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The Unprecedented Bifunctional Chemistry of Bis(acyl)phosphane Oxides in Aqueous and Alcoholic Media

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Abstract: Tailor-made photoinitiators will play an important role for efficient radical polymerisations in aqueous media, especially in hydrogel manufacturing. Bis(acyl)phosphane oxides (BAPOs) are among the most active initiators. Here we show that they display a remarkable photochemistry in aqueous and alcoholic media: Photolysis of BAPOs in the presence of water or alcohols provides a new delocalized π radical, which does not participate in the polymerization. It either converts into a monoacylphosphane oxide acting as a secondary photoactive species or it acts as one-electron reducing agent. Upon the electron-transfer process it again produces a dormant photoinitiator. We have established the structure and the chemistry of this π radical using steady-state and time-resolved (CIDEP) EPR together with electrospray-ionization mass spectrometry, NMR and DFT calculations. Our results show that bis(acyl)phosphane oxides act as bifunctional reagents when applied in aqueous and alcoholic media.

Bis(acyl)phosphane oxides (BAPOs) are widely employed and well investigated photoinitiators for radical polymerizations.[1[1–12]] The generation of a phosphanoyl/benzoyl (P•/B•) radical pair upon photolysis of BAPOs (Scheme 1) and the initiation of radical polymerizations by these radicals is well established.[7–9] An exceptional property of BAPOs is their wavelength dependent photochemistry, allowing diblock copolymer synthesis.[13–15] Recently, water soluble BAPO derivatives have been utilized to efficiently form functional polymers in aqueous media and at interfaces (e.g. in the fields of hydrogel production, inkjet printing, cell encapsulation and 3D printing).[14–25] Upon the photolysis of BAPOs in presence of alcohols time-resolved EPR spectra have been reported and phosphorus-containing radicals have been assigned to the EPR data.[24–25] Here, we undertake an in-depth investigation of the reactivity of BAPO derivatives 1–3 (Scheme 1) in aqueous and alcoholic media.

Specifically, we utilize an array of complementary techniques, i.e. time-resolved and continuous-wave electron paramagnetic resonance (CIDEP and CW-EPR), 31P-NMR, electrospray-ionization mass spectrometry (ESI-MS) and density functional theory (DFT) calculations.

It is well established that the photolysis of BAPOs yields the benzoyl radical B• and phosphanoyl radical P•, which have been characterized by time-resolved EPR (e.g. 1, Figure 1a). These are the radicals initiating macromolecular chain growth. However, in the presence of H2O or alcohols, two additional doublets (denoted as C• and M• in Figure 1) appear in the spectrum shortly after the primary P• and B• radicals are detected. One of these doublets persists substantially longer than the signals of B• and P• (C•, Figure 1, see also the Supporting Information, Figures S1 and S2).

Figure 1. a) TR-EPR spectrum observed 50 ns – 2 μs after laser flash photolysis (355 nm) of 1 (15 mM) in acetonitrile/ethanol, b) cross section along the field axis 300 ns after the laser flash and CW-EPR spectra attributed to radical C• obtained upon photolysing a solution of 1 in acetonitrile/ethanol (7:3) on an extended scale together with the highly resolved high-field line together with the corresponding simulations.

While the peaks of the primary phosphanoyl radical P1• decrease with increasing water or alcohol content (see Figure S3 in the Supporting Information), those associated with C• become dominating. The signal of the benzoyl radical B• remains unaffected, underpinning that the new radical is formed from P1• and contains a P atom. However, its 31P hyperfine-coupling constant (hfc) (ca. 3 mT (Figure 1b) is one order of magnitude smaller than that of P•-type radicals (~35 mT).

To test if such a reaction is specific for BAPOs, we have performed analogous experiments with monoacylphosphane...
oxide (MAPO) M (Figure S4), but the presence of water or alcohols did not affect its reactivity.

![MAPO M](image)

To investigate if the presence of monomers has an influence on the formation and decay rates of radicals \( P^•, M^•, B^•, \) and \( C^• \), we have photolysed mixtures containing \( 1 \) and butyl acrylate (BA) in \( \text{H}_2\text{O}/\text{acetonitrile} \), with \( \text{H}_2\text{O}/\text{BA} \) ratios of 0, 1:3, 1:1, and 15:2 (Figure 2). In the absence of \( \text{H}_2\text{O} \), TR-EPR spectra reveal primary radicals \( P^1•, B^•, \) together with radicals indicating the growing polymer chain based on \( \text{P}1^-\text{BA}^+ \) and \( \text{B}^•-\text{BA}^-\) (Figure 2 and Scheme 3). In the same way as observed in the absence of the acrylate (Figure 1), increasing the \( \text{H}_2\text{O} \) content leads to marked growth of EPR signals attributed to a radical \( C^• \) which becomes the dominating component. The signal representing the \( P1^-\text{BA}^+\)-based polymer chain (\( \text{P}1^-\text{BA}^+\)) disappears (Figure 2a). In analogy to the experiments performed in the absence of BA, the signals based on the primary benzoyl radical (\( B^•, \) and \( \text{B}^•-\text{BA}^-\)) remain unaffected. The compositions of the TR-EPR spectral components from \( P^1•, B^•, P1^-\text{BA}^+, \text{B}^•-\text{BA}^-\), and \( C^• \) depending on the \( \text{H}_2\text{O} \) content, are shown in Figure 2b (cf. Table S2).\(^1\) It is evident that the higher the water content, the more the EPR signal attributed to \( C^• \) grows whereas \( P1^-\text{BA}^+\)-gradually disappear. Kinetic traces calculated based on the addition rate coefficients of the primary radicals to BA and that of \( P1\) to \( \text{H}_2\text{O} \) are shown in Figure 2c. This kinetic simulation underpins that at the initial stages of the polymerization, \( P1^-\)predominately reacts with \( \text{H}_2\text{O} \) (\( k_{\text{H2O}} \) of 3.8 \( \times \) 10\(^8\) M\(^{-1}\)s\(^{-1}\)) is only slightly lower than the rate constant for the addition of \( P1^-\) to BA, \( k_{\text{BA}} = 1.1 \times 10^7\) M\(^{-1}\)s\(^{-1}\).\(^2\) Together with its substantial persistence, this explains the dominance of \( C^• \) (Figure 2). These results demonstrate that in alcoholic and aqeous solutions, polymerizations are, in the first instance, initiated by the benzoyl radical \( B^• \) whereas radicals of type \( P^• \) will be efficiently converted to \( C^• \). The substantially long lifetime of \( C^• \) allows its observation via steady-state CW-EPR using a flow system. This provides highly resolved EPR spectra with significantly improved resolution (not attainable by the time-resolved method, see Figure 1). Advantageously, the primary radicals \( B^• \) and \( P^• \) do not negatively affect the highly resolved spectra, since they are too short-lived to be detected in this latter experiment. The EPR spectrum obtained upon photolysis of \( 1 \) in water/acetonitrile is dominated by a \( ^{31}\text{P} \) hfc of 3.03 mT (identical with the doublet indicated with \( C^• \) in the TR-EPR spectra). Here, this markedly smaller \( ^{31}\text{P} \) hfc compared with \( P1^-\text{BA}^+\) indicates that \( C^• \) contains a phosphorus atom, yet without being a phosphorus-centred radical.

![Figure 2](image)

Importantly, the EPR patterns inside the \( ^{31}\text{P} \) doublet depend on:

i) The nature of the solvent; i.e. \( \text{H}_2\text{O} \) reveals a different pattern than \( \text{D}_2\text{O} \), which again differs from MeOH (Figures S7-S9 and Tables S4-S6) and ii) on the substituents \( R \) of the parent \( P^• \) radicals (Scheme 1). Consequently, the persistent radical \( C^• \) contains the residue \( R \) attached to the phosphorus atom (Scheme 1) of the BAPO and the OR’ group of the solvent (where \( R’ \) is H, D or the alkyl group of the alcohol). DFT calculations suggest that water/alcohols preferentially add to the \( P=O \) group of the \( P^• \) (rather than to the carbonyl \( C=O \) atom) leading to phosphorus-centred radical \( P^* \). Figure 3 shows the calculated conversion of \( P^* \), yielding the delocalized (benzoyl) radical \( C^• \), which is identified by its EPR data and their calculated counterparts (Figure S10) and resembles a protonated radical anion of a MAPO (Scheme S6). The tautomeration connecting \( P^* \) and \( C^• \) is a downhill process (~53.8 kJ mol\(^{-1}\)) with a low activation barrier of 8.2 kJ mol\(^{-1}\).

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\(^1\) Owing to the EPR spectral pattern being dominated by the “triplet effect”\(^3\), it is justified translating TR-EPR intensities into relative radical concentrations.
Further evidence for radical C• and insight into its fundamental reactivity arises from high-resolution electrospray ionization mass spectra (ESI-MS) obtained upon photolysis of BAPO 1 in acetonitrile/water, acetonitrile/ethanol, or acetonitrile/D2O (see Figures S15-S17). Here, radical recombination, H-transfer, and fragmentation are the dominating reaction pathways (Scheme 2). Recombination of C• with B•, P1• or another C• yields CB, CP1 and CC (Scheme 2). Alternatively, the C–OH atom of C• is transferred to B• or P1•, yielding a mono(acyl)phosphane oxide (MAPO, M1–M3) and aldehydes BH and P1H.[2,29] In the presence of D2O the corresponding deuterated derivatives appear in the mass spectrum (Scheme S4, Table S9, Figure S16) underpinning C• as the source of the transferred hydrogen (deuterium) atom. Cleavage of the C–P bond of C• (fragmentation) results in phosphinic and phosphonic acid derivatives P1A1 and P1A2. We have additionally investigated this fragmentation reaction via DFT. Upon elongation of the C=P bond of C•, the hydrogen atom of the C–O–H group is transferred to the P=O, producing a further benzoyl radical B• and species P(III), which tautomerises to the more stable phosphinic acid derivative PA1. Alternatively, P(III) can be oxidized to the phosphonic acid derivative PA2 (see the Supporting Information, Scheme S2 and Figure S13).

The very efficient formation of a MAPO is substantiated by irradiating 1 in ethanol at wavelengths > 410 nm. 31P NMR reveals a photoproduc with δ = 17.52 ppm, (Figure S19), which perfectly corresponds with the 31P NMR signal of the commercially available MAPO photoinitiator Irgacure® TPO-L (M1, R’ = OEt in Scheme 2, Figure S20). Additional proof arises from the TR-EPR spectrum obtained upon photolysis of 1 in H2O/acetonitrile at 355 nm. An additional doublet with an 31P hfc of 48.9 mT (see Figure 1) occurs exactly matching the P-centred radical detected upon photolysis of MAPO Irgacure® TPO-L, M1•, R’ = OEt, (Figure S21). Accordingly, the formation of a MAPO via P•-type radicals in alcohol or H2O is highly likely.

The preferred formation of a MAPO upon long-wavelength irradiation resembles the wavelength selective reactivity of BAPOs: light of wavelengths > 410 nm does not cause the photocleavage of MAPOs, since they absorb below 410 nm.[15,13] This formation of a MAPO is decisive for the use of BAPOs in aqueous media, since this compound again is a photoinitiator and will remain in the polymer as a (dormant) photoactive species.[19]

Radical C• is inert towards radical addition reactions. However, C• acts as an electron transfer agent. Tetracyanoethene (TCNE) was added to an aqueous acetoneitrile solution of BAPO 1, which was irradiated at 430 nm (LED). Immediately the TCNE radical anion [TCNE]• was detected (Scheme 3 and Figure S22). This reactivity is observed in the presence and in the absence of BA.

![Figure 3. Calculated reaction pathway for the formation of C• via P•, which is formed by the addition of H2O to the P=O group. The distance between the carbonyl oxygen atom and the added proton from H2O serves as the reaction coordinate (for details, see the Supporting Information).](image)

![Scheme 2. Formation and follow-up reactions of C•. Recombination, H-transfer and fragmentation products identified via ESI-MS. For residues R of BAPOs 1–3 and the resulting MAPOs M1–M3 refer to Scheme 1. Residues R’ correspond to H, D or the alkyl group of the alcohol.](image)

![Scheme 3. Bifunctional reactivity of P• in non-aqueous and aqueous (R’OH) solution: polymerization and electron transfer.](image)

The photochemistry of bis(acyl)phosphane oxides in aqueous and alcoholic media indicates unexpected transformations of phosphanyl radicals into the rather persistent radical C•, consistently characterized by EPR, TR-EPR, ESI-MS, and theoretical calculations. Radical C• resembles a ketyl radical with spin delocalization onto the adjacent phosphorus centre. This radical is also closely related to the radical anion of monoacylphosphane oxides. The hyperfine data of these two radical types are closely related (refer the Supporting Information, section 7, Scheme S6).
In aqueous/alcoholic media, the formation of C• competes with radical photopolymerizations initiated by radical P•. Although C• is unreactive towards monomers it is converted to a MAPO derivative. The latter serves as a secondary photoinitiator and may allow the synthesis of complex polymer architectures by performing simple polymerization steps with a single photoinitiator in aqueous media. The unprecedented reaction pathway involving radical C•, which serves as a reducing agent, opens the opportunity to initiate light-induced simultaneous radical and electron-transfer reactions.

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