Using the phospha-Michael reaction for making phosphonium phenolate zwitterions

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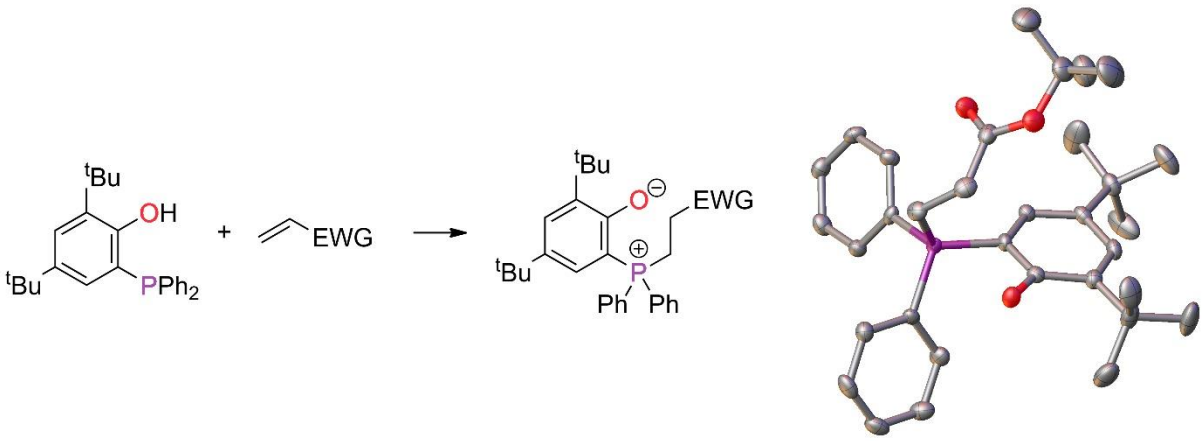


Abstract

The reactions of 2,4-di-*tert*-butyl-6-(diphenylphosphino)phenol and various Michael acceptors (acrylonitrile, acrylamide, methyl vinyl ketone, several acrylates, methyl vinyl sulfone) yield the respective phosphonium phenolate zwitterions at room temperature. Nine different zwitterions were synthesized and fully characterized. Zwitterions with the poor Michael acceptors methyl methacrylate and methyl crotonate formed, but could not be isolated in pure form. The solid-state structures of two phosphonium phenolate

molecules were determined by single-crystal X-ray crystallography. The bonding situation in the solid state together with NMR data suggests an important contribution of an ylidic resonance structure in these molecules. The phosphonium phenolates are characterized by UV-Vis absorptions peaking around 360 nm and exhibit a negative solvatochromism. An analysis of the kinetics of the zwitterion formation was performed for three Michael acceptors (acrylonitrile, methyl acrylate and acrylamide) in two different solvents (chloroform and methanol). Results revealed the proton transfer step necessary to stabilize the initially formed carbanion as the rate determining step. A preorganization of the carbonyl bearing Michael acceptors allowed for reasonable fast direct proton transfer from the phenol in aprotic solvents. In contrast, acrylonitrile not capable of forming a similar preorganization, is hardly reactive in chloroform solution, while in methanol the corresponding phosphonium phenolate is formed.

Keywords

Lewis-base catalysis, phosphonium phenolate zwitterion, phospha-Michael reaction, Michael acceptor reactivity

Introduction

Organocatalysis has emerged as a valuable and powerful tool for performing organic reactions [1] and polymerizations [2] in recent years. In this context phosphines have proven to be potent Lewis-base catalysts [3,4] for a variety of reactions [5], including but not limited to Rauhut-Currier [6], Morita-Baylis Hillman [7] and Michael reactions [8,9,10]. In all the mentioned reactions, the first step of the catalytic cycle is the nucleophilic attack of the phosphine on the electrophile, in many cases an electron deficient olefin. The zwitterion formed from this conjugate addition can subsequently act as a nucleophile or as a base [3-5]. The efficiency of this zwitterion formation is of great importance since it is the initiation step for the catalytic cycle in Michael reactions [8]. Generally, the conjugate addition is favored for strong nucleophiles, which is why electron-rich trialkylphosphines were among the first catalysts used in this type of reaction [11,12]. Recently, our working group has investigated electron-rich triarylphosphines [13,14,15] as viable alternatives to alkylphosphines, which often suffer from their pronounced susceptibility to oxidation. In this regard, we wanted to explore hydroxyl-substituted arylphosphines as potential candidates as well. Ortho-

hydroxyl substituted phosphines have been mainly used as chelating ligands for metal complexes until recently [16,17,18]. Further, ortho-hydroxyl phosphines have been used for the synthesis of probes in metabolic labeling [19], as a photocatalyst in the defluoroalkylation of trifluoromethyl groups [20] and the cross-coupling of aryl halides [21]. Like phosphonium salts in general are used as catalysts [22,23], phosphonium salts based on ortho-hydroxy substituted phosphines received particular attention because of their zwitterionic nature and have been used as catalysts in the synthesis of carbonates from CO_2 [24,25,26] and the synthesis of oxazolidines from isocyanates and epoxides [27]. Furthermore, their application in primary hydroxyl group selective acylation of diols [28] and their use as organophotoredox catalyst [29,30] is known. The latter mentioned catalysts are regarded as stable phosphonium enolate zwitterions. The first example of an isolable phosphonium enolate zwitterion was reported in 2007 by Zhu et al. who synthesized the compound via a three-component coupling between an alkylphosphine, an aldehyde and an alkyne [31]. Another example resulting from phosphine addition to α,β-unsaturated aldehydes was published shortly afterwards [32]. Phosphonium carboxylate zwitterions have been obtained by the reaction of phosphines with acrylic acid [8] and ortho-carboxylated aryl phosphines with several Michael acceptors [33].

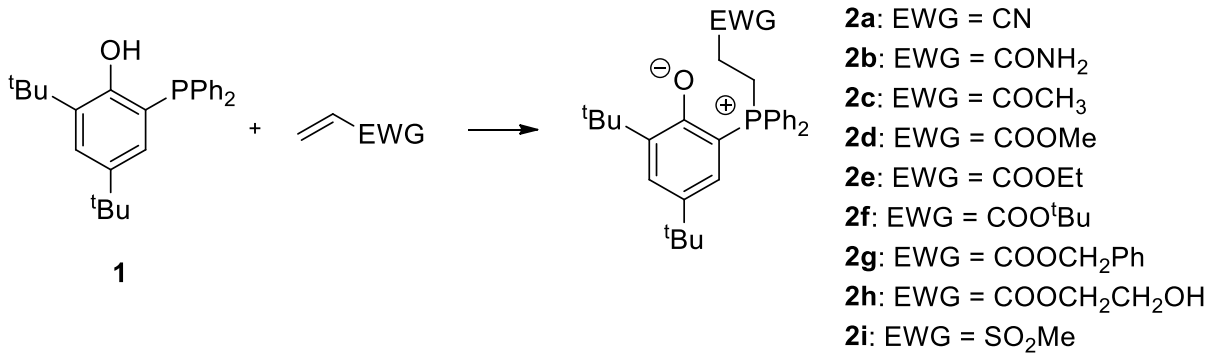
In this work we present the formation of stable zwitterions from the reaction of 2,4-di-*tert*-butyl-6-(diphenylphosphino)phenol (**1**) and a variety of different Michael acceptors and disclose kinetic investigations on the zwitterion formation with carbonyl and non-carbonyl-based Michael acceptors.

Results and Discussion

Synthesis

During our endeavors to identify potent Lewis base catalysts for the oxa-Michael reaction [13,14], the triarylphosphine **1** was tested in a model reaction (2 equiv. allyl alcohol, 1 equiv. acrylonitrile, 0.05 equiv. **1**). However, no conversion toward the desired product 3-(allyloxy)propanenitrile was observed after stirring the reaction mixture for 24 h at room temperature. Analyzing the reaction mixture with ^{1}H-NMR spectroscopy revealed the formation of a minor amount of a novel compound characterized by two multiplets centered at 3.31 and 3.09 ppm, respectively and two

novel signals for tertiary butyl groups. Accordingly, we reasoned that the phosphine has reacted presumably with acrylonitrile forming a stable species not suited to catalyze the oxa-Michael reaction. In order to identify this compound, we reacted **1** with acrylonitrile or with allyl alcohol (in both cases using a molar ratio of 1:1.05 and dichloromethane as the solvent). While in the latter case only the starting materials were observed after 24 h at room temperature, the reaction of **1** with acrylonitrile turned yellow during the same time and exclusively yielded the product of interest **2a**. Compound **2a** was identified by a combination of NMR spectroscopic methods and single-crystal X-ray structure analysis (vide infra) as the zwitterionic phospha-Michael adduct of **1** and acrylonitrile, formally stabilized by proton transfer from the phenol group to the initially formed carbanion [13,14]. Also with other Michael-acceptors such as methyl vinyl ketone, several acrylates as well as methyl vinyl sulfone the reaction proceeds smoothly under the same reaction conditions (Scheme 1).



Scheme 1. *Reaction of **1** with various Michael acceptors (EWG = electron withdrawing group) forming the zwitterions **2a-i**; the reactions were performed in dichloromethane at room temperature*

Conversions of **1** are usually quantitative within 24 h and all phosphonium phenolates can be purified by recrystallization whereby the solvents used vary depending on the parent Michael acceptor (for details, see SI). Yields are not optimized and given in Table 1. The synthesized zwitterions were investigated via ^{1}H-, ^{13}C- and ^{31}P-NMR spectroscopy. All synthesized compounds exhibit similar features and characteristic resonances, like a set of two multiplets in the region between 3.00 and 2.70 as well as 3.50 and 3.10 ppm corresponding to the two methylene groups in between the phosphonium and the electron withdrawing group (see Figure 1 for the case of **2a**). All compounds share a characteristic doublet of doublet pattern centered in the range of 6.21 to 6.09 ppm depending on the Michael acceptor used. This signal is attributed to the aromatic proton in position 5 of the 2,4-di-*tert*-butylphenol substituent, that

experiences a meta coupling to the aromatic proton on position 3 ($^4J_{HH}$ ≈ 2.5 Hz) as well as coupling with the phosphonium center ($^3J_{PH}$ ≈ 14 Hz). In comparison to phosphine **1**, in which the same proton displays a resonance at 6.88 ppm ($^4J_{HH}$ = 2.5 Hz, $^3J_{PH}$ = 5.8 Hz; [34]), this signal is characteristically up-field shifted in every adduct **2a**-**2j** (Table 1). The similar phosphonium salt 2,4-di-*tert*-butyl-6-(triphenylphosphonium)phenolate features this particular signal at 6.27 ppm ($^4J_{HH}$ = 2.7 Hz, $^3J_{PH}$ = 14.4 Hz; [30]).

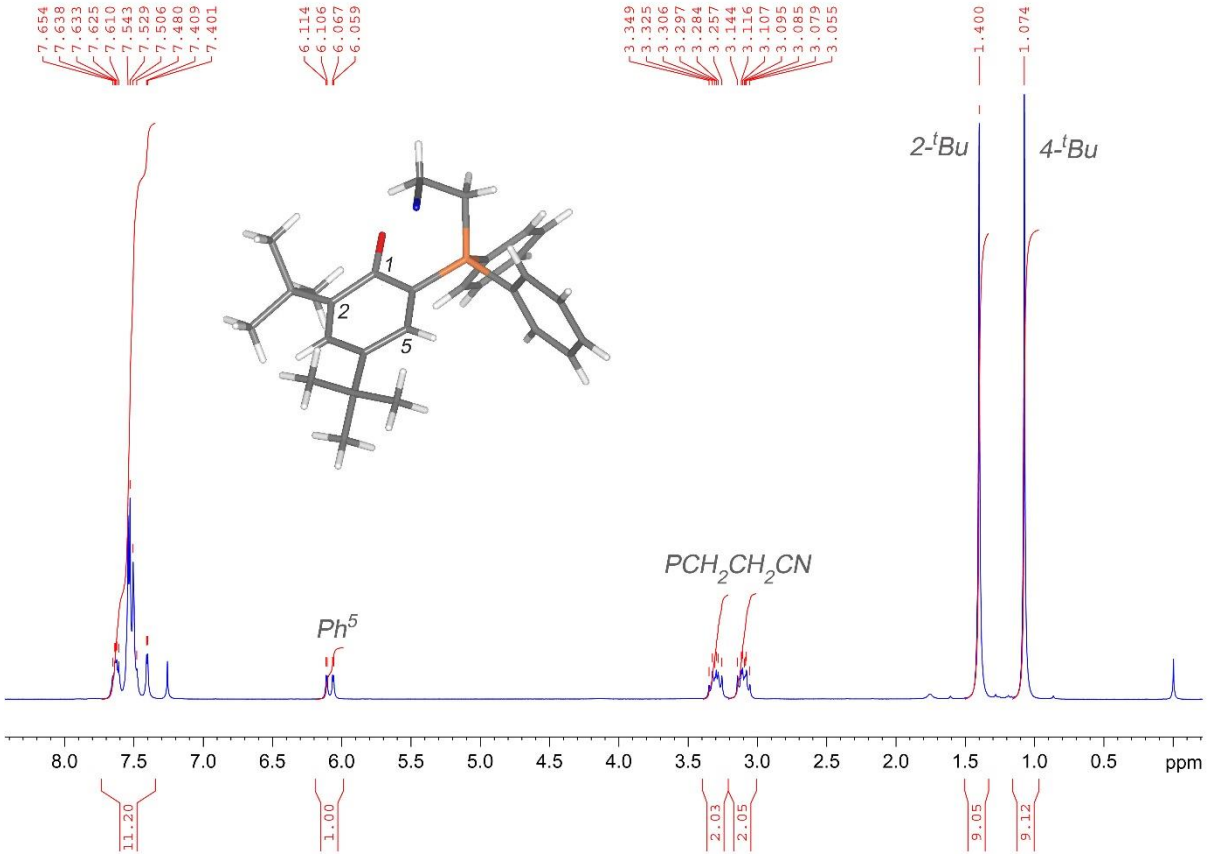


Figure 1. *^{1}H-NMR spectrum of **2a** recorded on a 300 MHz-spectrometer in $CDCl_3$ at 23°C; the inset shows a 3D-model based on the solid-state structure of **2a** and the numbering scheme of the phenolate moiety.*

In the ^{13}C-NMR spectra, the chemical shifts of the carbon atoms in positions 1 and 6 of the phenolate unit are particularly noteworthy. In the adducts **2a**-**2i**, the carbon atom 1, featuring the phenolate oxygen atom attached, shows a doublet ($^2J_{PC}$ ≈ 4 Hz) in the range of 175.0-173.9 ppm (Table 1). In the closely related 2,4-di-*tert*-butyl-6-(triphenylphosphonium)phenolate the chemical shift for the corresponding carbon atom appears at 173.8 ppm ($^2J_{PC}$ = 3.9 Hz) [30].

Table 1. Yields and characteristic ^{1}H-, ^{13}C-, and ^{31}P-NMR shifts of compounds **2a**-**2i**.

Number	EWG	Yield [%]	^{1}H-NMR shift of Ph[5] [ppm]	^{13}C-NMR shift of Ph[1] [ppm]	^{13}C-NMR shift of Ph[6] [ppm]	^{31}P-NMR shift [ppm]
2a	CN	85	6.09	175.0	95.5	18.9
2b	$CONH_2$	42	6.14	174.1	96.6	25.1
2c	$COCH_3$	61	6.13	174.8	96.9	20.7
2d	COOMe	46	6.20	174.9	96.1	19.4
2e	COOEt	49	6.19	174.9	96.2	19.4
2f	$COO^{t}Bu$	75	6.21	174.8	96.3	19.6
2g	$COOCH_2Ph$	43	6.19	174.8	96.1	19.5
2h	$COO(CH_2)_2OH$	61	6.15	173.9	96.8	20.9
2i	SO_2Me	18	6.14	175.0	95.3	19.7

Compared to the parent phosphine **1** (155.9 ppm, $^{2}J_{PC}$ = 19.3 Hz) [34] a pronounced down-field shift occurred upon adduct formation, which suggests a considerable contribution of a quinonic resonance structure as benzoquinones exhibit ^{13}C-NMR shifts of about 188 ppm and hydroquinones of about 150 ppm [35]. The opposite is true for the resonance of the carbon atom 6 having the phosphonium center attached, which is distinctly more shielded in **2a**-**2i** (96.9-95.3 ppm, $^{1}J_{PC} \approx$ 100 Hz) then in **1** (119.9 ppm, $^{1}J_{PC}$ = not observed) [34]. Likewise, the two ipso-carbons of the phenyl groups attached to the phosphonium center in **2a**-**2i** are somewhat more shielded (≈ 124-125 ppm, $^{1}J_{PC} \approx$ 85-90 Hz) than in the starting material **1** (134.4 ppm, $^{1}J_{PC}$ = 9 Hz). Comparison to alkyltriphenylphosphonium bromides reveals even more shielding of the ipso-carbons in these derivatives (117-116 ppm, $^{1}J_{PC} \approx$ 86 Hz) [36]. Concerning the ^{13}C chemical shift for the aliphatic carbons directly attached to the phosphorus atom a slight down-field shift is found for **2a**-**2i** (24-20 ppm, $^{1}J_{PC} \approx$ 64 Hz) when compared to similar alkyltriphenylphosphonium bromides (20-18 ppm, $^{1}J_{PC} \approx$ 54 Hz) [36]. Finally, the ^{31}P-NMR shift (against H_3PO_4, 85%) of the adducts is in the range of 20.9-18.9 ppm. Only the acrylamide derived phosphonium phenolate **2b** is an exception, showing a ^{31}P-NMR shift of 25.1 ppm. The ^{31}P-NMR signal of 2,4-di-*tert*-butyl-6-(triphenyl-phosphonium)phenolate appears at 19.6 ppm [30]. Surprisingly, the ^{31}P-NMR shifts of the phosphonium phenolates are largely unaffected by changing a phenyl group for an alkyl group like in **2a**-**2i**. Also other similarly substituted phosphonium salt species give

the phosphorus signal in the range of 26-19 ppm [28,36,37]. For comparison, the phosphine **1** exhibits a ^{31}P-NMR shift of -29.7 ppm [34].

Additionally to the Michael acceptors presented in Scheme 1, the very weak Michael acceptors methyl methacrylate (electrophilicity parameter (E) for ethyl methacrylate is -22.77) and methyl crotonate (E for ethyl crotonate = -23.59) [38] were also tested as partner in the reaction with **1**. In these cases, the zwitterion formed to some extent (as evidenced by characteristic signals in the proton NMR spectra of the crude reaction mixture) but could not be isolated in pure form. In case of methyl methacrylate, the reaction is accompanied by oligomerization of the Michael acceptor (SI, Fig. S47). A similar oligomerization reaction has been reported for cyanoacrylates [39]. Apart from the adducts of these two very weak Michael acceptors, the zwitterionic species **2a**-**2i** described herein are quite stable. In the solid state, they can be stored under ambient conditions for several weeks without any sign of decomposition upon evaluation of redissolved samples with NMR spectroscopy. However, in solution, the zwitterions are less stable. Over hours, liberation of the Michael acceptor accompanied by formation of the phosphine oxide of **1** as identified by ^{31}P NMR spectroscopy [40] can be observed.

Crystal Structures

The solid-state structures of **2a** and **2f** were determined by single-crystal X-ray diffraction. The crystals were grown from concentrated solutions in toluene. A representation of the molecular structure of **2a** is shown in Figure 2a (for **2f** see Fig. S1). Both molecules crystallize in a conformation in which the phenolate is oriented toward the methylene group in α–position (C16 in Figure 2b) to the electron-withdrawing group (either CN in case of **2a** or COO^{t}Bu in case of **2f**). The O1-C15 and O1-C16 distances are in **2a** 3.128(3) and 3.162.3(3) Å and in **2f** 3.098(4) and 3.019(4) Å, suggesting a weak hydrogen bonding interaction between O1 and the protons of the methylene groups [41]. The P1-O1 distances of 2.750(1) Å in **2a** and 2.693(3) Å in **2f** suggest an electrostatic interaction between the anionic phenolate and the cationic phosphonium center [31]. Other stable phosphonium enolate or phenolate zwitterions feature P-O distances in the range of 2.60-2.95 Å [28,31]. For comparison, in 1,2-oxaphosphetanes, the covalent bond between P-O is characterized by a distinctly shorter distance between the two atoms of 1.85 Å [42]. The bonding situation in the phenolate ring is of particular interest for understanding the zwitterions. The P1-C6

distances are with 1.758(2) Å in **2a** and 1.774(3) Å in **2f** significantly shorter than in the parent phosphine (1.825 Å) [34].

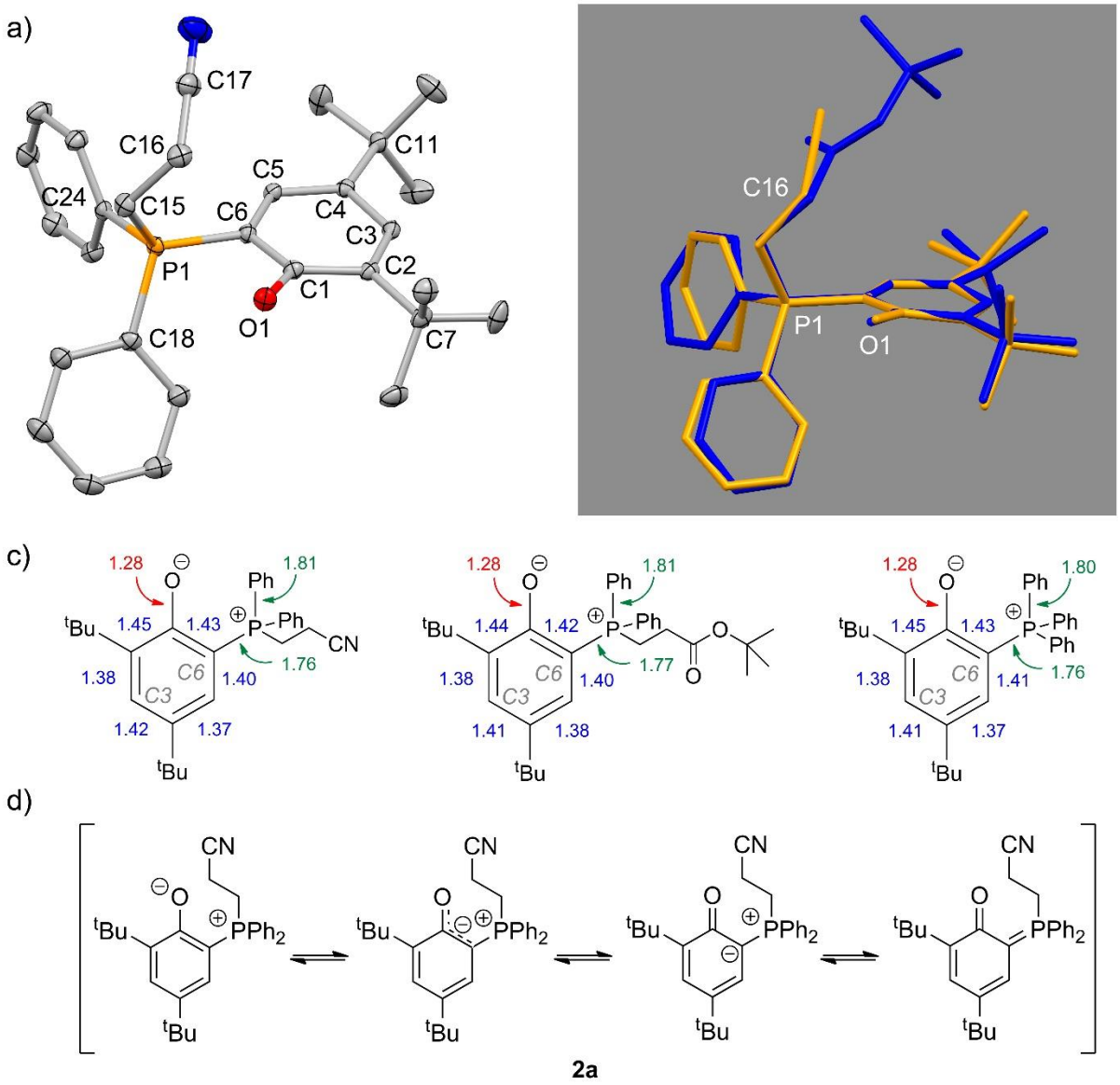


Figure 2. *a) Molecular structure of* ***2a****, hydrogen atoms omitted for clarity, thermal ellipsoids drawn at 30 % probability level. Selected distances (Å) and angles (deg): P1-C6 = 1.758(2), P1-C15 = 1.824(2), P1-C18 = 1.814 (2), P1-C24 = 1.806 (2), O1-C1 = 1.281 (2), C15-C16 = 1.533 (3), C16-C17 = 1.456 (3), C17-N1 = 1.136 (3), C6-C1-O1 = 118.6(2), C2-C1-O1 = 126.0(2), C6-P1-C24 = 107.64(8), C6-P1-C18 = 112.89(9), C15-P1-C24 = 108.88(9), C15-P1-C18 = 106.55(9), C15-P1-C6 = 115.33(9), C15-C16-C17 = 114.1(2); b) overlay of the molecular structures of* ***2a*** *(orange) and* ***2f*** *(blue); c) bond length of the phenolate substituent for* ***2a****,* ***2f*** *and 2,4-di-tert-butyl-6-(triphenylphosphonium)phenolate [30]; d) resonance structures for the description of the bonding situation in* ***2a****.*

This points to a ylidic bonding situation in **2a** and **2f** similar to that observed in the related (triphenylphosphonium)phenolate [28,30] (Figure 2c). Also the O1-C1

distances (**2a**: 1.281(2) Å and **2f**: 1.279(3) Å) are very similar and between the values expected for a phenolate or a quinonic bonding [35].

The phosphonium center exhibits a somewhat distorted tetrahedral conformation in both zwitterions. The largest angles found are 115.3(1)° in **2a** and 114.0(2)° in **2f** (in both cases C6-P1-C15) and the smallest angles are 105.0(1)° in **2a** and 104.3(2)° in **2f** (C18-P1-C24). A marginal shortening of about 0.02-0.03 Å of the bonds between P1 and the ipso-carbons of the aryl substituents in comparison to the parent phosphine **1** is observed. The alkyl groups attached to the phosphonium center do not show any special features. The distance between P1 and C15 is slightly longer (1.824(2) Å in **2a**; 1.828(3) in **2f**) when compared to the P-CH_2 distance of a tetra-*n*-butylphosphonium cation [43].

UV Vis Spectroscopy

All phosphonium phenolate compounds exhibit a bright yellow color in solution (see inset in Figure 3). Investigating the absorption properties in chloroform solution revealed an absorption feature ranging from about 310 to 420 nm peaking at 360±3 nm (with molar absorption coefficients (ε) between 4000 and 6000 L mol^{-1} cm^{-1}) for all zwitterions except **2b** and **2h** (Figure 3 and Figure S56).

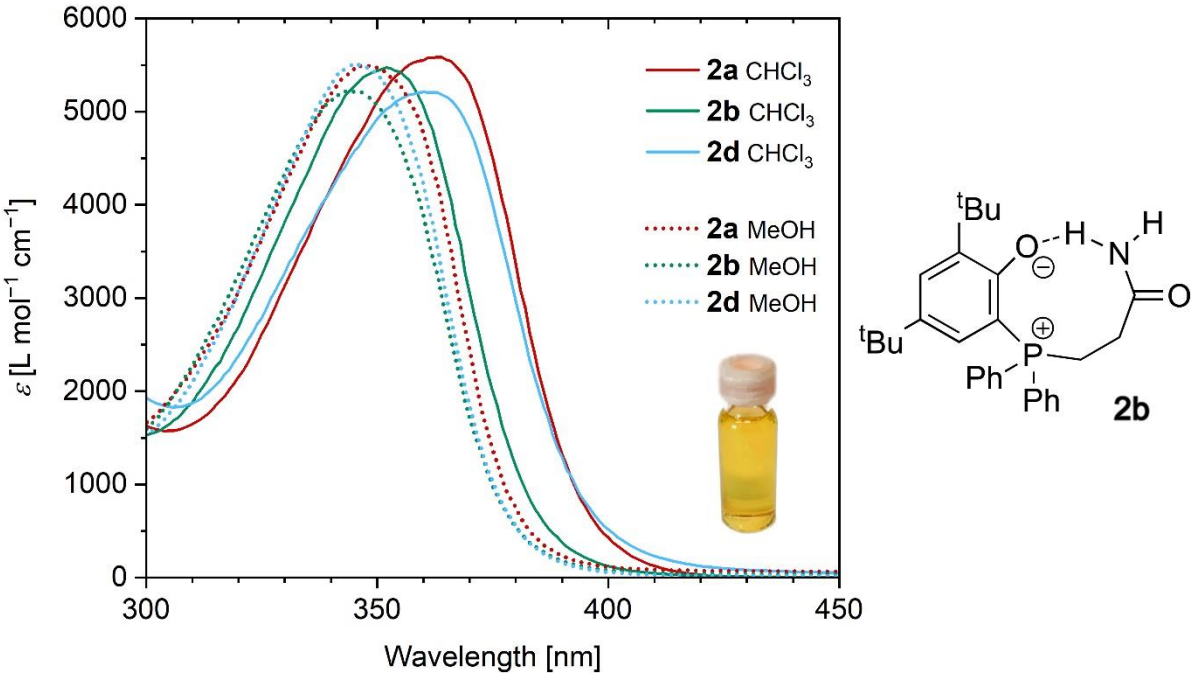


Figure 3. Left: UV-Vis spectra of **2a**, **2b** and **2d** in chloroform (straight lines) and **2a**, **2b** and **2d** in methanol (dotted lines); the inset shows a photograph of a vial containing a solution of **2a** in chloroform; right: proposed hydrogen bonding interaction in **2b** in $CHCl_3$.

Compounds **2b**, the Michael adduct of acrylamide, and **2h**, the Michael adduct of 2-hydroxyethyl acrylate, show blue shifted absorption maxima of 352 nm and 356 nm, respectively. Upon increasing the solvent polarity by using methanol instead of chloroform, a hypsochromic shift of the absorption maximum occurs (dotted lines in Figure 3). The blue shift is more pronounced for those zwitterions not bearing any hydrogen bond donating functional groups. Accordingly, it is plausible to explain the blue shifted absorption maxima of **2b** and **2h** in chloroform by a more polar environment of the chromophore caused by the hydrogen bond donors attached to the alkyl substituent of the phosphonium center (Figure 3b). This hypothesis is further supported by the observation of two very different chemical shifts for the two amide-protons the ^{1}H-NMR spectrum of **2b** in $CDCl_3$ giving resonance at 5.21 and 8.58 ppm.

Kinetic Studies

In the next step the kinetics of the formation of the Michael adducts were studied. For this purpose, we used two strong and one weak Michael acceptor, which were selected according to their electrophilicity parameters (E) [38], their performance in previous testing [14] and the nature of the functional group. The strong Michael acceptors were methyl acrylate (E = -18.84) bearing a carbonyl-based electron-withdrawing group and acrylonitrile (E = -19.05) featuring a geometrically different electron withdrawing group. Acrylamide was selected as a weak (for dimethylacrylamide E = -23.54), carbonyl-based Michael acceptor. The kinetic study was performed by monitoring the appearance of the zwitterion absorption by means of UV-Vis spectroscopy in chloroform or in methanol as the solvent. The concentration of the respective Michael acceptor was varied ([Michael acceptor] = 2.5 mmol/L – 10 mmol/L) and was at least ten-fold higher than the concentration of the phosphine **1** ([**1**] = 0.25 mmol/L) to obtain pseudo first-order kinetics. Figure 4 shows typical time vs. conversion plots for an initial Michael acceptor concentration of 7.5 mmol/L. Time conversion plots were then evaluated using COPASI [44]. To obtain second-order rate constants, we performed kinetic modelling (Figs. S50-S55), fitting the experimental time traces by considering the second-order reaction shown in Scheme 1. The strong Michael acceptor methyl acrylate quite readily yields the corresponding zwitterion **2d** in chloroform (k_{CHCl3} = 3.2 mM^{-1} s^{-1}). Upon changing to methanol, the reaction becomes almost four times faster (k_{MeOH} = 11.6 mM^{-1} s^{-1}). The reaction of **1** with the poor Michael acceptor acrylamide

yielding **2b** in chloroform (k_{CHCl3} = 2.2 mM^{-1} s^{-1}) is somewhat slower than the reaction with methyl acrylate.

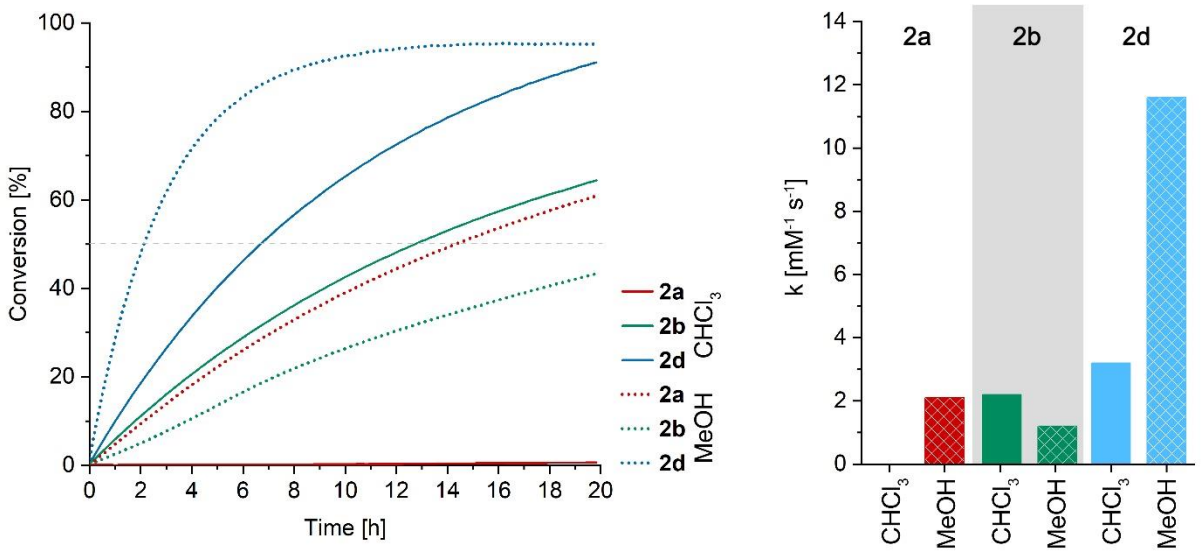
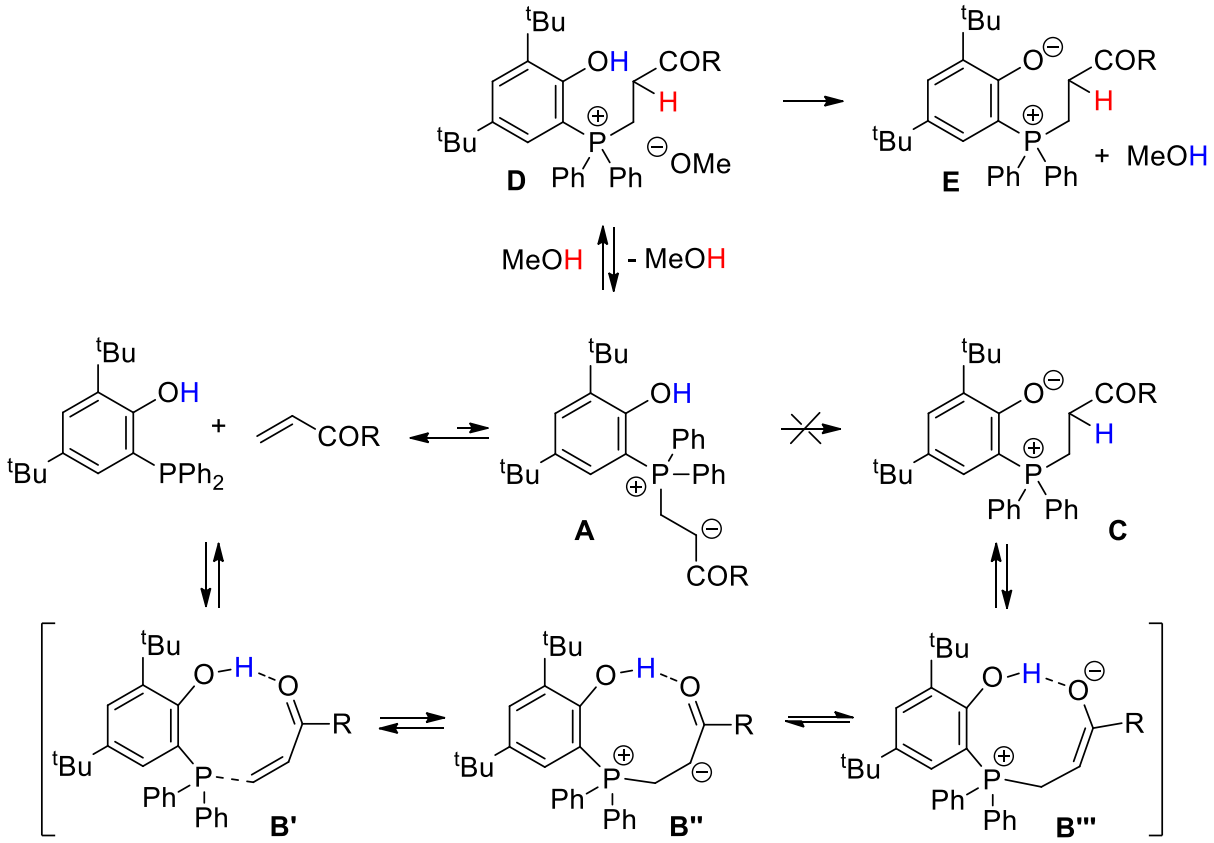


Figure 4. Conversion of **1** (initial *c* = 0.25 mM) toward **2a**, **2b** or **2d** in the presence of the respective Michael acceptors (initial *c* = 7.5 mM) *vs*. time as determined by the increase of the absorption band centered at 350-360 nm at 23 °C in either chloroform (solid lines) or methanol (dotted lines); right: 2nd order rate constants determined for the formation of **2a**, **2b** and **2d** in chloroform (solid bars) and in methanol (checkered bars) at 23 °C.

In this case, methanol has a detrimental effect on the reaction velocity as the rate constant (k_{MeOH} = 1.2 mM^{-1} s^{-1}) is almost halved compared to chloroform. The strong Michael acceptor acrylonitrile reacts only very slowly in chloroform (k_{CHCl3} = 5.6 10^{-3} mM^{-1} s^{-1}). In methanol, **2a** is formed with a similar rate constant (k_{MeOH} = 2.1 mM^{-1} s^{-1}) as **2b** the product of the poor Michael acceptor acrylamide in $CHCl_3$. Results show no correlation of the rate constant with the electrophilicity parameter of the Michael acceptors.

The low rate constant for the acrylonitrile reaction in chloroform suggests that the primary adduct **A** (see Scheme 2) is too short-lived that an intramolecular hydrogen transfer toward **2a** (**C**, in Scheme 2) is occurring [45]. Instead, in case of acrylonitrile another hydrogen bond donor, which is the solvent methanol [46], is necessary to trap intermediate **A** forming the ion pair **D**. Finally, deprotonation of the phenol moiety by the methoxide gives the final product **E** (**2a** when acrylonitrile is used as the Michael acceptor). In this case, the proton at the α-position to the electron-withdrawing group is stemming from the protic solvent.



Scheme 2. Proposed mechanism for intramolecular proton transfer in zwitterion formation with Michael acceptors bearing a carbonyl moiety and for the intermolecular proton transfer in the presence of the hydrogen donor solvent methanol.

Performing the reaction with methanol-d_4 leads to incorporation of 0.7 equiv. of deuterium in the α-position to the cyano group. However, this experiment does not allow for a conclusive distinction between the two postulated hydrogen transfer pathways as the phenolic hydrogen is quickly exchanged for deuterium under these conditions. The evenly strong Michael acceptor methyl acrylate reacts much faster in chloroform than acrylonitrile. A likely explanation is the preorganization of the Michael acceptor and donor by hydrogen bonding between the phosphine's hydroxyl group and the carbonyl group of the ester **B'**. Such a preorganization facilitates the proton transfer [33] from the hydroxy group to the initial zwitterion via **B''** and **B'''** resulting in **C**. In this case, the proton at the α-position to the electron-withdrawing group is stemming from the phenol moiety. Methyl acrylate in methanol is the fastest reaction presumably because both pathways, the intramolecular proton transfer and the methanol mediated proton transfer, can occur. It has been described that intermediate **B** is more stable with enolizable electron-withdrawing groups such as esters [47] when compared to e.g. a nitrile [45]. Accordingly, the intermolecular proton transfer pathway should be more

accessible with methyl acrylate than with acrylonitrile. The lower reactivity of acrylamide in chloroform compared to methyl acrylate is in accordance with its lower electrophilicity. The observed rate reduction in methanol suggests the importance of the intramolecular hydrogen transfer pathway for the conversion of acrylamide, which is probably disturbed when the hydrogen bond donor solvent methanol is interacting with the amide group and/or the hydroxyl group.

Conclusion

The conjugate addition of 2,4-di-*tert*-butyl-6-(diphenylphosphino)phenol to Michael acceptor molecules allows for a facile modular synthesis of stable phosphonium phenolate zwitterions bearing additional functional groups. The bonding situation in the zwitterions was studied by NMR and UV-Vis spectroscopies and single-crystal X-ray analysis of selected representatives. The zwitterions exhibit negative solvatochromism and feature considerable contribution of an ylidic resonance structure in the solid state and in aprotic solution. Kinetic studies revealed that the proton transfer from the phenolic hydroxyl group to the initially formed zwitterionic adduct bearing the negative charge at the *α*-carbon to the electron-withdrawing group is the rate determining step of the reaction. In an aprotic solvent, Michael acceptors bearing a carbonyl group allow for a preorganization of the reactants facilitating the proton transfer from the phenol and therefore a comparatively fast formation of the product. In protic solvents, the initial proton transfer stems predominantly from the solvent and Michael acceptors not suited for a preorganization react much faster compared to the aprotic solvent case.

Experimental

All experiments were performed under ambient conditions. Chemicals were purchased from Sigma-Aldrich, Carl Roth, Merck, or TCI and were used as received. 2,4-Di-*tert*-butyl-6-(diphenylphosphino)phenol (**1**) was prepared according to a published procedure [48]. Stabilizers present in the Michael acceptors were not removed. NMR spectra were recorded on a Bruker AVANCE III 300 spectrometer or a JEOL JNM-ECZ 400 MHz spectrometer and are referenced to tetramethylsilane (^{1}H, ^{13}C), and 85% H_3PO_4 (^{31}P). Deuterated solvents were obtained from Cambridge Isotope Laboratories Inc. UV-Vis spectra were recorded on an Agilent Cary 60 UV-Vis spectrophotometer. Kinetic evaluation was conducted assuming a second-order reaction as displayed in

Scheme 1. All simulations were performed with COPASI, an open-source software [44]. The second-order rate constants were obtained by fitting the experimental time traces until a fully consistent data set, being valid for all experimental conditions, was established. For X-ray structure analyses the crystals were mounted onto the tips of glass fibres. Data collection was performed with a Bruker-AXS SMART APEX CCD diffractometer using graphite-monochromated Mo-K_α radiation (0.71073 Å). The data were reduced to F_o^2 and corrected for absorption effects with SAINT (*Version 6.45, Bruker AXS Inc., 1997-2003*) and SADABS (*Version 2.10. Bruker AXS Inc.*) respectively [49]. The structures were solved by direct methods and refined by full-matrix least-squares method (SHELXL97 or SHELXL19) [50]. If not noted otherwise all non-hydrogen atoms were refined with anisotropic displacement parameters. All hydrogen atoms were located in calculated positions to correspond to standard bond lengths and angles. Figures of solid state molecular structures and the overlay of the molecular structures were generated using Mercury 2022.3.0 (Build 364735) [51]. Crystallographic data for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC 2287962 (**2a**) 2287963 (**2f**).

Synthesis of zwitterions exemplarily given for 2b. In a standard procedure **1** (0.2 mmol, 78 mg, 1 equiv.) was dissolved in 0.5 mL dichloromethane in a 4 mL screw-cap vial. The Michael acceptor acrylamide (14.9 mg, 0.21 mmol, 1.05 equiv.) was dissolved in 0.5 mL dichloromethane in a separate vial and then added dropwise to the solution of **1**. Zwitterion formation was indicated by a color change to yellow of the solution. The reaction mixture was stirred at room temperature for 24 h and the solvent evaporated. The product was recrystallized from a hot toluene/THF mixture. Yield: 38.8 mg (42 %) off-white solid.

^{1}H NMR (δ in ppm, $CDCl_3$, 298 K): 1.07 (s, 9H, C*H*$_3$), 1.40 (s, 9H, C*H*$_3$), 2.66-2.81 (m, 2H, C*H*$_2$), 3.30-3.46 (m, 2H, C*H*$_2$), 5.21 (br, 1H, NH_2), 6.14 (dd, $^3J_{P\text{-}H}$ = 14.4 Hz, $^4J_{H\text{-}H}$ = 2.6 Hz, 1H, H5), 7.41-7.56 (m, 9H, Ar-*H*), 7.58-7.67 (m, 2H, Ar-*H*), 8.58 (br, 1H, NH_2). ^{13}C{^{1}H} NMR (δ in ppm, $CDCl_3$, 298 K): 24.2 (d, $^1J_{P\text{-}C}$ = 60.7 Hz, *C*H_2), 29.4 (s, *C*H_3), 30.9 (d, $^2J_{P\text{-}C}$ = 4.0 Hz, *C*H_2), 31.4 (s, *C*H_3), 33.9 (d, $^4J_{P\text{-}C}$ = 1.2 Hz, *C*CH_3), 35.0 (d, $^4J_{P\text{-}C}$ = 2.2 Hz, *C*CH_3), 96.6 (d, $^1J_{P\text{-}C}$ = 99.0 Hz, C6), 124.6 (d, $^1J_{P\text{-}C}$ = 86.0 Hz, $C_{i\text{-}Ph}$), 127.3 (d, $^2J_{P\text{-}C}$ = 12.5 Hz, C5), 129.4 (d, $^3J_{P\text{-}C}$ = 11.9 Hz, C4), 131.3 (d, $^4J_{P\text{-}C}$ = 1.4 Hz, C3), 132.6 (d, $^3J_{P\text{-}C}$ = 9.3 Hz, C2), 132.9 (d, $^3J_{P\text{-}C}$ = 2.7 Hz, $C_{m\text{-}Ph}$), 133.4 (d, $^2J_{P\text{-}C}$ = 14.8 Hz,

$C_{o\text{-}Ph}$), 140.5 (d, $^{4}J_{P\text{-}C}$ = 8.0 Hz, $C_{p\text{-}Ph}$), 174.1 (d, $^{2}J_{P\text{-}C}$ = 4.4 Hz, C1), 174.8 (d, $^{3}J_{P\text{-}C}$ = 13.9 Hz, CO). $^{31}P\{^{1}H\}$ NMR (δ in ppm, $CDCl_3$, 298 K): 25.1. UV-Vis ($CHCl_3$): λ_{max} = 352 nm (ε = 5.53 * 10^3 L mol^{-1} cm^{-1}).

Supporting Information

Containing experimental procedures, plot of the solid-state structure of 2f, crystallographic data, NMR spectra, UV-Vis spectra and experimental and simulated time conversion plots for the zwitterion formation.

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