Acylation Reactions of Dibenzo-7-phosphanorbornadiene: DFT Mechanistic Insights

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Extensive DFT calculations provide deep mechanistic insights into the acylation reactions of tert-butyl dibenzo-7-phosphanorbornadiene with PhCOX (X=Cl, Br, I, OTf) in CH₂Cl₂ solution. Such reactions are initialized by the nucleophlic P−C attack to the carbonyl group to form the acylphosphonium intermediate A⁺ together with X⁻ anion, followed either by nucleophlic X−P attack (X=Cl, Br, I) toward A⁺ to eliminate anthracene or by slow rearrangement or decomposition of A⁺ (X=OTf). In contrast to the first case (X=Cl) that is rate-limited by the initial P−C attack, other reactions are rate-limited by the second X−P attack for X=Br and I and even thermodynamically prevented for X=OTf, leading to isolable phosphonium salts. The rearrangement of phosphonium A⁺ is initiated by a P−C bond cleavage, followed either by sequential proton-shifts to form anthracenyl acylphosphonium or by deprotonation with additional base Et₃N to form neutral anthracenyl acylphosphine. Our DFT results strongly support the separated acylphosphonium A⁺ as the key reaction intermediate that may be useful for the transfer of acylphosphonium in general.

Acylphosphines and their oxides are useful photo-initiators for radical polymerization reactions,[1] usually synthesized by using nucleophlic sources of phosphorus such as PH₃, MPH₂ (M=Li, Na, K), PTMS₃ (TMS=trimethylsilyl), and transition metal-supported phosphines and phosphides.[2] Very recently, novel acylation reactions of tert-butyl dibenzo-7-phosphanorbornadiene (R or RPA, A=anthracene C₁₆H₁₀)[3] with both benzoyl chloride (PhCOCl) and benzoyl triflate (PhCOOTF, OTf=OSO₂CF₃) in dichloromethane CH₂Cl₂ solution were reported (Scheme 1),[4] leading to neutral acyl(chloro)phosphine B (together with anthracene C₁₆H₁₀) and acylphosphonium A⁺ (together with a triflate anion OTf⁻), respectively. The cation A⁺ is stable in the solid state at low temperature but does rearrange or decompose slowly at ambient temperature, putatively leading to an anthracenyl (acyl)hydrophosphonium F⁺ that can be further deprotonated by the base triethylamine Et₃N.[4] Gas-phase DFT calculations supported the ion-pair A⁺Cl⁻ but precluded the phosphonium E⁺ as potential intermediates in the reaction with PhCOCl.[4] As will be shown below, inclusion of solvation effects in the theoretical treatment for ionic species is essential to provide reliable energetics for such reactions in solution. The present DFT study thus may provide deep mechanistic insights that are useful for the design of more efficient synthesis of acylphosphine compounds of broad scope.

Extensive state-of-the-art DFT calculations at the well-established PW6B95-D3 + COSMO-RS/TPSS-D3 + COSMO level in CH₂Cl₂ solution (see below for computational details) are performed for the reactions of R with various acylation reagents of PhCOX (X=Cl, Br, I, OTf), with an emphasis on the role of different anionic leaving groups X⁻ and the unclear decomposition mechanism of acylphosphonium A⁺ in solution. The PW6B95-D3 free energies (at 298 K in CH₂Cl₂) are used in our discussion unless specified otherwise.

As shown in Figure 1A, two ways of P−C nucleophilic attacks of R to the acyl carbonyl group of PhCOCl are found in our DFT calculations, with the leaving chloride anion Cl⁻ being either distant from (via TSA) or close to (via TSAc) the anthracene moiety. The former way is kinetically 4.4 kcal/mol more favorable mainly due to better π−π stacking interactions. Such nucleophlic P/C⁻ replacement at the carbonyl group is 1.2 kcal/mol endergonic to form the acylphosphonium cation A⁺ and Cl⁻ over a barrier of 20.1 kcal/mol. The transition structure TSA was also found in recent gas-phase DFT

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Scheme 1. Acylation reactions of tert-butyl dibenzo-7-phosphanorbornadiene R with PhCOCl and PhCOOTF.
higher in free energy than the overall reaction is thus rate-limited by the initial $\text{P} \cdots \text{C}$ attack 

The nucleophilic $\text{P} \cdots \text{C}$ and $\text{X}$ replacements at the carbonyl group become more and more exergonic in the series by $-4.1$, $-7.2$, and $-17.1$ kcal/mol to form $\text{A}^+$. Since the transition structures (such as $\text{TSBo}$) for further $\text{X} \cdots \text{P}$ attacks to $\text{A}^+$ remain almost unchanged in free energy with respect to the initial reactants, the preceding, exergonic $\text{P} \cdots \text{C}$ addition step do effectively increase the transition barriers for the $\text{X} \cdots \text{P}$ reaction step: such barriers are increased to 19.8, 22.7, and 33.8 kcal/mol for $\text{X} = \text{Br}$, I and OTf, which are 2.4, 6.2 and 19.6 kcal/mol higher than those required for the first $\text{P} \cdots \text{C}$ attack step, respectively. Moreover, the $\text{X} \cdots \text{P}$ attacks toward $\text{A}^+$ to eliminate anthracene are decreasingly exergonic by $-14.5$, $-12.7$ and 2.5 kcal/mol for $\text{X} = \text{Br}$, I and OTf, respectively, with reversed reaction spontaneity for $\text{X} = \text{OTf}$. Note that the conformational energies of acylphosphine $\text{PhCOP}(\text{X}) \text{tBu}$ are also subtly changed by the size of $\text{X}$-group: the cis-conformer is $1.4$ and $0.7$ kcal/mol more stable for small $\text{X} = \text{Cl}$ and Br, while the trans-conformer is $0.1$ and $3.8$ kcal/mol more stable for larger $\text{X} = \text{I}$ and OTf, respectively. It is clear that the nucleophilic OTf $\cdots \text{P}$ attack toward $\text{A}^+$ is kinetically and thermodynamically unfavourable to form the OTf-substituted acylphosphine $\text{Bo}$, making the isolation of stable salt $\text{A}^+\text{OTf}^-$ possible. Note that the $\text{A}^+\text{OTf}^-$ contact ion-pair is still $10.9$ kcal/mol less stable than the separated ions $\text{A}^+$ and OTf$^-$ in solution.

Experimentally, the acylphosphonium cation $\text{A}^+$ (with OTf$^-$ counter-anion) is only meta-stable in solution and may decompose slowly (complete in 36 hours at 23°C in CH$_2$Cl$_2$), putatively leading via an unclear mechanism to the anthracenyl (acyl)hydridophosphonium $\text{E}^+$. [4] Nucleophilic attack by OTf$^-$ is unlikely due to barriers higher than $30$ kcal/mol mentioned above. As shown in Figure 2, direct ring-opening of $\text{A}^+$ through

![Figure 1. DFT computed free energy paths (in kcal/mol, 298 K in CH$_2$Cl$_2$) for the acylation reactions of tert-butyl dibenzo-7-phosphanorbornadiene (R) with (A) $\text{PhCOCl}$, and (B) $\text{PhCOOTf}$ (results for $\text{PhCOX}$ with $\text{X} = \text{I}$ and Br shown in parentheses and in brackets for comparison). Crucial C, H, P and O atoms are highlighted as grey, white, yellow and red balls, with grey tube indicating carbon backbones and with mostly omitted H-atoms for clarity. Partially broken bonds of transition structures are indicated by dashed lines, with selected bond lengths shown in Å.](image)

![Figure 2. DFT computed free energy paths (in kcal/mol, 298 K in CH$_2$Cl$_2$) for the rearrangement/decomposition of phosphonium $\text{A}^+$ (together with OTf$^-$) without and with base NEt$_3$ (in red line). Other details see Figure 1.](image)
is prevented by a higher barrier of 35.5 kcal/mol and required heating at about 95°C. It is thus obvious that the highly electrophilic acylphosphonium E+ should be easily accessible from A+ in solution upon moderate heating, in stark contrast to the conclusion based on previous gas-phase DFT calculations. Alternatively, the activation of one antrachene C–H bond within the complex C+ may occur via proton-shift to adjacent carbonyl oxygen (via TSDh*), which is ~14 kcal/mol exergonic over a low barrier of 9.1 kcal/mol to form Dh+, followed by the OTf−-mediated proton-shift to form F+ as main product. The overall (A+ − F+) conversion is ~2.3 kcal/mol exergonic over a barrier of 23.6 kcal/mol, consistent with the slow rearrangement of A+ observed in solution at ambient temperature. When the base Et3N is also present, proton transfer from F+ to Et3N is ~9.6 kcal/mol exergonic over a barrier of only 6.3 kcal/mol (via TSDnF*) to form the anthracenyl acylphosphine D as main product. Proton transfer from C+ to Et3N is also possible (via TSDn*) but kinetically slightly less favourable than an intramolecular proton-shift to carbonyl oxygen (via TSDh*). Thus, our DFT calculations confirmed the formation of F+ (D being deprotonated by base Et3N) putatively assigned from the experimental 31P{1H} NMR doublet at ~15.5 ppm (singlet at ~8.1 ppm) as the main product of the A+ rearrangement. Moreover, the minor product Et3H*− PhOP(C2H5)2Bu+ or Et PhOPH2Bu when deprotonated by Et3N, tentatively assigned from the experimental 31P{1H} NMR triplet at ~62.1 ppm (and doublet at ~59.1 ppm), is very likely formed from hydride abstraction by the reactive acylphosphonium intermediate E+ with (without) additional protonation at the P-site. This fact suggests that stable acylphosphonium salts such as A+OTf− may be useful acylphosphonium transfer reagent in general, especially when nucleophile stronger than Cl− is used as acceptor.

In summary, detailed DFT mechanistic insights are provided into the acylation reactions of tert-butyl dibenzo-7-phosphanoboradiene R with PhCOX (X=Cl, Br, I, and OTf) in CH2Cl2 solution. All such reactions are initialized by nucleophilic P−C attack to form the acylphosphonium A+ together with free anion X−, followed by either nucleophilic X−→P attack (for X=Cl, Br, and I) to eliminate antrachene or by slow rearrangement/decomposition of A+ (X=OTf). Though the reaction with PhCOCl is rate-limited by the initial P−C attack, other reactions with more reactive acylation reagents are rate-limited by either the second X−→P attack (for X=Br and I) or by slow rearrangement/decomposition of A+ (X=OTf) instead. Our results strongly support the separated acylphosphonium A+ as the key intermediate that may be useful for the transfer of acylphosphonium E+ in general.

Computational Methods

All DFT calculations are performed with the TURBOMOLE 7.3 suite of programs. The initial structures are screened with the GGN-xTB method and fully optimized at the TPSS-D3/def2-TZVP + COSMO (CH2Cl2) level, which combines the TPSS meta-GGA density functional with the B3-damped DFT-D3 dispersion correction and the def2-TZVP basis set, using the Conductor-like Screening Model (COSMO) for CH2Cl2 solvent (dielectric constant ε = 8.93 and diameter Rm=2.94 Å). The density-fitting RI-J approach is used to accelerate the DFT calculations. The optimized structures are characterized by frequency analysis (no imaginary frequency for true minima and only one imaginary frequency for transition states) to provide thermal free-energy corrections (at 298.15 K and 1 atm) according to the modified ideal gas-rigid rotor-harmonic oscillator model.

More accurate solvation free energies in CH2Cl2 are computed with the COSMO-RS model (parameter file: BP_TZVP_C30_16001.cdt) using the COSMOTHERM package based on the TPSS-D3 optimized structures, corrected by ~1.89 kcal/mol to account for the 1 mol/L reference concentration in solution. To check the effects of the chosen DFT functionals on the reaction energies and barriers, single-point calculations at both TPSS-D3 and hybrid-meta-GGA PW6B95-D3 levels are performed using larger def2-QZVP basis set. Final reaction free energies (ΔG) are determined from the electronic single-point energies plus TPSS-D3 thermal corrections and COSMO-RS solvation free energies. The results from both DFT functionals are in good mutual agreement but on average 3.5 ± 2.0 kcal/mol higher reaction barriers (as expected) are found at the hybrid PW6B95-D3 level compared to the TPSS-D3 results (see ESII). In the discussion, more reliable PW6B95-D3+COSMO-RS free energies (in CH2Cl2 at 298.15 K and 1 mol/L reference concentration) are used unless specified otherwise.

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Conflict of Interest

The authors declare no conflict of interest.

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[1] L. Gonsalvi, M. Peruzzi, Angew. Chem. Int. Ed. 2012, 51, 7895–7897; Angew. Chem. 2012, 124, 8017–8019; b) K. Dietliker, T. Jung, J. Benkhoff, H. Kura, A. Matsumoto, H. Oka, D. Hristova, G. Gescheidt, G. Rist, Macromol. Symp. 2004, 217, 77–98.

[2] a) A. Eibel, M. Schmallegger, M. Zalibera, A. Huber, Y. Bürkl, H. Grützmacher, G. Gescheidt, Eur. J. Inorg. Chem. 2017, 2017, 2469–2478; b) A. Huber, A. Kuchel, T. Ott, G. Santisio-Quinones, D. Stein, J. Bräuer, R. Kniss, F. Krumefich, H. Schönberg, J. Levalois-Grützmacher, H. Grützmacher, Chem. Commun. 2016, 52, 2823–2826; c) G. Becker, W. Schwarz, N. Seidler, M. Westerhausen, Z. Anorg. Allg. Chem. 1992, 612, 72–82; e) C. L. Liotta, M. L. McLaughlin, B. A. O’Brien, Tetrahedron Lett. 1984, 25, 1249–1252; f) C. L. Liotta, M. L. McLaughlin, D. G. Van Derveer, B. A. O’Brien, Tetrahedron Lett. 1984, 25, 1665–1668; g) A. Antolato, S. García-Yuste, A. Otero, R. Realgui-Carmona, M. I. Tercero-Morales, C. R. Chem. 2010, 13, 929–934; h) J.-J. Brunet, R. Chauvin, B. Donnadieu, E. Thépaut, J. Organomet. Chem. 1999, 579, 198–205; i) J.-J. Brunet, A. Capperucci, R. Chauvin, B. Donnadieu, J. Organomet. Chem. 1997, 533, 79–81; j) D. S. Bohle, G. R. Clark, C. E. F. Rickard, W. R. Roper, J. Organomet. Chem. 1990, 393, 243–264; k) D. S. Bohle, G. R. Clark, C. E. F. Rickard, W. R. Roper, J. Organomet. Chem. 1988, 353, 355–381; l) J. M. Goicoechea, H. Grützmacher, Angew. Chem. Int. Ed. 2018, 57, 16968–16994.
[3] a) A. Velian, C. C. Cummins, J. Am. Chem. Soc. 2012, 134, 13978–13981; b) W. J. Transue, A. Velian, M. Nava, C. García-Iriepa, M. Temprado, C. C. Cummins, J. Am. Chem. Soc. 2017, 139, 10822–10831.

[4] K. M. Szkop, M. B. Geeson, D. W. Stephan, C. C. Cummins, Chem. Sci. 2019, 10, 3627–3631.

[5] F. Furche, R. Ahlrichs, C. Haettig, W. Klopper, M. Sierka, F. Weigend, Wiley Interdiscip. Rev.: Comput. Mol. Sci. 2014, 4, 91–100.

[6] S. Grimme, C. Bannwarth, P. Shushkov, J. Chem. Theory Comput. 2017, 13, 1989–2009.

[7] J. Tao, J. P. Perdew, V. N. Staroverov, G. E. Scuseria, Phys. Rev. Lett. 2003, 91, 146401.

[8] a) S. Grimme, J. Antony, S. Ehrlich, H. Krieg, J. Chem. Phys. 2010, 132, 154104–154119; b) S. Grimme, S. Ehrlich, L. Goerigk, J. Comput. Chem. 2011, 32, 1456–1465.

[9] F. Weigend, R. Ahlrichs, Phys. Chem. Chem. Phys. 2005, 7, 3297–3305.

[10] A. Klamt, G. Schüürmann, J. Chem. Soc. Perkin Trans. 2 1993, 799–805.

[11] a) F. Weigend, Phys. Chem. Chem. Phys. 2006, 8, 1057–1065; b) K. Eischkorn, F. Weigend, O. Treutler, R. Ahlrichs, Theor. Chem. Acc. 1997, 97, 119–124.

[12] S. Grimme, Chem. Eur. J. 2012, 18, 9955–9964.

[13] F. Eckert, A. Klamt, AIChE J. 2002, 48, 369–385.

[14] F. Eckert, A. Klamt in COSMOtherm, Version 3.1.0, Release 16.01; COSMOlogic GmbH & Co. KG, Leverkusen, Germany Vol. 2015.

[15] Y. Zhao, D. G. Truhlar, J. Phys. Chem. A 2005, 109, 5656–5667.

[16] F. Weigend, F. Furche, R. Ahlrichs, J. Chem. Phys. 2003, 119, 12753–12762.

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