ChemPubSoc Europe

DOI: 10.1002/open.201900176

Open Access ChemistryOPEN Communications

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

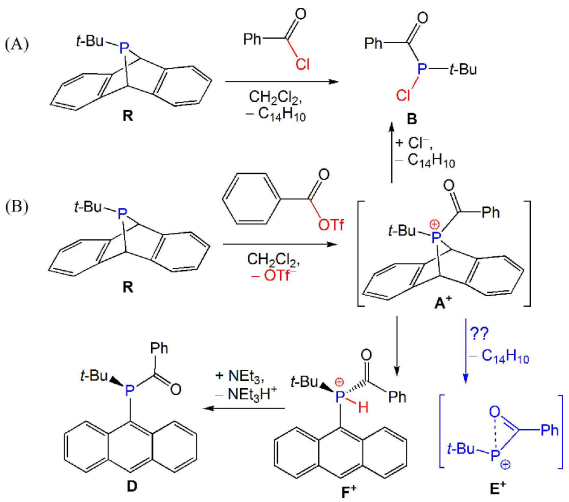
Zheng-Wang Qu,* Hui Zhu, and Stefan Grimme[a]

Extensive DFT calculations provide deep mechanistic insights into the acylation reactions of *tert*-butyl dibenzo-7-phosphanobornadiene with PhCOX (X = Cl, Br, I, OTf) in CH_2Cl_2 solution. Such reactions are initialized by the nucleophilic P···C attack to the carbonyl group to form the acylphosphonium intermediate $\mathbf{A}^+$ together with X^- anion, followed either by nucleophilic X^-···P attack (X = Cl, Br, and I) toward $\mathbf{A}^+$ to eliminate anthracene or by slow rearrangement or decomposition of $\mathbf{A}^+$ (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 $\mathbf{A}^+$ is initiated by a P-C bond cleavage, followed either by sequential proton-shifts to form anthracenyl acylphosphonium or by deprotonation with additional base Et_3N to form neutral anthracenyl acylphosphine. Our DFT results strongly support the separated acylphosphonium $\mathbf{A}^+$ as the key reaction intermediate that may be useful for the transfer of acylphosphenium in general.

Acylphosphines and their oxides are useful photo-initiators for radical polymerization reactions,[1] usually synthesized by using nucleophilic sources of phosphorus such as PH_3, MPH_2 (M=Li, Na, K), $P(TMS)_3$ (TMS = trimethylsilyl), and transition metal-supported phosphines and phosphides.[2] Very recently, novel acylation reactions of *tert*-butyl dibenzo-7-phosphanobornadiene (**R** or RP**A**, **A** = anthracene $C_{14}H_{10}$)[3] with both benzoyl chloride (PhCOCl) and benzoyl triflate (PhCOOTf, OTf = OSO_2CF_3) in dichloromethane CH_2Cl_2 solution were reported (Scheme 1),[4] leading to neutral acyl(chloro)phosphine **B** (together with anthracene $C_{14}H_{10}$) and acylphosphonium $\mathbf{A}^+$ (together with a triflate anion OTf^-), respectively. The cation $\mathbf{A}^+$ is stable in the solid state at low temperature but does rearrange or decompose slowly at ambient temperature, putatively leading to an anthracenyl (acyl)hydridophosphnium $\mathbf{F}^+$ that can be further deprotonated by the base triethylamine Et_3N.[4] Gas-phase DFT calculations supported the ion-pair $\mathbf{A}^+Cl^-$ but precluded the phosphenium $\mathbf{E}^+$ 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 CH_2Cl_2 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 $\mathbf{A}^+$ in solution. The PW6B95-D3 free energies (at 298 K in CH_2Cl_2) 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 nucleophilic P/Cl^- replacement at the carbonyl group is 1.2 kcal/mol endergonic to form the acylphosphonium cation $\mathbf{A}^+$ and Cl^- over a barrier of 20.1 kcal/mol. The transition structure **TSA** was also found in recent gas-phase DFT



Scheme 1. Acylation reactions of *tert*-butyl dibenzo-7-phosphanorbornadiene **R** with PhCOCl and PhCOOTf.

[a] *Dr. Z.-W. Qu, Dr. H. Zhu, Prof. S. Grimme*
Mulliken Center for Theoretical Chemistry
University of Bonn
Beringstr. 4, 53115 Bonn, Germany
E-mail: qu@thch.uni-bonn.de

Supporting information for this article is available on the WWW under https://doi.org/10.1002/open.201900176

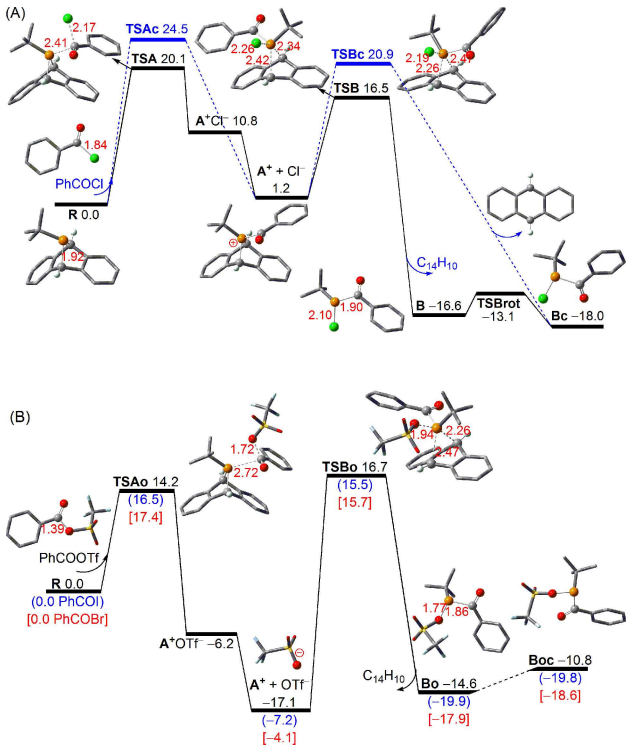


Figure 1. DFT computed free energy paths (in kcal/mol, 298 K in CH_2Cl_2) for the acylation reactions of *tert*-butyl dibenzo-7-phosphanorbornadiene (**R**) with (A) PhCOCl, and (B) PhCOOTf (results for PhCOX with X = I and Br shown in parentheses and in brackets for comparison). Crucial C, H, P and 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.

calculations and connected to the contact ion-pair[4] $\mathbf{A}^+Cl^-$ that turns out to be 9.6 kcal/mol less stable than the separated ions $\mathbf{A}^+$ and Cl^- in solution. Further elimination of the anthracene moiety from $\mathbf{A}^+$ can be induced in two ways of nucleophilic Cl^-···P attack towards $\mathbf{A}^+$, with the incoming Cl^- being either distant from (via **TSB**) or close to (via **TSBc**) the carbonyl oxygen. The transition structure **TSBc** was also found in recent DFT calculations[4] but in our calculations is actually 4.4 kcal/mol higher in free energy than **TSB**. The Cl^-···P attack via **TSB** is −16.6 kcal/mol exergonic over a low barrier of 15.3 kcal/mol to form the *trans*-conformer **B** of acyl (chloro)phosphine PhCOP(Cl)*t*Bu together with the anthracene by-product, followed by a rapid P–C bond rotation into the *cis*-conformer **Bc** that is 1.4 kcal/mol more stable. In contrast, the *trans*-conformer **B** is preferred as P-ligand within the corresponding Ru-complex,[4] likely due to increased steric interactions around the P-center. The overall reaction is thus rate-limited by the initial P···C attack via **TSA** over a moderate barrier of 20.1 kcal/mol.

As shown in Figure 1B, very similar reaction steps (sequential nucleophilic P···C and X^-···P attacks) are also found for the reactions of **R** with more reactive acylation reagents PhCOX (X = Br, I and OTf), as indicated by the decreasing reaction barrier of 17.4, 16.5 and 14.2 kcal/mol for the initial P···C attack. Due to increasing solubility of leaving anions X^-, such nucleophilic P/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 $\mathbf{A}^+$. Since the transition structures (such as **TSBo**) for further X^-···P attacks to $\mathbf{A}^+$ remain almost unchanged in free energy with respect to the initial reactants, the preceding, exergonic P···C addition step do effectively increase the transition barriers for the X^-···P reaction step: such barriers are increased to 19.8, 22.7, and 33.8 kcal/mol for X = Br, I and OTf, which are 2.4, 6.2 and 19.6 kcal/mol higher than those required for the first P···C attack step, respectively. Moreover, the X^-···P attacks toward $\mathbf{A}^+$ to eliminate anthracene are decreasingly exergonic by −14.5, −12.7 and 2.5 kcal/mol for X = Br, I and OTf, respectively, with reversed reaction spontaneity for X = OTf. Note that the conformational energies of acylphosphine PhCOP(X)*t*Bu are also subtly changed by the size of X-group: the *cis*-conformer is 1.4 and 0.7 kcal/mol more stable for small X = Cl and Br, while the *trans*-conformer is 0.1 and 3.8 kcal/mol more stable for larger X = I and OTf, respectively. It is clear that the nucleophilic OTf^-···P attack toward $\mathbf{A}^+$ is kinetically and thermodynamically unfavourable to form the OTf-substituted acylphosphine **Bo**, making the isolation of stable salt $\mathbf{A}^+OTf^-$ possible. Note that the $\mathbf{A}^+OTf^-$ contact ion-pair is still 10.9 kcal/mol less stable than the separated ions $\mathbf{A}^+$ and OTf^- in solution.

Experimentally, the acylphosphonium cation $\mathbf{A}^+$ (with OTf^- counter-anion) is only meta-stable in solution and may decompose slowly (complete in 36 hours at 23 °C in CH_2Cl_2), putatively leading via an unclear mechanism to the anthracenyl (acyl)hydridophosphonium $\mathbf{F}^+$.[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 $\mathbf{A}^+$ through

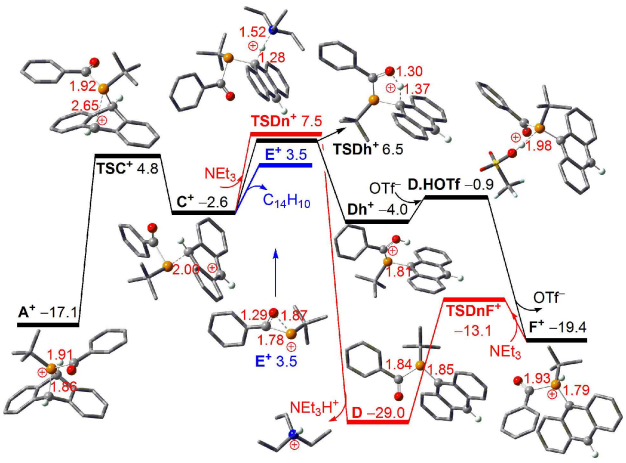


Figure 2. DFT computed free energy paths (in kcal/mol, 298 K in CH_2Cl_2) for the rearrangement/decomposition of phosphonium $\mathbf{A}^+$ (together with OTf^-) without and with base NEt_3 (in red line). Other details see Figure 1.

a P–C cleavage (via $\mathbf{TSC}^+$) is 14.5 kcal/mol endergonic over a barrier of 21.9 kcal/mol to form the transient complex $\mathbf{C}^+$ that may dissociate further into the acylphosphenium $\mathbf{E}^+$ together with anthracene with a binding affinity of only 6.1 kcal/mol. For comparison, similar ring-opening of neutral **R** (via **TSR**, see ESI)

is prevented by a higher barrier of 35.5 kcal/mol and required heating at about 95 °C.[3a] It is thus obvious that the highly electrophilic acylphosphenium $\mathbf{E}^+$ should be easily accessible from $\mathbf{A}^+$ in solution upon moderate heating, in stark contrast to the conclusion based on previous gas-phase DFT calculations.[4] Alternatively, the activation of one anthracene C–H bond within the complex $\mathbf{C}^+$ may occur via proton-shift to adjacent carbonyl oxygen (via $\mathbf{TSDh}^+$), which is −1.4 kcal/mol exergonic over a low barrier of 9.1 kcal/mol to form $\mathbf{Dh}^+$, followed by the OTf^--mediated proton-shift to form $\mathbf{F}^+$ as main product. The overall ($\mathbf{A}^+ \rightarrow \mathbf{F}^+$) conversion is −2.3 kcal/mol exergonic over a barrier of 23.6 kcal/mol, consistent with the slow rearrangement of $\mathbf{A}^+$ observed in solution at ambient temperature.[4] When the base Et_3N is also present, proton transfer from $\mathbf{F}^+$ to Et_3N is −9.6 kcal/mol exergonic over a barrier of only 6.3 kcal/mol (via $\mathbf{TSDnF}^+$) to form the anthracenyl acylphosphine **D** as main product. Proton transfer from $\mathbf{C}^+$ to Et_3N is also possible (via $\mathbf{TSDn}^+$) but kinetically slightly less favourable than an intramolecular proton-shift to carbonyl oxygen (via $\mathbf{TSDh}^+$). Thus, our DFT calculations confirmed the formation of $\mathbf{F}^+$ (**D** when deprotonated by base Et_3N) putatively assigned from the experimental $^{31}P\{^1H\}$ NMR doublet at −15.5 ppm (singlet at −8.1 ppm) as the main product of the $\mathbf{A}^+$ rearrangement.[4] Moreover, the minor product $\mathbf{Eh_2}^+$ $PhCOPH_2tBu^+$ (or **Eh** PhCOPH*t*Bu when deprotonated by Et_3N), tentatively assigned from the experimental $^{31}P\{^1H\}$ NMR triplet at −62.1 ppm (and doublet at −59.1 ppm),[4] is very likely formed from hydride abstraction by the reactive acylphosphenium intermediate $\mathbf{E}^+$ with (without) additional protonation at the P-site. This fact suggests that stable acylphosphonium salts such as $\mathbf{A}^+OTf^-$ may be useful acylphosphenium 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-phosphanobornadiene **R** with PhCOX (X = Cl, Br, I, and OTf) in CH_2Cl_2 solution. All such reactions are initialized by nucleophilic P···C attack to form the acylphosphonium $\mathbf{A}^+$ together with free anion X^-, followed by either nucleophilic X^-···P attack (for X = Cl, Br, and I) to eliminate anthracene or by slow rearrangement /decomposition of $\mathbf{A}^+$ (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 $\mathbf{A}^+$ (X = OTf) instead. Our results strongly support the separated acylphosphonium $\mathbf{A}^+$ as the key intermediate that may be useful for the transfer of acylphosphenium $\mathbf{E}^+$ in general.

Computational Methods

All DFT calculations are performed with the TURBOMOLE 7.3 suite of programs.[5] The initial structures are screened with the GFN-xTB method[6] and fully optimized at the TPSS–D3/def2-TZVP + COSMO ($CHCl_3$) level, which combines the TPSS meta-GGA density functional[7] with the BJ-damped DFT–D3 dispersion correction[8] and the def2-TZVP basis set,[9] using the Conductor-like Screening Model (COSMO)[10] for CH_2Cl_2 solvent (dielectric constant ε = 8.93 and diameter R_{solv} = 2.94 Å). The density-fitting RI-J approach[11] is used to accelerate the 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.[12]

More accurate solvation free energies in CH_2Cl_2 are computed with the COSMO-RS model[13] (parameter file: BP_TZVP_C30_1601.ctd) using the COSMOtherm package[14] 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[7] and hybrid-meta-GGA PW6B95-D3[15] levels are performed using larger def2-QZVP[9,16] 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 ESI). In the discussion, more reliable PW6B95-D3 + COSMO-RS free energies (in CH_2Cl_2, at 298.15 K and 1 mol/L reference concentration) are used unless specified otherwise.

Acknowledgements

The German Science Foundation (DFG) is gratefully acknowledged for financial support (Gottfried Wilhelm Leibnitz prize to S.G.).

Conflict of Interest

The authors declare no conflict of interest.

Keywords: acylphosphine · acylation reactions · reaction mechanism · norbornadienes · phosphenium

[1] a) L. Gonsalvi, M. Peruzzini, *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. Kuschel, T. Ott, G. Santiso-Quinones, D. Stein, J. Bräuer, R. Kissner, F. Krumeich, H. Schönberg, J. Levalois-Grützmacher, H. Grützmacher, *Angew. Chem. Int. Ed.* **2012**, *51*, 4648–4652; *Angew. Chem.* **2012**, *124*, 4726–4730; c) J. Wang, G. Siqueira, G. Müller, D. Rentsch, A. Huch, P. Tingaut, J. Levalois-Grützmacher, H. Grützmacher, *Chem. Commun.* **2016**, *52*, 2823–2826; d) G. Becker, W. Schwarz, N. Seidler, M. Westerhausen, *Z. Anorg. Allg. Chem.* **1992**, *612*, 72–82; e) C. L. Liotta, M. L. MeLaughlin, 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. Antiñolo, S. García-Yuste, A. Otero, R. Reguillo-Carmona, M. T. Tercero-Morales, *C. R. Chim.* **2010**, *13*, 929–934; h) J.-J. Brunet, R. Chauvin, B. Donnadieu, E. Thepaut, *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*, 243–285; 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. Garcia-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. Eichkorn, 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 C3.0, 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.

Manuscript received: May 20, 2019
Revised manuscript received: June 6, 2019