CH_3).

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