First Characterisation of Enol Carbonate and Enol Carbamate Radical Cations in Solution. Kinetics and Selectivity of the Mesolytic Cleavage of the O-CO Bond[1]

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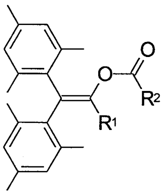
For the first time enol carbonate and enol carbamate radical cations are characterised in solution by CV and EPR; the sterically congested radical cations undergo an unprecedented mesolytic cleavage of the O–CO bond, the kinetics of which are determined.

While enol and enol O-X derivatives have already adopted a paramount standing in organic synthesis as versatile reactive nucleophiles,[2] the chemistry of the corresponding radical cations has still to be developed. It is to be expected that the radical cations promise a wealth of electrophilic reactivity,[3] although at present only a handful of interesting synthetic applications has been elaborated.[4-7] C-C bond formation with π-nucleophiles and enol radical cations as electrophiles can take place either at the stage of the radical cation itself or the α-carbonyl radical after mesolytic O-X-bond cleavage. Importantly, only the former should allow to run the reaction in an diastereoselective way (using X*), emphasising the importance of understanding the kinetics of mesolytic bond fragmentations.

As enol carbonates and carbamates could easily accomodate a chiral auxiliary for future stereoselective carbon-carbon bond formation processes, we now report on the first characterisation of such radical cations in solution and the kinetics of their mesolytic O-CO bond cleavage. As model compounds we have chosen the sterically congested enol derivatives **1a-c** and **2a,b** (Table 1.).[8] Due to the steric hindrance about the β-carbon exerted by the mesityl groups undesired side reactions of the radical cations, in particular dimerisation and attack by nucleophiles, are completely excluded, thus facilitating enormously the study of the O-CO bond cleavage.

The oxidation of **1a-c** and **2a,b** was first investigated by cyclic voltammetry (CV). All model compounds exhibit irreversible anodic peak potentials E_{pa} in acetonitrile at $v = 20 - 500$ mV s^{-1} indicative of a rapid follow-up reaction and a decrease of $i_{pa}v^{-1/2}$ with increasing v characteristic of an EC-mechanism.[10] In comparison with similar enol derivatives, the anodic peak potentials display a remarkable potential difference of $\Delta E_{pa} \approx 0.5$ V in the sequence: E_{pa} (carbamate **1a**) < E_{pa} (acetate **1d**) < E_{pa} (carbonate **1b**) < E_{pa} (carbonate **1c**) < E_{pa} (trifluoroacetate **1e**). Accordingly, enol carbamates with their low E_{pa} are best suited for preparative purposes as they allow for a selective oxidation in the presence of several other functional groups.

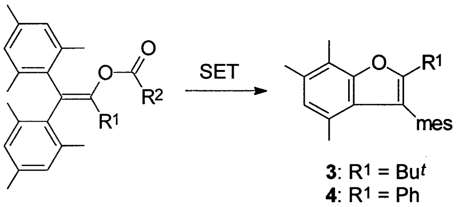
Table 1. Peak potentials (E_{pa}) of compounds **1** and **2**



R^1	R^2	Nr	E_{pa}/V^a	R^1	R^2	Nr	E_{pa}/V^a
Bu^t	NH-Bu^t	**1a**	1.02	Ph	NH-Bu^t	**2a**	0.99
Bu^t	O-Bu^t	**1b**	1.21	Ph	O-Bu^t	**2b**	1.06
Bu^t	O-CH$_2$Ph	**1c**	1.32				
Bu^t	CH$_3$	**1d**	1.16^b	Ph	CH$_3$	**2d**	1.04^b
Bu^t	CF$_3$	**1e**	1.51^c	Ph	CF$_3$	**2e**	1.26^c

^{a} in V *vs* Fc at 100 mV s^{-1} in CH$_3$CN/Bu$_4$NPF$_6$. ^{b} data from Ref.[9] ^{c} data from Ref.[1]

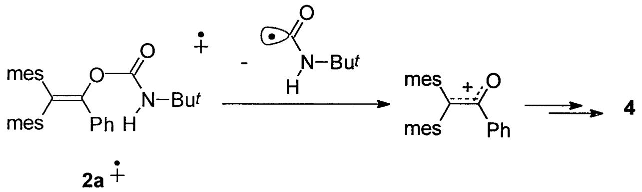
To understand their radical cation reactivity, model compounds **1a,b** and **2a,b** were oxidised with either thianthrenium perchlorate or Fe(phen)$_3$(PF$_6$)$_3$. In all cases, the benzofuran derivatives **3** or **4**[11] were afforded as exclusive products in 41 - 73 % yield. No products derived from nucleophilic attack in β–position[12] of the enol or from direct cyclisation reaction[1] of the radical cation could be detected.



3: R1 = Bu*t*
4: R1 = Ph

Notably, formation of benzofurans **3** or **4** could equally be detected in the CV studies. Both, enol carbamate **1a** as well as carbonates **1b,c** and **2b** showed an intriguing curve crossing in the reverse scan at slow scan rates (20 - 50 mV s^{-1}) caused by oxidation of electroactive follow-up products which are formed on the timescale of the experiment. In multisweep experiments, the oxidation waves of the benzofurans **3** ($E_{1/2} = 0.93$ V) and **4** ($E_{1/2} = 0.87$ V) showed up during the oxidation of compounds **1b,c** and **2b**, respectively. This interpretation of the CV experiments has been supported by digital simulation.[9,13]

For EPR characterisation, the enol radical cations were generated by oxidation of the neutral compounds with O$_2$AsF$_6$ in CHClF$_2$ at 130 K, since they decomposed at slightly elevated temperatures. For example, at 130 K the dark green radical cation **2a**$^{•+}$ exhibited an unresolved spectrum at $g = 2.0023$ but upon warming to ca. 200 K for a few seconds a sudden change to a dark violet colour occurred. The EPR spectrum of this solution now showed a broad triplet with a coupling constant of $a^N = 22.9$ G and a g value of $g = 2.0017$, which could be assigned to the (Z)-*tert*-butylaminoacyl radical, generated by mesolytic O-CO bond scission from **2a**$^{•+}$.[15] In a different experiment, the EPR signal of **2a**$^{•+}$ was followed at 130 K for a longer time. It finally converted into a novel highly resolved signal at $g = 2.0026$ that could unambiguously be assigned to the radical cation of the corresponding benzofuran **4**.[16]



2a $^{•+}$

Table 2. Thermodynamic half-wave potentials of the enol derivatives, rates (k_f) of the mesolytic O–CO bond cleavage and EPR data of their radical cations

System	**1a**	**2a**	**1b**	**2b**
$E_{1/2}$ (CH_3CN) / V	1.00	0.99	1.20	1.06
k_f (CH_3CN) / s^{-1}	2870	1650	2020	<1500[14]
k_f (CH_2Cl_2) / s^{-1}	502	228	104	<2 [14]
g value	2.0015	2.0023	2.0014	2.0023

The kinetic reactivity of **1a-c**$^{\bullet+}$ and **2a,b**$^{\bullet+}$ was investigated at room temperature using fast scan CV. By increasing scan rates from 100 mV s^{-1} up to 5000 V s^{-1}, the irreversible oxidation waves of all model enols turned reversible in both acetonitrile ($E_{1/2}$, see Table 2) and dichloromethane. The different degrees of reversibility at various scan rates were utilised for the determination of the rate constants k_f (except for **1c**) applying the Nicholson-Shain formalism[10] and assuming a first-order process. The small solvent effect (only a rate increase of 5 - 20, when switching from CH_3CN to CH_2Cl_2) precludes definitely a nucleophile-assisted bond cleavage process.[17]

The above results from preparative one-electron oxidation, CV and EPR provide a lucid picture of the radical cation chemistry. All enol systems undergo a monomolecular O-CO bond cleavage leading to the formation of the corresponding α-carbonyl cations and acyl radicals, thus following a homolytic cleavage mode.[18] After cyclisation of the α-carbonyl cations, the benzofurans are formed after a 1,2-methyl shift and subsequent deprotonation.[9,12] The oxidation potentials provide a clear trend dependent on the electron-withdrawing nature of R^2. Interestingly, in series **2a-e** (R^1 = Ph) the influence of R^2 on the oxidation potentials is much lower than in series **1a-e** (R^1 = Bu^t). While in series **1a-e** the electrophore is depicted by the enolate $Mes_2C{=}C{-}OC(O)R^2$, apparently there is a gradual change in **2a-e** from the $Mes_2C{=}C{-}OC(O)R^2$ to the $Mes_2C{=}C{-}Ph$ electrophore with increasing electron-withdrawing influence of R^2. Accordingly, in the electron-rich enol carbamate **2a** the electrophore is best represented by the $Mes_2C{=}C{-}O$ moiety, whereas in trifluoroacetate **2e** it rather resides on the $Mes_2C{=}C{-}Ph$ substructure.

Remarkably, in dichloromethane the difference in the rates of mesolytic cleavage is very small in the case of enol carbamates **1a**$^{\bullet+}$ and **2a**$^{\bullet+}$ (k_f(**1**)/k_f(**2**) = 2.2), whereas it is markedly increased for enol carbonates **1b**$^{\bullet+}$ and **2b**$^{\bullet+}$ (k_f(**1**)/k_f(**2**) = 52).[19] Such a rate difference can readily be explained from the thermodynamics of the mesolytic bond cleavage.

$$\begin{tikzcd}
Mes_2C{=}C(R1)O{-}C(O)R2^{\bullet+} \arrow[r, "\Delta G_{Meso}"] & Mes_2C{=}C(R1)O^{+} + {}^{\bullet}C(O)R2 \\
Mes_2C{=}C(R1)O{-}C(O)R2 \arrow[u, "E_{1/2}\,(enol)"'] \arrow[r, "\Delta G_{Homo}"] & Mes_2C{=}C(R1)O^{\bullet} + {}^{\bullet}C(O)R2 \arrow[u, "E_{1/2}\,(CR)"']
\end{tikzcd}$$

5^+ : R1 = Bu^t
6^+ : R1 = Ph

$5^{\bullet}$: R1 = Bu^t
$6^{\bullet}$: R1 = Ph

According to thermochemical cycle calculations,[20] the mesolytic bond energy ΔG_{Meso} can be derived from the homolytic bond energy and the oxidation potentials of reactant and the α-carbonyl radical (CR): $\Delta G_{Meso} = \Delta G_{Homo} - nF[E_{1/2}(enol) - E_{1/2}(CR)]$.

Because of the cross conjugation of the phenyl group, ΔG_{Homo} in both the carbamates and the carbonates is expected to be roughly 8 kJ mol^{-1} lower for series **2** (R^1 = Ph) molecules as compared to those of series **1** (R^1 = Bu^t).[21] However, this difference in homolytic bond energies $\Delta\Delta G_{Homo} = \Delta G_{Homo}(\mathbf{2}) - \Delta G_{Homo}(\mathbf{1})$ is basically compensated by the difference in the oxidation potentials of the α-carbonyl radicals $\Delta E_{1/2}(CR) = E_{1/2}(\mathbf{6}^{\bullet}) - E_{1/2}(\mathbf{5}^{\bullet})$ = 0.09 V (≙ 8 kJ mol^{-1}).[22] As a consequence, the differences in mesolytic bond cleavage energies $\Delta\Delta G_{Meso} = \Delta G_{Meso}(\mathbf{2}) - \Delta G_{Meso}(\mathbf{1})$ are determined only by $nF[E_{1/2}(\mathbf{2}) - E_{1/2}(\mathbf{1})]$. Hence, the small difference in the oxidation potentials of the enol carbamates leads to similar values of ΔG_{Meso} for **1a**$^{\bullet+}$ and **2a**$^{\bullet+}$, whereas ΔG_{Meso} is increased in enol carbonate **2b**$^{\bullet+}$ with respect to **1b**$^{\bullet+}$ by 14.5 kJ mol^{-1} because of $\Delta E_{1/2}$ = 0.15 V.

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