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Dealkanative Main Group Couplings Across the peri-Gap

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Abstract

Here, we highlight the ability of peri-substitution chemistry to promote a series of unique P–P/P–As coupling reactions, which proceed with concomitant C–H bond formation. This dealkanative reactivity represents an interesting and unexpected expansion to the established family of main-group dehydrocoupling reactions. These transformations are exceptionally clean, proceeding essentially quantitatively at relatively low temperatures (70–140 °C), with 100% diastereoselectivity in the products. The reaction appears to be radical in nature, with the addition of small quantities of a radical initiator (azobisisobutyronitrile) increasing the rate dramatically, as well as altering the apparent order of reaction. DFT calculations suggest that the reaction involves dissociation of a phosphorus centred radical (stabilised by the peri-backbone) to the P–P coupled product and a free propyl radical, which carries the chain. This unusual reaction demonstrates the powerful effect that geometric constraints, in this case a rigid scaffold, can have on the reactivity of main group species; an area of research that is gaining increasing prominence in recent years.

1 – Introduction

Coupling reactions, in which two species are linked together with the elimination of a small molecule, have revolutionised many areas of chemical research. In the field of main group chemistry, dehydrocoupling reactions (E–H + H–E′ → E–E′ + H_2) have provided an alternative to traditional reductive strategies for the formation of E–E bonds. These reactions have been invaluable not only in inorganic synthesis; but also in polymer formation, transfer hydrogenation, and hydrogen storage.[1–3] Dehydrocoupling reactions utilise element hydrides as the principal starting materials; the preparation and reactivity of such species (in the case of phosphorus) have been reviewed extensively.[4,5]

Coupling reactions are typically catalysed by transition metals. This has several drawbacks; many of the metals used are non-abundant and thus expensive, which limits their sustainability and economy. Often, the metals are toxic,[6,7] which leads to problems when these catalysts are used in the synthesis of pharmaceuticals.[8] As such, the replacement of transition metals with cheaper and more readily available main group reagents is a tantalising prospect.

In recent years, there has been a push towards the use of heavier main group elements as catalysts, and a number of reactions which had previously been considered the domain of transition metals have been observed with p-block species.[9] The work of the Radosevich group in this area is particularly exciting, as it demonstrates the profound effect that geometric constraints can have on reactivity.[10–14]

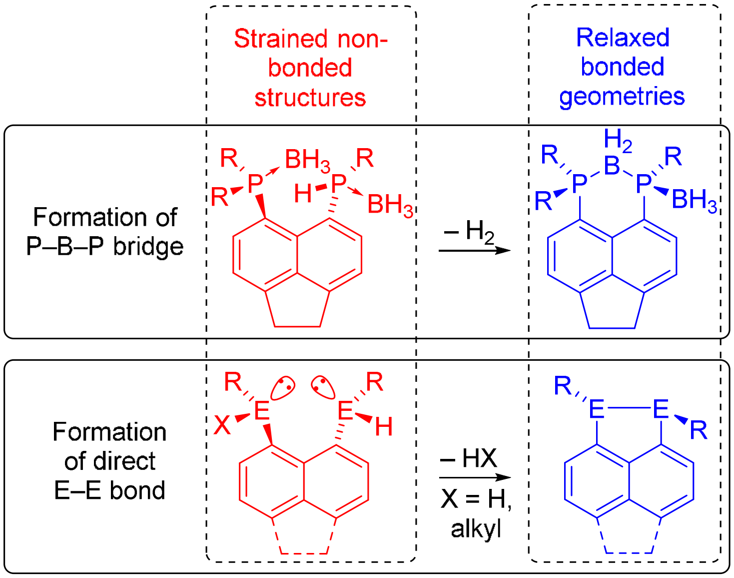
Focusing on dehydrocoupling, a number of main group reagents now exist to effect such transformations, with both stoichiometric[15,16] and catalytic[17–19] examples being known. The majority of these catalytic reagents carry out B–N bond formation, with Si–E bond forming reactions (E = C, N, O, S) also being a major area of research.[3,20] While many of these reactions initially appeared disparate in mechanism, general trends in the reactivity of such species are now being identified as more examples are published.[20]

The work of our group has focused on peri-substitution, which is a double substitution in the 1,8 positions of naphthalene, or the 5,6 positions of acenaphthene.[21] The rigid scaffold and enforced proximity this provides is useful in thermodynamically stabilising bonding motifs which are typically unstable at room temperature, such as subvalent or redox metastable species.[21–24] Other groups have used peri-substitution to stabilise free radicals,[25–28] and to generate strong Lewis acids for frustrated Lewis pair chemistry.[29–31]

Lately, we have become interested in using peri-substitution to substantially reduce the *kinetic* barrier to certain reactions, thus eliminating the need for an external catalyst. If successful, we feel that this concept could open an exciting new avenue of research into peri-substitution chemistry. This idea relies on the fact that the two peri-atoms (E) are forced into close proximity, closer than the sum of their van der Waals radii. This introduces significant strain into the system, which is thermodynamically unfavourable.[32] If possible, the system will seek to relieve that strain, and one way to achieve that is to undergo a coupling reaction. By forming a direct E–E bond, or by bonding via a bridging atom, the peri-backbone can achieve a far more relaxed geometry. In such a reaction, the peri-scaffold emulates the role of a catalyst by fixing the two reacting groups in place (reducing conformational entropy), destabilising the starting material relative to the transition state and, potentially, by stabilising the transition state. Thus, the overall kinetic energy barrier is reduced, allowing the reactions to proceed at a reduced temperature.

This concept has already been demonstrated in our recent work on peri-substituted phosphine-borane adducts. These molecules were found to undergo a spontaneous P–B dehydrocoupling reaction to afford P–B–P bridged species (Scheme 1, top).[33] This reaction occurred at room temperature and in the absence of a catalyst, something which had never been observed previously.[34,35]

In this paper, we extend this "enforced proximity coupling" concept to a series of highly unusual dehydrocoupling and dealkacoupling reactions, in which a direct E–E bond (E = P, As) is formed with concomitant elimination of either dihydrogen or a C–H coupled product, propane (Scheme 1, bottom).



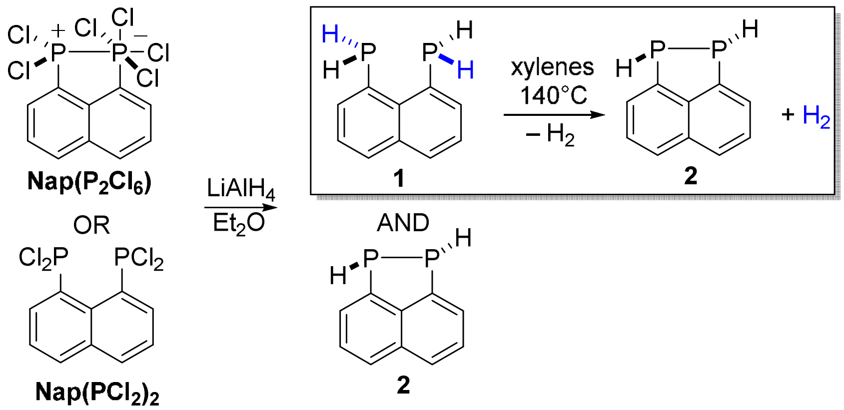
Scheme 1 Relaxation of the strained peri-geometry via P–B[33] or E–E coupling (E = P, As; as reported herein) with concurrent formation of either H_2 or an alkane.

2 – Results and Discussion

2.1 – Thermally Induced Dehydrocoupling

To date, only two examples of direct E–E dehydrocoupling on a peri-substituted scaffold (Scheme 1, bottom) have been reported. In 2004, Schmidbaur synthesised the primary bis(phosphine) **1** by reduction of $Nap(PCl_2)_2$ with $LiAlH_4$ (Nap = naphthalene-1,8-diyl), and observed diphosphane **2** as a minor by-product (Scheme 2). This compound was proposed to form via a dehydrogenative P–P coupling reaction from **1**. However, this transformation was not studied in detail, and compound **2** was characterised in the mixture with **1** by mass spectrometry and $^{31}P\{^1H\}$ NMR only.[36]

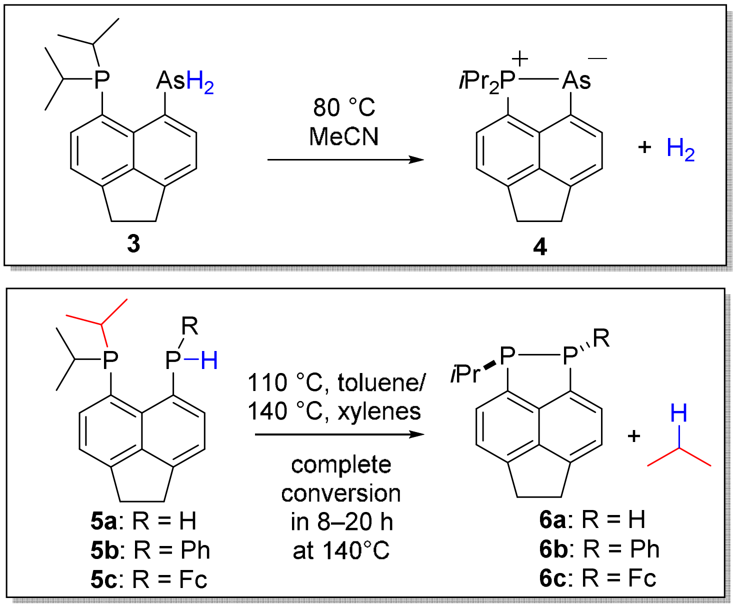
The transformation of bis(phosphine) **1** to diphosphane **2** has been reinvestigated by us and, in the process, a new route to **1** and **2** *via* the phosphonium-phosphoride $Nap(P_2Cl_6)$ has been developed (Scheme 2).[37] In our hands, both reductions (of $Nap(PCl_2)_2$ or $Nap(P_2Cl_6)$) afforded mixtures of **1** and **2** in variable ratios. Heating a mixture of **1** and **2** (with an initial ratio of 1:4) to 140° C in an inert solvent (xylenes) for 5 days gave complete, clean conversion to compound **2** (Scheme 2) as judged by $^{31}P\{^1H\}$ NMR. This confirmed that catalyst-free dehydrocoupling of **1** is possible at moderate temperatures, and allowed pure **2** to be isolated and fully characterised, including by single crystal X-ray diffraction (Figure 1).



Scheme 2: Synthetic transformations leading to Nap(PH)$_2$ (**2**). Complete conversion of **1** to **2**, from an initial mixture of **1** and **2** containing approximately 80% **2**, took 5 days at 140 °C. The dehydrocoupling step is highlighted in the frame.

To put this reactivity into context, we highlight here the *catalytic* dehydrocoupling of a closely related bis(phosphine), *o*-$C_6H_4(PH_2)_2$. The mildest conditions for this substrate (as reported by Stephan) were 75 °C for 48 hours in the presence of 5 mol% [CpTi(NP*t*Bu)(CH$_2$)$_2$], which gave the dimer $[C_6H_4P(PH)]_2$ in 75% isolated yield.[38] Waterman carried out the same transformation using a zirconium catalyst, with full conversion requiring temperatures of 100 °C for 4–6 weeks.[39] We presume the related uncatalysed reaction would require harsher conditions, presumably significantly harsher than those used in our uncatalysed transformation of **1** to **2**. In short, the clean thermal dehydrocoupling of bis(phosphine) **1** is unusual, as it is comparable (in terms of rate and reaction temperatures) to the transition metal catalysed dehydrocoupling of electronically similar substrates.

The only other example of a direct E–E dehydrocoupling arising from peri-substitution is the synthesis of the stable arsanylidene-σ^4-phosphorane **4**, recently published by our group.[23] Compound **4** was obtained by dehydrogenative coupling of the primary arsine **3** (Scheme 3, top). This reaction is very unusual, representing both a rare 1,1-hydrogen elimination and an example of dehydrocoupling being employed in the synthesis of a low-valent main group species.



Scheme 3: Contrasting outcomes of the dehydrogenative P–As coupling to afford arsanylidene-σ^4-phosphorane **4** (top) and of the dealkanative P–P couplings of bis(phosphines) **5a**–**c** (bottom).

2.2 – Thermally Induced Dealkacoupling

2.2.1 – Phosphorus-Phosphorus Dealkacoupling

As the primary arsine **3** (Scheme 3, top) had displayed such interesting reactivity on heating, the thermal decomposition of the phosphorus congener (the primary phosphine **5a**) was investigated, with unexpected results. On refluxing **5a** in toluene for 3 days (or xylenes for 8 h), clean conversion to the diphosphane **6a** was observed (Scheme 3, bottom). In this reaction, **5a** undergoes P–P coupling with concomitant C–H bond formation to evolve propane gas. The evolution of propane was confirmed by trapping the gaseous byproducts and subsequent analysis by ^{1}H NMR (see supporting information (SI), section S6.1). No evidence of propene or hydrogen formation was observed in this experiment. The reaction proceeded essentially quantitatively, with very minor amounts of other phosphorus compounds being co-formed (< 2% as judged by ^{31}P NMR).

As an extension to this, two other secondary phosphines (**5b–c**) were synthesised via previously published procedures[40,41] and heated in toluene or xylenes. These compounds also underwent propane elimination to yield the novel diphosphanes **6b–c** in quantitative yield (Scheme 3, bottom). These reactions are exceptionally clean, with no phosphorus containing byproducts being observed. X-ray crystallography demonstrated that these diphosphanes form exclusively as the trans isomers (Figure 1). Both structures show a decrease in strain compared to the parent bis(phosphines) **5b–c**, with reduced P···P distances (**6b**: 2.232(2) Å, **6c**: 2.220(2) Å; c.f. **5b**: 3.028(1) Å, **5c**: 3.050(2) Å),[40] splay angles (**6b**: −7.8(13)°, **6c**: −8.2(4)°; c.f. **5b**: +11.0(10)°, **5c**: +12.2(9)°)[40] and almost no out-of-plane displacement of the peri-atoms (see Table 1).

Whilst approximately the same rate of elimination was observed for both **5a** and **5b**, the rate of propane elimination for the ferrocenyl compound (**5c**) was substantially slower. Complete conversion was achieved after 20 hours of reflux in xylenes, or 15 days in toluene (c.f. 3 days in toluene for **5a**).

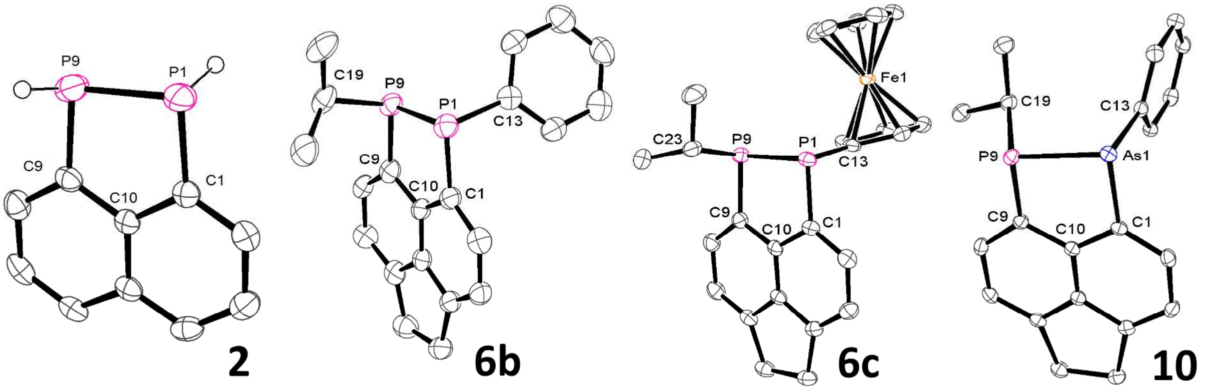


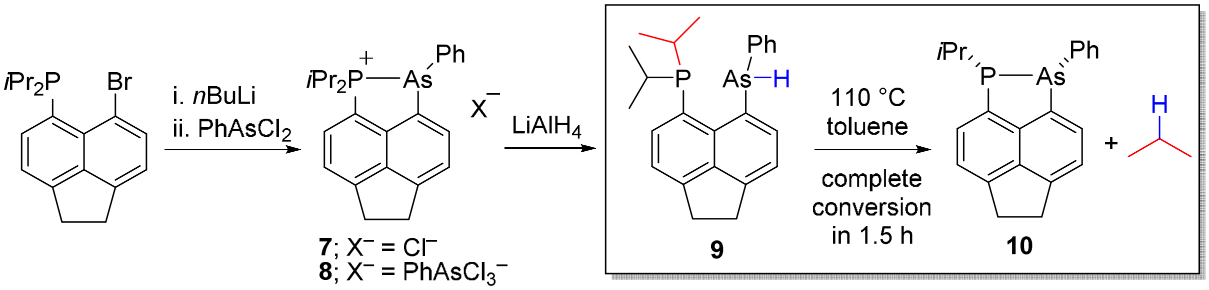
Figure 1 Structures of **2**, **6b**, **6c** and **10** in the solid state. Carbon-bound hydrogen atoms and second molecule in asymmetric unit (**6b**, **10**) omitted for clarity. The phosphorus-bound hydrogens of compound **2** are disordered over two positions, but are believed to be trans to one another. For clarity, only one pair of H atoms is shown.

This C–H bond forming reaction is unexpected and rather intriguing. Almost all work on E–E couplings thus far has involved the evolution of hydrogen,[1–3] whilst related main group dealkanative reactivity (E–H + E–R → E–E + R–H; E = main group element, R = alkyl) is mostly limited to systems involving highly energised and polar M–C bonds. Examples of this include the reaction of metal alkyls (M = Li, Al, Mg, Zn) with protic substrates.[42] In contrast to M–C bonds, P–C bonds are rather non-polar ($\chi(P) = 2.19$; $\chi(C) = 2.55$ on the Pauling scale)[43] and are considered to be one of the most stable bonds in chemistry.[44]

The authors could find only one literature example of P–C bond cleavage with concurrent P–P and C–H bond formation, which was published very recently.[45] However, this was a rhodium catalysed isomerisation reaction, and thus mechanistically distinct from the reaction presented here. Somewhat more distant from pnictogen chemistry, an intriguing example of ambient temperature demethanative Ge–Ge coupling [$n(HGeMe_3) \rightarrow H(GeMe_2)_nMe + (n-1)CH_4$] was reported by Berry in 1996.[46,47] More recently, the group of Hill has reported a catalytic B–N coupling reaction proceeding with concurrent formation of a Si–H bond (elimination of Me_2PhSiH, a "desilacoupling" reaction).[48] Again, both of these reactions differ mechanistically from this propane elimination. The demethanative coupling requires a ruthenium metal catalyst, while the "desilacoupling" is mediated by strongly basic group 2 metal reagents.

2.2.2 – Phosphorus-Arsenic Dealkacoupling

As an initial expansion of this work, we decided to move down group 15 to the heavier pnictogens. These elements form weaker E–H and E–C bonds and, as such, might be expected to eliminate more readily than the P/P system. To this end, an arsenic analogue of the bis(phosphine) **5b** (**9**) was synthesised, to see if it underwent propane elimination at an increased rate.[49] To synthesise **9**, Acenap(P*i*Pr_2)(Br) (Acenap = acenaphthene-5,6-diyl) was treated with *n*BuLi and then reacted with 1 equivalent of $PhAsCl_2$. This afforded a mixture of compounds **7** and **8**,[50] which were then reduced with $LiAlH_4$ to obtain the target compound (Scheme 4).



Scheme 4: Synthesis of arsenic compounds **7**, **8**, and **9,** followed by propane elimination to give **10** (highlighted in the frame).

Compound **9** was subjected to heating and, as predicted, eliminated propane to give the P–As bonded compound **10** at a far faster rate than its phosphorus congener. Complete clean conversion to **10** was achieved after 1.5 h of reflux in toluene, with **5b** requiring 3 days under the same conditions. Intriguingly, the crystal structure of **10** (Figure 1) demonstrated that compound **9** eliminated propane to give exclusively the cis product, whereas bis(phosphines) **5b–c** gave exclusively the trans isomer (Figure 1). In the crystal structure, compound **10** (as with the related diphosphanes **6b–c**) is relatively unstrained with a slightly negative splay angle and minimal out-of-plane displacements (Table 1). The P–As bond length (2.387(1) Å) is typical of a standard P–As single bond.[51]

To the best of our knowledge, the mild thermal elimination of an alkane from P–H/As–H and P–C functionalities is without precedent in the literature. Most notably, this reactivity involves the cleavage of a strong, non-polar P–C bond without the need for bond activation via the addition of a catalyst. We have undertaken a detailed mechanistic investigation into this reaction, as presented below.

Table 1: Selected bond lengths (Å), out-of-plane displacements (Å) and angles (°) for **2**, **5b**, **6b**, **6c** and **10**.

Compound	**2**	**5b**	**6b**[a]	**6c**	**10**[a]
E1···P9[b]	2.199(1)	3.028(1)	2.232(2) [2.231(2)]	2.220(2)	2.3867(8) [2.3870(9)]
Out of plane displacement (E1)[b]	0.024	0.351	0.013 [0.032]	0.247	0.008 [0.173]
Out of plane displacement (P9)	0.027	0.323	0.026 [0.104]	0.089	0.164 [0.111]
Splay angle[c]	−7.8(6)	+11.0(10)	−7.8(13) [−8.1(13)]	−8.2(4)	−4.2(6) [−4.5(6)]

a) Measurements for second molecule in asymmetric unit shown in square brackets; b) E = P, As; c) Splay angle = sum of the three bay-region angles – 360°. Example (for compound **2**): P9–C9–C10 + C9–C10–C1 + C10–C1–P1 – 360°.

2.3 – Mechanistic Studies of Propane Elimination

In our mechanistic studies we focused on the conversion of **5b** to **6b** (Scheme 3, bottom), as this reaction was considered representative, and the synthesis and purification of **5b** could be conducted on a relatively large scale with little difficulty.

As judged by quantitative $^{31}\text{P}\{^{1}\text{H}\}$ NMR spectroscopy, the reaction of **5b** to **6b** in xylenes proceeded cleanly, with no observable intermediates or by-products (Figure 2, A). The reaction was found to be second order with respect to **5b**, with a rate constant of 57 ± 2 $\text{M}^{-1}\ \text{h}^{-1}$ (T_{rxn} = 131 ± 1 °C) (Figure 2, B). Changing to a more polar reaction solvent (benzonitrile) did not change the order of reaction, but resulted in a substantial drop in rate to 7.4 $\text{M}^{-1}\ \text{h}^{-1}$ (T_{rxn} = 128 ± 1 °C). This suggests that the rate controlling step does not involve a significant build-up of charge, and makes an ionic mechanism unlikely.[52]

Second order rate constants were obtained for the reaction in xylenes over a temperature range of 94–131 °C (Figure 2, C). Plotting an Eyring graph over this temperature range affords activation parameters of $\Delta^{\ddagger}H°$ = +75 ± 5 kJ mol^{-1} and $\Delta^{\ddagger}S°$ = −97 ± 10 J $\text{K}^{-1}\ \text{mol}^{-1}$. However, a better linear fit is obtained with data in the range 114–131 °C only (Figure 2, D; see section S6.4 for details). This affords activation parameters of $\Delta^{\ddagger}H°$ = +57 ± 7 kJ mol^{-1} and $\Delta^{\ddagger}S°$ = −140 ± 20 J $\text{K}^{-1}\ \text{mol}^{-1}$. This activation enthalpy is remarkably low, much lower than the bond dissociation energies of either of the bonds being cleaved in this reaction. The negative entropy of activation could indicate some degree of ordering in the transition state, perhaps the association of two molecules.

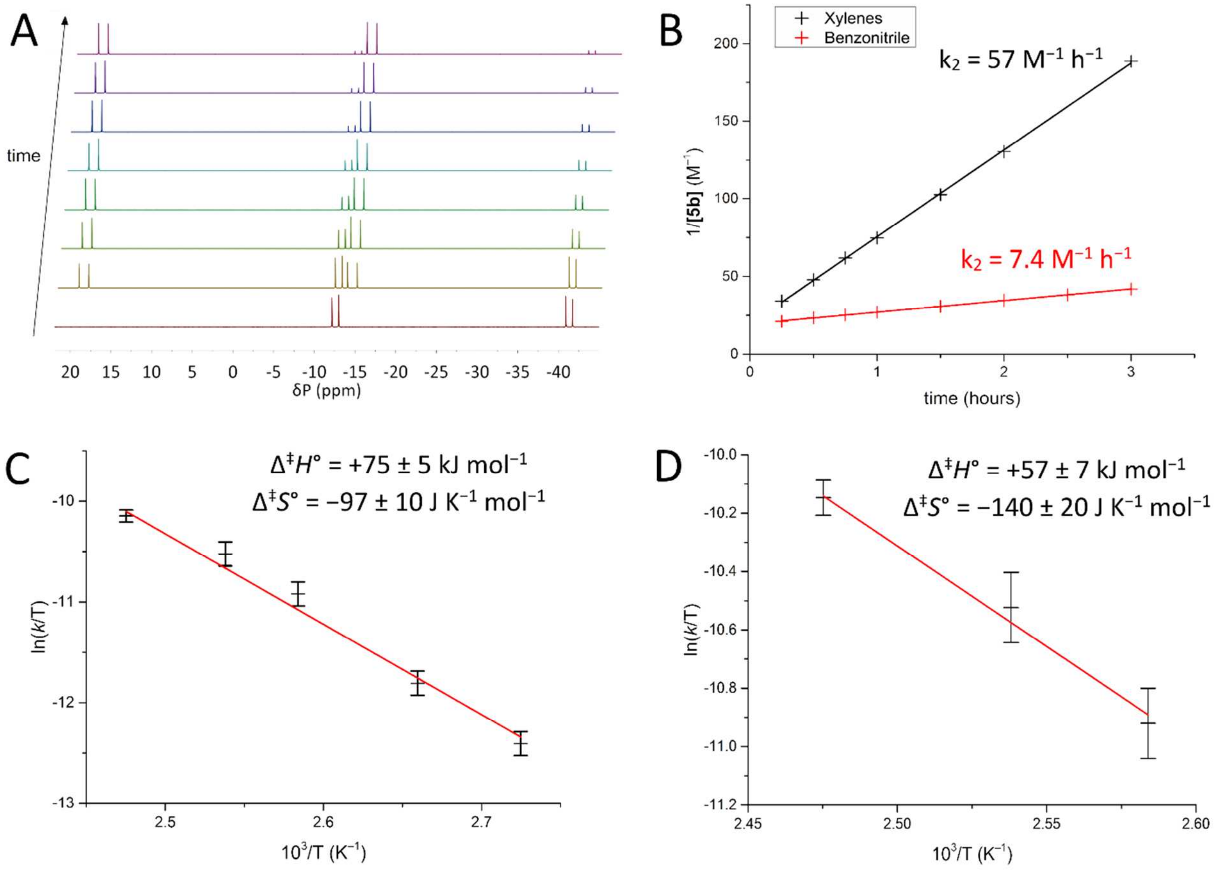


Figure 2: Mechanistic data for dealkanative coupling of **5b** to **6b**. (A) Time-stacked quantitative $^{31}\text{P}\{^{1}\text{H}\}$ NMR spectra showing the consumption of **5b** and formation of **6b**. (B) Second order rate plot (inverse concentration vs. time) for reactions in xylenes (T_{rxn} = 132 ± 1 °C) and benzonitrile (T_{rxn} = 128 ± 1 °C). (C) Eyring plot for data collected over the temperature range 94–132 °C in xylenes. (D) Eyring plot for data collected over the temperature range 114–131 °C in xylenes. Error bars set to 3σ for T_{rxn} = 131 °C (based on 3 independent measurements at this temperature) and twice this value for all other data points (which were measured once only).

The P-deuterated analogue of **5b**, compound **5d** (Scheme S16) was synthesised, and the kinetic isotope effect (KIE) measured for the transformation of **5d** to **6b**. This afforded a KIE of approximately 5 (see section S6.5). Given the magnitude of this KIE, we conclude that cleavage of the P–D/P–H bond is likely involved in the rate controlling step of this reaction.

Isotope labelling has also been used to ascertain that the P-bonded hydrogen is selectively transferred to C-2 of the formed propane molecule; $^{2}H\{^{1}H\}$ and ^{2}H NMR spectroscopy clearly showed the presence of the expected elimination product, propane-2-*d* (see section S6.6). No other deuterated compounds were observed, indicating no isotope scrambling had occurred during the reaction.

The thermal reaction of **5b** was also carried out in the presence of an excess (≈ 10 equivalents) of the radical scavenger 1,4-cyclohexadiene.[53] This had a rather dramatic effect, resulting in no propane elimination when the reaction was run for over an hour in xylenes (T_{rxn} = 128 ± 1 °C).[54] During this time, no phosphorus containing compounds (other than the starting material) were observed by $^{31}P\{^{1}H\}$ NMR spectroscopy.

The reaction was then performed in the presence of the radical initiator azobisisobutyronitrile (AIBN). With the addition of 10 mol% AIBN at 72 °C in benzene, a solution of **5b** underwent complete conversion to **6b** within 15 minutes; a huge increase in reaction rate. The reaction was still exceptionally clean, with no other significant peaks observed in the $^{31}P\{^{1}H\}$ NMR. With 0.5 mol% AIBN, the reaction was still accelerated, but could be monitored by the method employed previously. The reaction was now found to be pseudo-first order in **5b** (k_{obs} = 0.055 min^{-1}, T_{rxn} = 72 ± 1 °C, see section S6.4).

This result is interesting from a synthetic perspective, as well as a mechanistic one. The addition of a very small amount of radical initiator has allowed the reaction to occur faster, under milder conditions, with no loss of stereoselectivity or increase in side-products. Given the substantial changes observed on addition of both a radical initiator and radical scavenger, it seems highly likely that this reaction occurs via a radical mechanism. In particular, one would not expect 1,4-cyclohexadiene to have any effect on the reaction, unless it was proceeding via a radical chain.

Electron Paramagnetic Resonance (EPR) spectroscopy was employed to help identify any transient radical intermediates. Radicals were generated in situ by either raising the temperature or irradiating with UV light in the presence of an initiator (see section S2 for details). However, no appreciable signal was observed in either experiment. This is most likely due to the radicals being too short lived, or giving signals that are too broad to resolve.

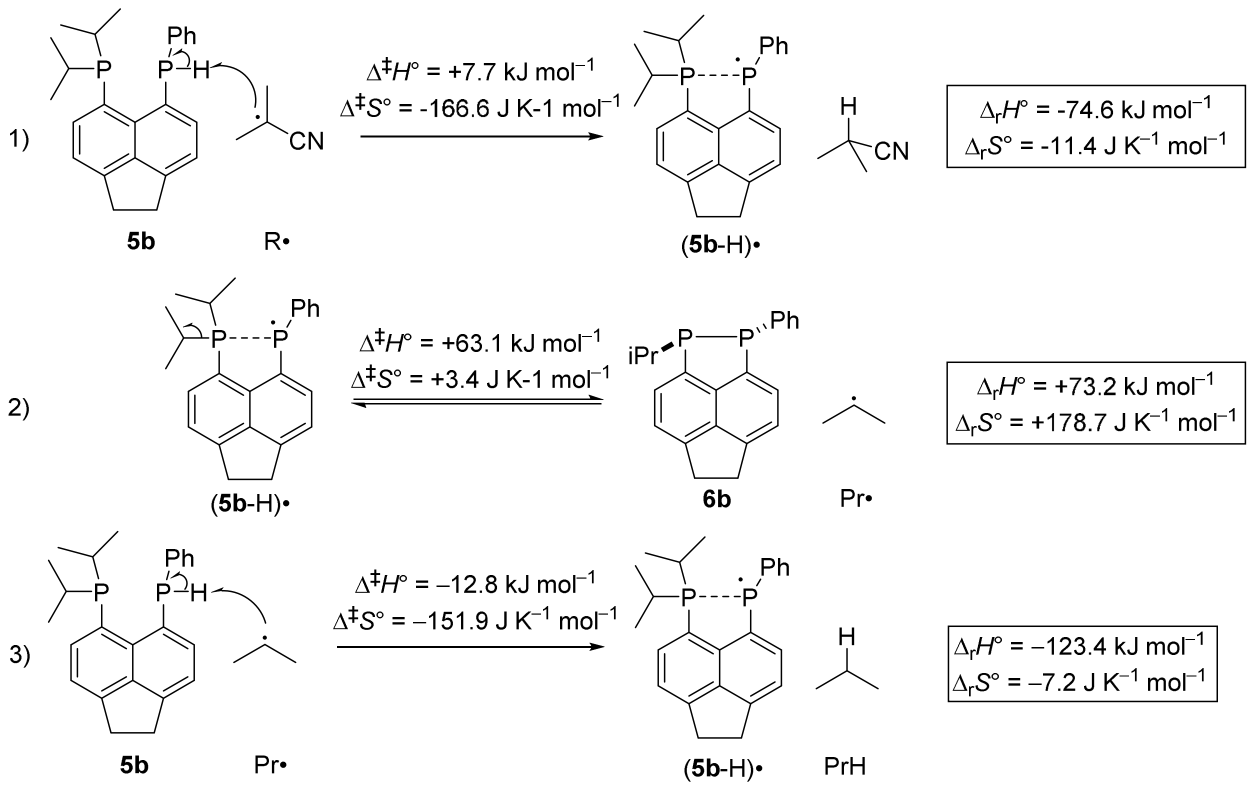
2.4 – Mechanistic Discussion

2.4.1 – Mechanism with a Radical Initiator

With the aid of DFT calculations, we can propose a plausible mechanism for this transformation which is consistent with the above mechanistic data. In the presence of the radical initiator AIBN, the initiation step (dissociation of AIBN into two 2-cyanopropyl radicals, R·) is likely followed by hydrogen abstraction from **5b** by R·, to afford a new phosphorus centred radical, (**5b**-H)· (Scheme 5, Reaction 1). Such hydrogen abstraction reactions are well established for secondary phosphines.[4] Calculations reveal that the reaction has a modest activation barrier ($\Delta^{\ddagger}G°$ = +57.5 kJ mol^{-1} at 345 K), which is achievable under the reaction conditions. In the next step, (**5b**-H)· can undergo P–C bond cleavage, affording **6b** and the propyl radical, Pr· (Scheme 5, Reaction 2). This is an equilibrium process ($\Delta_{r}G°$ ca. +11.5 kJ mol^{-1}

at 345 K) with a surmountable energy barrier ($\Delta^{\ddagger}H°$ = +63.1 kJ mol^{-1}). It should be noted that elimination to form the trans-diphosphane is more favourable than formation of the cis-isomer ($\Delta\Delta^{\ddagger}G°$ = 10.7 kJ mol^{-1} at 345 K), which correlates with the observed stereoselectivity.

Once formed, the propyl radical (Pr·) can abstract a hydrogen atom from another molecule of **5b**, affording (**5b**-H)· and propane (PrH). This step has a very strong driving force ($\Delta_rG°$ ca. −120.9 kJ mol^{-1} at 345 K), and is essentially diffusion controlled with no enthalpic barrier (Scheme 5, Reaction 3; see Figure S8 for full reaction profile).



Scheme 5: Proposed radical chain for propane elimination in the presence of AIBN, with computed activation parameters and thermodynamic driving forces shown.

The proposed radical chain mechanism is consistent with the following rate equation (see section S7.1 for details):[55]

$$rate = k[\mathbf{5b}][AIBN]^{\frac{1}{2}} \#(1)$$

This is first order in **5b**, as observed experimentally. Running the reaction with a two-fold increase in AIBN concentration (1.0 mol%) resulted in the observed rate constant increasing by a factor of 1.5 (≈ $\sqrt{2}$). This is taken as further support for the mechanism shown in Scheme 5.

The structure of the proposed radical (**5b**-H)· was probed in silico, to determine if it is a plausible intermediate for the reaction. Formation of the radical results in a partial relaxation of strain (with respect to **5b**), as seen in the reduction of the P···P peri-distance (2.94 Å in (**5b**-H)· vs. 3.028(1) Å in **5b**; see Figure S9). There is an increase in the calculated Wiberg bond index (WBI = 0.18 in (**5b**-H)·; c.f. 0.01 in **5b**), consistent with a weakly bonding interaction between the two P atoms. The radical also shows significant spin delocalisation across both phosphorus atoms (calculated spin densities; P1 = 0.80, P9 = 0.11; see Figure S9).

From this, we conclude that (**5b**-H)· is somewhat stabilised by the peri-backbone. In fact, peri-substitution has previously been used to stabilise several radical species for this reason, including boryl[25] and chalcogen[26–28] radicals.

2.4.2 – Mechanism without a Radical Initiator

Given that the propagation steps proposed above (Scheme 5, Reactions 2 and 3) account for the observed products and are energetically accessible, it seems reasonable that the same propagation steps operate in the absence of an initiator. While the experimentally determined activation parameters will be dependent on every step in the radical chain, and therefore are difficult to interpret directly, it is interesting to note that the computed enthalpic barrier for the dissociation of radical (**5b**-H)· ($\Delta^{\ddagger}H°$ = +63.1 kJ mol^{-1}, Equation 2 in Scheme 5), and the entropic barrier for hydrogen abstraction by Pr· ($\Delta^{\ddagger}S°$ = −151.9 J K^{-1} mol^{-1}, Equation 3 in Scheme 5) correlate well with the experimentally determined activation parameters ($\Delta^{\ddagger}H°$ = +57 ± 7 kJ mol^{-1}, $\Delta^{\ddagger}S°$ = −140 ± 20 J K^{-1} mol^{-1}, see section 2.3).

Identification of the initiation step is, however, more complex. We have computationally assessed several possibilities consistent with the observed second order kinetics. These include bimolecular initiation steps (such as those based on dehydrogenative coupling) and single electron transfer reactions (see section S7.2). However, none of the proposed mechanisms is fully consistent with our observations, with prohibitive thermodynamic or kinetic barriers established computationally.

Several possible termination steps have also been identified. These are discussed in more detail in the SI, section S7.3.

3 – Conclusions

By exploiting the steric strain and enforced proximity conferred by peri-substitution, a set of thermally initiated main group coupling reactions have been discovered. These reactions appear quite unique in the context of the literature, both in the “dealkanative” nature of the coupling, and the apparent involvement of radical intermediates. They are remarkably clean, diastereoselective, and occur under relatively mild conditions. In at least one case, the reaction can be facilitated by the addition of trace amounts of a radical initiator, which enhances the rate and lowers the required temperature. While the exact mechanism of radical formation (in the absence of an initiator) remains unclear, a plausible series of propagation steps have been proposed, which are supported by DFT calculations and consistent with experimental observations. The unusual geometry of the coupling precursors is likely the key to these reactions being kinetically accessible; it reduces the conformational entropy of the reacting groups, destabilises the starting material relative to the product through strain, and stabilises the proposed radical intermediates of the reaction. We expect that this reactivity could find more general applications, although this will require a more thorough understanding of the reaction, its mechanism, and its limitations. We are particularly interested in the small molecule evolved during the coupling reaction (propane, in this case). The elimination of a C–H coupled product suggests that other couplings may be possible, and future work will focus on synthetically valuable coupling targets (i.e. C-heteroatom coupling), as well as the use of heavier main-group elements.

4 – Associated Content

Supporting Information: All synthetic procedures, experimental details, spectral characterisation, additional crystallographic information, kinetic procedures, data and additional discussion, and computational details can be found in the supporting information. This material is available free of charge at WEB ADDRESS HERE

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Notes: the authors declare no competing financial interest

6 – Acknowledgements

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7 – Dedication

This work is dedicated to Professor Evamarie Hey-Hawkins.

8 – Notes and References

(1) Greenberg, S.; Stephan, D. W. *Chem. Soc. Rev.* **2008**, *37*, 1482.

(2) Waterman, R. *Curr. Org. Chem.* **2008**, *12*, 1322.

(3) Leitao, E. M.; Jurca, T.; Manners, I. *Nat. Chem.* **2013**, *5*, 817.

(4) Nell, B. P.; Tyler, D. R. *Coord. Chem. Rev.* **2014**, *279*, 23.

(5) Fleming, J. T.; Higham, L. J. *Coord. Chem. Rev.* **2015**, *297–298*, 127.

(6) Moore, W.; Hysell, D.; Hall, L.; Campbell, K.; Stara, J. *Environ. Heal. Persp.* **1975**, *10*, 63.

(7) Kruszynka, H.; Kruszynka, R.; Hurst, J.; Smith, R. P. *J. Toxicol. Environ. Heal.* **1980**, *6*, 757.

(8) ICH. *Q3D Elemental Impurities Guidance for Industry*; 2014.

(9) Power, P. P. *Nature* **2010**, *463*, 171.

(10) Reichl, K. D.; Dunn, N. L.; Fastuca, N. J.; Radosevich, A. T. *J. Am. Chem. Soc.* **2015**, *137*, 5292.

(11) Zhao, W.; Yan, P. K.; Radosevich, A. T. *J. Am. Chem. Soc.* **2015**, *137*, 616.

(12) McCarthy, S. M.; Lin, Y. C.; Devarajan, D.; Chang, J. W.; Yennawar, H. P.; Rioux, R. M.; Ess, D. H.; Radosevich, A. T. *J. Am. Chem. Soc.* **2014**, *136*, 4640.

(13) Dunn, N. L.; Ha, M.; Radosevich, A. T. *J. Am. Chem. Soc.* **2012**, *134*, 11330.

(14) Zhao, W.; McCarthy, S. M.; Lai, T. Y.; Yennawar, H. P.; Radosevich, A. T. *J. Am. Chem. Soc.* **2014**, *136*, 17634.

(15) Naseri, V.; Less, R. J.; Mulvey, R. E.; McPartlin, M.; Wright, D. S. *Chem. Commun.* **2010**, *46*, 5000.

(16) Miller, A. J. M.; Bercaw, J. E. *Chem. Commun.* **2010**, *46*, 1709.

(17) Less, R. J.; Melen, R. L.; Naseri, V.; Wright, D. S. *Chem. Commun.* **2009**, 4929.

(18) Less, R. J.; Melen, R. L.; Wright, D. S. *RSC Adv.* **2012**, *2*, 2191.

(19) Johnson, H. C.; Hooper, T. N.; Weller, A. S. *Top. Organomet. Chem.* **2015**, *49*, 153.

(20) Melen, R. L. *Chem. Soc. Rev.* **2016**, *45*, 775.

(21) Kilian, P.; Knight, F. R.; Woollins, J. D. *Chem. Eur. J.* **2011**, *17*, 2302.

(22) Surgenor, B. A.; Bühl, M.; Slawin, A. M. Z.; Woollins, J. D.; Kilian, P. *Angew. Chem. Int. Ed.* **2012**, *51*, 10150.

(23) Chalmers, B. A.; Bühl, M.; Arachchige, K. S. A.; Slawin, A. M. Z.; Kilian, P. *J. Am. Chem. Soc.* **2014**, *136*, 6247.

(24) Chalmers, B. A.; Bühl, M.; Athukorala Arachchige, K. S.; Slawin, A. M. Z.; Kilian, P. *Chem. Eur. J.* **2015**, *21*, 7520.

(25) Rosenthal, A. J.; Devillard, M.; Miqueu, K.; Bouhadir, G.; Bourissou, D. *Angew. Chem. Int. Ed.* **2015**, *54*, 9198.

(26) Zhang, S.; Wang, X.; Sui, Y.; Wang, X. *J. Am. Chem. Soc.* **2014**, *136*, 14666.

(27) Zhang, S.; Wang, X.; Su, Y.; Qiu, Y.; Zhang, Z.; Wang, X. *Nat. Commun.* **2014**, *5*, 4127.

(28) Knight, F. R.; Randall, R. A. M.; Roemmele, T. L.; Boeré, R. T.; Bode, B. E.; Crawford, L.; Bühl, M.; Slawin, A. M. Z.; Woollins, J. D. *ChemPhysChem* **2013**, *14*, 3199.

(29) Holthausen, M. H.; Hiranandani, R. R.; Stephan, D. W. *Chem. Sci.* **2015**, *6*, 2016.

(30) Holthausen, M. H.; Bayne, J. M.; Mallov, I.; Dobrovetsky, R.; Stephan, D. W. *J. Am. Chem. Soc.* **2015**, *137*, 7298.

(31) Devillard, M.; Brousses, R.; Miqueu, K.; Bouhadir, G.; Bourissou, D. *Angew. Chem. Int. Ed.* **2015**, *54*, 5722.

(32) For a quantitative evaluation of strain in some representative peri-substituted systems, see DFT calculations in: Somisara, D. M. U. K.; Bühl, M.; Lebl, T.; Richardson, N. V; Slawin, A. M. Z.; Woollins, J. D.; Kilian, P. *Chem. Eur. J.* **2011**, *17*, 2666.

(33) Taylor, L. J.; Surgenor, B. A.; Wawrzyniak, P.; Ray, M. J.; Cordes, D. B.; Slawin, A. M. Z.; Kilian, P. *Dalton Trans.* **2016**, *45*, 1976.

(34) For an example of spontaneous N–B dehydrocoupling, see: Helten, H.; Robertson, A. P. M.; Staubitz, A.; Vance, J. R.; Haddow, M. F.; Manners, I. *Chem. Eur. J.* **2012**, *18*, 4665.

(35) For a recent example of transition metal catalysed P–B dehydrocoupling, see: Pandey, S.; Lönnecke, P.; Hey-Hawkins, E. *Inorg. Chem.* **2014**, *53*, 8242.

(36) Reiter, S. A.; Nogai, S. D.; Karaghiosoff, K.; Schmidbaur, H. *J. Am. Chem. Soc.* **2004**, *126*, 15833.

(37) Kilian, P.; Philp, D.; Slawin, A. M. Z.; Woollins, J. D. *Eur. J. Inorg. Chem.* **2003**, 249.

(38) Masuda, J. D.; Hoskin, A. J.; Graham, T. W.; Beddie, C.; Fermin, M. C.; Etkin, N.; Stephan, D. W. *Chem. Eur. J.* **2006**, *12*, 8696.

(39) Ghebreab, M. B.; Shalumova, T.; Tanski, J. M.; Waterman, R. *Polyhedron* **2010**, *29*, 42.

(40) Ray, M. J.; Slawin, A. M. Z.; Bühl, M.; Kilian, P. *Organometallics* **2013**, *32*, 3481.

(41) The crystal structure of **5b** was obtained and is shown in Figure S9, with data in Table 1.

(42) For a recent example of alkane elimination from metal alkyl species, see: Bradley, M. A.; Birchall, C.; Blake, A. J.; Lewis, W.; Moxey, G. J.; Kays, D. L. *Dalton Trans.* **2017**, *46*, 4101.

(43) Allred, A. L. *J. Inorg. Nucl. Chem.* **1961**, *17*, 215.

(44) Quin, L. D. *A Guide to Organophosphorus Chemistry*, 1st ed.; Wiley-Interscience: New York, 2000.

(45) Scheetz, P. M.; Glueck, D. S.; Rheingold, A. L. *Organometallics* **2017**, *36*, 3387.

(46) Reichl, J. A.; Popoff, C. M.; Gallagher, L. A.; Remsen, E. E.; Berry, D. H. *J. Am. Chem. Soc.* **1996**, *118*, 9430.

(47) Katz, S. M.; Reichl, J. A.; Berry, D. H. *J. Am. Chem. Soc.* **1998**, *120*, 9844.

(48) Liptrot, D. J.; Arrowsmith, M.; Colebatch, A. L.; Hadlington, T. J.; Hill, M. S.; Kociok-Köhn, G.; Mahon, M. F. *Angew. Chem. Int. Ed.* **2015**, *54*, 15280.

(49) The arsenic analogue of the bis(phosphine) **5a**, compound **3**, was already shown to eliminate H_2 to give the arsanylidene-σ^4-phosphorane **4** (Scheme 3, top). It was hoped that replacement of one arsenic-bound hydrogen with a Ph group would preclude H_2 elimination.

(50) The novel compounds **7** and **8** are rather interesting, but they are not the focus of this paper. As such, a discussion of these compounds (including their crystal structures) is given in section S3.2.

(51) Thomas, I. R.; Bruno, I. J.; Cole, J. C.; Macrae, C. F.; Pidcock, E.; Wood, P. A. *J. Appl. Cryst.* **2010**, *43*, 362.

(52) Anslyn, E. V; Dougherty, D. A. *Modern Physical Organic Chemistry*, 1st ed.; University Science Books: Sausalito, CA, 2006.

(53) Hawari, J. A.; Engel, P. S.; Griller, D. *Int. J. Chem. Kinet.* **1985**, *17*, 1215.

(54) Under these conditions, approximately 75% of the starting material is consumed after 1 hour in the absence of 1,4-cyclohexadiene.

(55) Stevens, M. P. *Polymer Chemistry: An Introduction*; Oxford University Press USA: New York, 1999; pp 176–186.

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