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Phenyl Radical Cleavage from Tetraphenylphosphoranyl Radicals

Alex Larrabee
Winona State University

Thomas Nalli
Winona State University

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Alex Larrabee
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Research Advisor: T. Nalli

Introduction

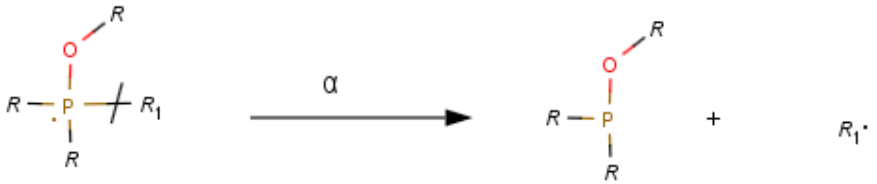
Phosphoranyl radicals ($Z_4P\cdot$) were first proposed as an intermediate in 1957 and later studied extensively in the 1960's by electron spin resonance (ESR) spectroscopy.[1] Phosphoranyl radicals are common intermediates and they are important in many different biological and synthetic processes.[2] These phosphoranyl radicals can be created in a number of ways but the following reactions show the most common pathways.[3]

$$Z_3P + Z\cdot \rightarrow Z_4P \qquad (1)$$

$$Z_5P + \text{-}Z\cdot \rightarrow Z_4P\cdot \qquad (2)$$

$$Z_4P^+ + e\text{-} \rightarrow Z_4P\cdot \qquad (3)$$

These radicals are able to undergo both α- and β-cleavage reactions (eq 4, 5) especially when the cleaved radical is stable[4] as in phenoxy and t-butyl.



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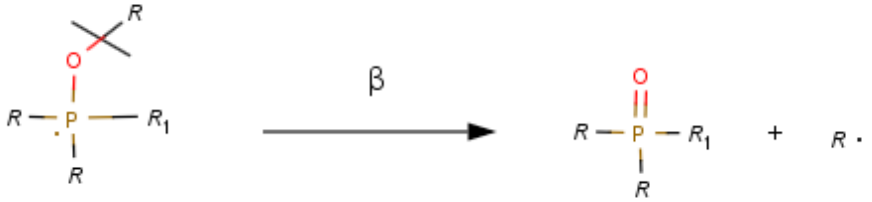


(5)

Tetraphenylphosphoranyl radicals (TPPRs) can be formed by the rapid addition of a phenyl radical to PPh_3 (eq 6).[3] However, the only known mode of reaction for TPPRs formed in this manner is electron transfer to acceptors such as diaryliodonium salts (eq 7).[4] TPPRs formed by γ-ray irradiation of tetraphenylphosphonium salts ($^+PPh_4$) (eq 3) and detected by ESR were reported to disproportionate (eq 8) rather than undergo unimolecular cleavage reactions. However, TPPRs formed via reduction may have different structures than those formed through phenyl radical addition to phosphines.[5]

$$Ph\cdot + PPh_3 \rightleftharpoons \cdot PPh_4 \qquad (6)$$

$$\cdot PPh_4 + Ar_2I^+ \rightarrow {}^+PPh_4 + Ar_2I\cdot \qquad (7)$$

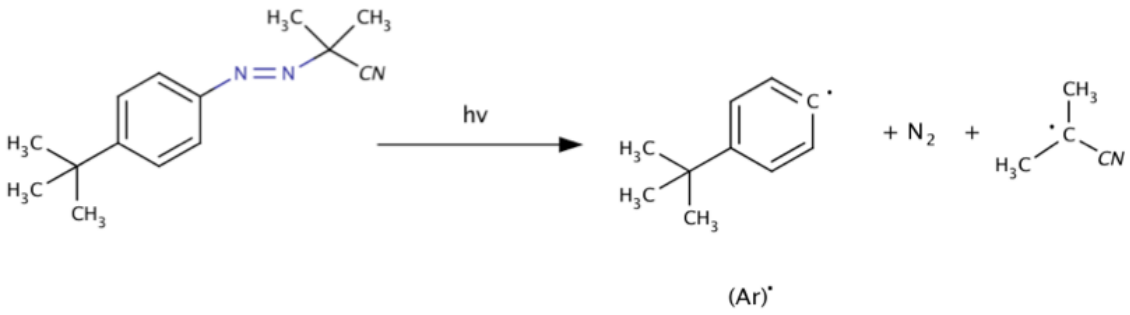
$$2\ Ph_4P\cdot \rightarrow Ph_5P + Ph_3P \qquad (8)$$

The purpose of this research was to determine whether a phenyl radical, other than the one just added, can cleave off from a tetraphenylphosphoranyl radical formed by phenyl radical addition. A literature procedure for the preparation of phenylazoisobutyronitrile ($PhN{=}NCMe_2CN$) was adapted for the preparation of 4-*tert*-butylphenylazoisobutyronitrile (BPAIN). This compound was used as a photochemical source of *tert*-butyl substituted phenyl radicals (Ar ·) that were allowed to react with triphenylphosphine (PPh_3) or tris(4-fluorophenyl)phosphine (TFP) (eq 1). ^1H NMR and ^{31}P NMR were used to check for the formation of 4-*tert*-butyltriphenyltriphosphine ($ArPPh_2$) according to equation 9.

$$Ar\cdot + PPh_3 \rightleftharpoons ArP\cdot Ph_3 \rightarrow ArPPh_2 + Ph\cdot \qquad (9)$$

Results and Discussion

A literature procedure[6] for the preparation of phenylazoisobutyronitrile ($PhN{=}NCMe_2CN$) was adapted for the preparation of 4-*tert*-butylphenylazoisobutyronitrile (BPAIN), which was used as a photochemical source of phenyl radicals (eq 10).



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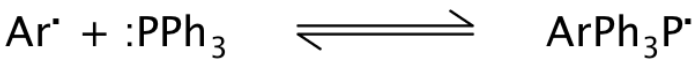

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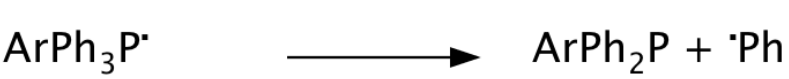

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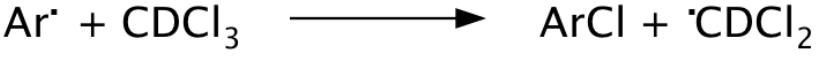

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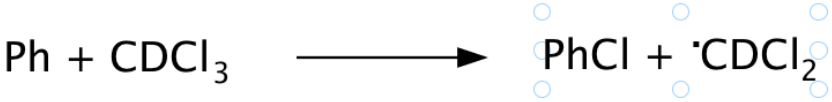
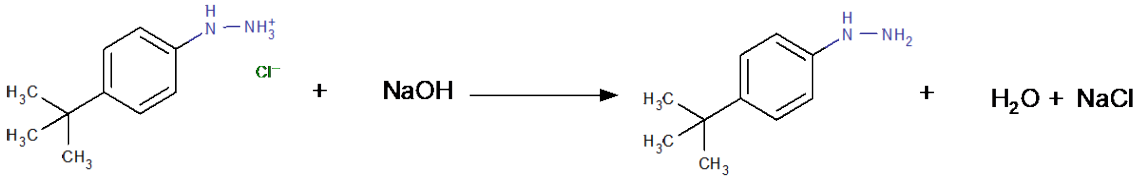


(10d)

Preparation of 4-*tert*-Butylphenylazoisobutyronitrile (BPAIN).

NaOH was used to deprotonate the ammonium salt of 4-tert-butylphenylhydrazine to form the free base amine (eq 11), which was then reacted with acetone cyanohydrin (eq 12) to give 3.5 g (59%) yield of the desired product, 4-*tert*-butylphenylhydrazinoisobutylnitrile, as orange/yellow crystals.



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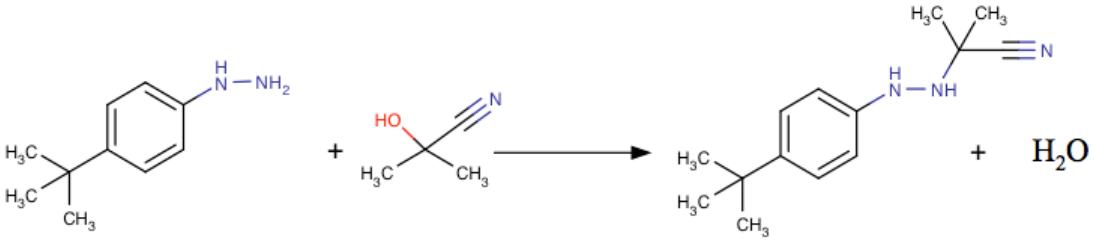
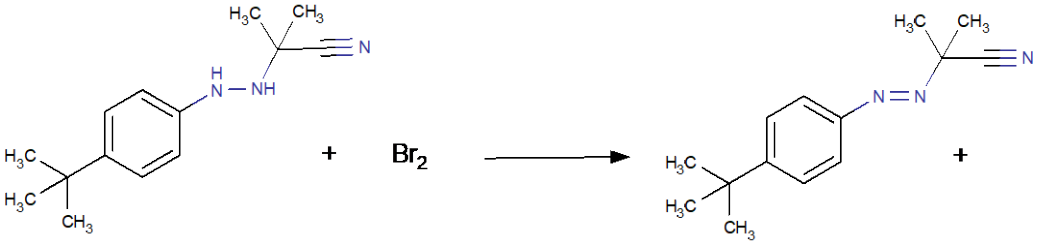


(12)

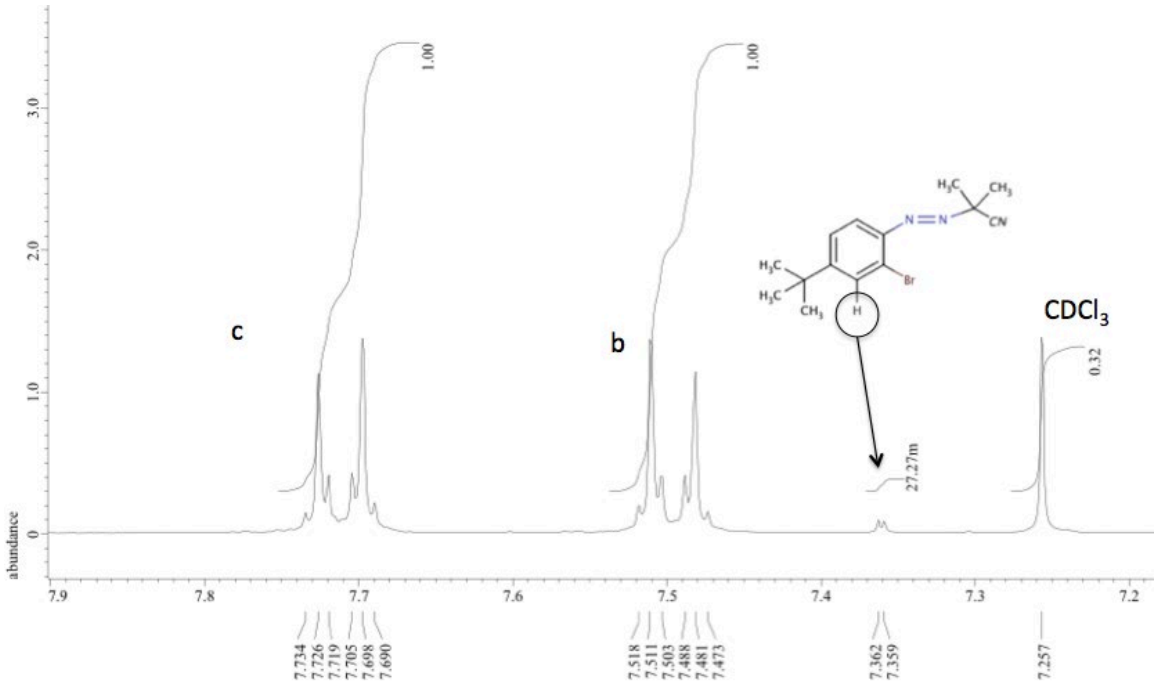
^{1}H NMR analysis of the crystals showed a relatively pure crude product with little to no obvious impurity peaks (Appendix, 1H NMR of 4-tert-butylphenylhydrazinoisobutylnitrile). The hydrazino compound was oxidized with Br_2 to form BPAIN (eq 13).



(13)

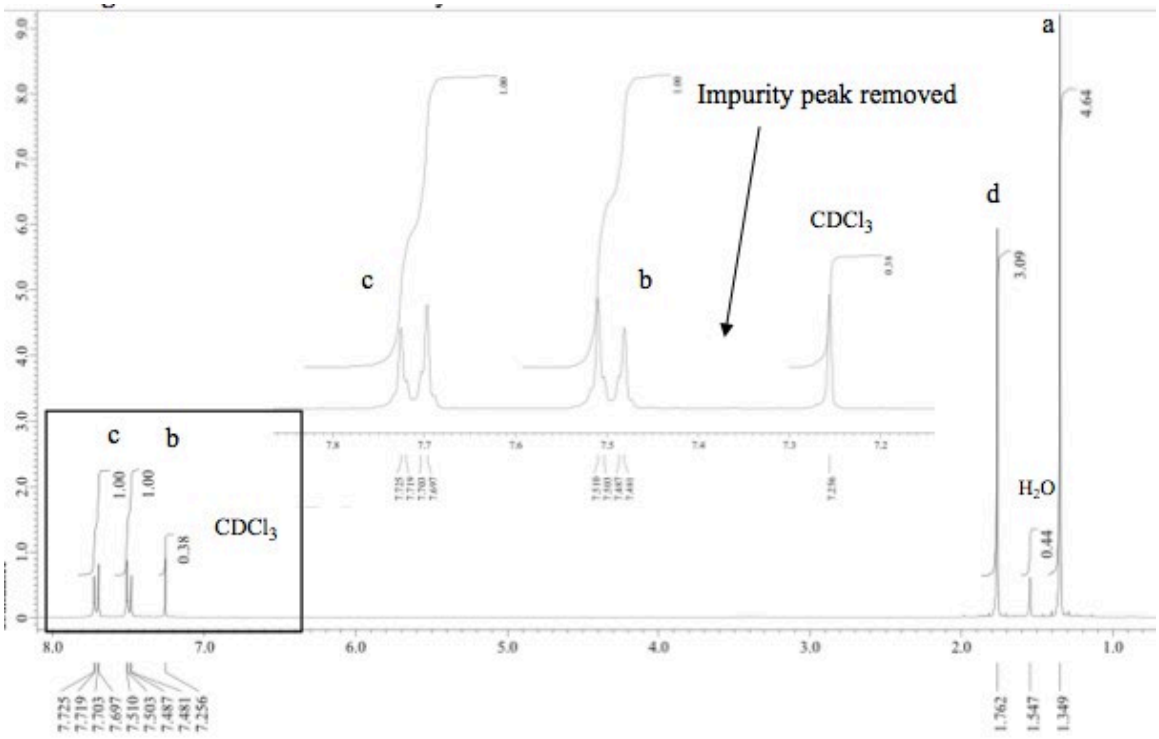
The crude ^{1}H NMR lacked the NH singlets of the hydrazino compound (5.35 and 3.80 ppm), showing that the oxidation of the hydrazino starting material was complete. However, there were obvious impurity peaks at 7.35 (d, J=1.0 Hz), 1.77 (s), and 1.33 (s) ppm (Figure 2). The impurity was thought to be due to ring bromination, forming 2-bromo-4-*tert*-butylphenylazoisobutyronitrile (Figure 1).

Figure 1. ^{1}H NMR BPAIN Unpurified Crude Product



The oxidation reaction was very exothermic and this side reaction can probably be reduced by keeping the reaction mixture cold with the addition of ice, which we did not do. Removal of this impurity was achieved by recrystallization from dichloromethane (Figure 2) giving a pure yield of 0.87 g (26%) yield.

Figure 2. ^{1}H NMR BPAIN Recrystallized Product

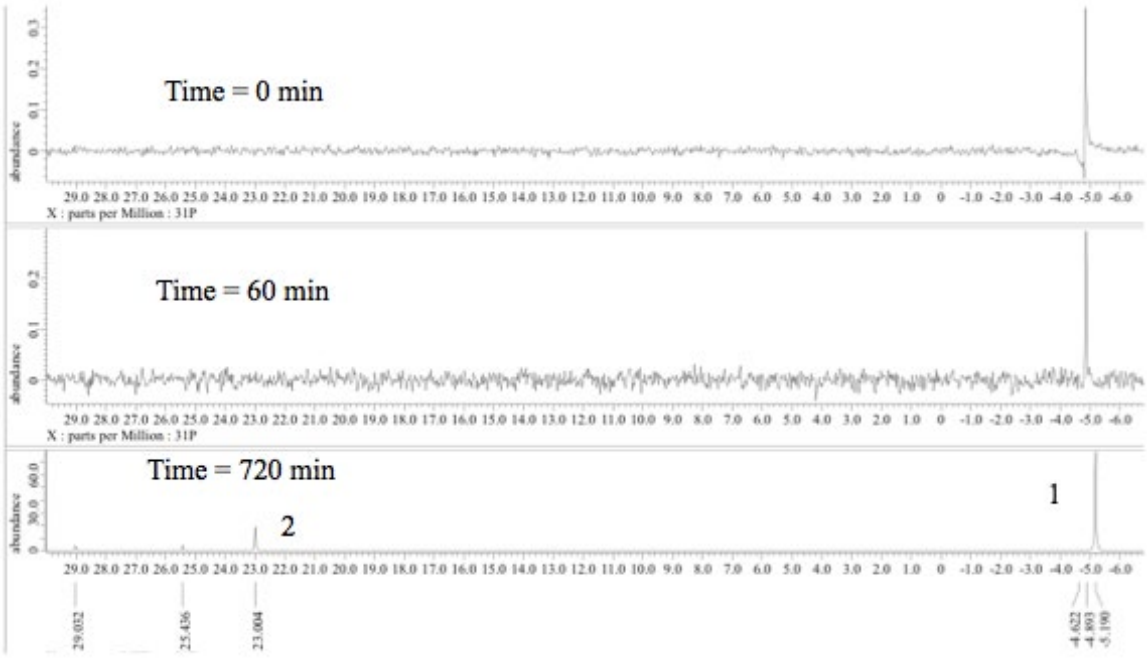


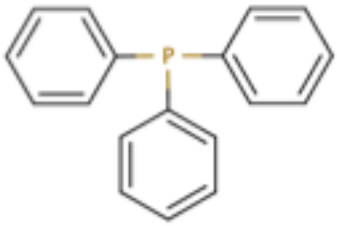
Test for phenyl radical cleavage from TPPRs radicals.

Triphenylphosphine. When an equimolar solution of BPAIN and triphenylphosphine (PPh_3) (0.0001 mol) in $CDCl_3$ (1 mL) was irradiated with visible light, the reaction was very sluggish but new peaks showed up in the ^{31}P NMR at 29.0, 25.4, and 23.0 ppm. The peak at 23.0 ppm is triphenylphosphine oxide (2) formed by air oxidation of Ph_3P. The other two peaks are unidentified. These peaks may be due to the triphenylphosphine phenyl radicals reacting with 1-cyano-1-methylethyl radicals in the solution. Five peaks showed up in the GC-MS. The peak at 5.6 min with M+ at m/z = 134 is *tert*-butylbenzene seemingly consistent with *tert*-butylphenyl radical formation. However, it was expected the M+ value would be m/z

= 135 due to the abstraction of deuterium from $CDCl_3$. It is puzzling that H is reacting instead of deuterium. A possible explanation is that the observed peaks came primarily from decomposition of BPAIN in the GC injection port. The peak at 6.1 min with M+ at m/z = 134 appears to be an isomer of *tert*-butylbenzene. The peak at 6.8 min with M+ at m/z = 81 is unknown. The peak at 15.9 min with M+ at m/z = 186 is unreacted BPAIN and the peak at 26 min with M+ at m/z = 277 is triphenylphosphine. There is no evidence for phenyl radical cleavage of $ArPPh_2$.

Figure 3. ^{31}P NMR of PPh_3 and BPAIN in $CDCl_3$ under visible illumination.





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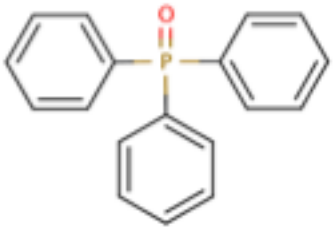

2

Tris(4-fluorophenyl)phosphine. When an equimolar solution of BPAIN and tris(4-fluorophenyl)phosphine (TFP) (0.0001 mol) in $CDCl_3$ (1 mL) was irradiated with visible light, the reaction was much faster than with PPh_3 and new peaks showed up in the ^{31}P NMR at 27.51. 21.97, and -8.56 ppm. One of the latter two peaks was confirmed with GC-MS to be tris(4-fluorophenyl)phosphine oxide (4). Peaks 5 and 6 were thought to possibly be (4-*tert*-butylphenyl)bis(4-fluorophenyl)phosphine (5) and (4-*tert*-butylphenyl)bis(4-fluorophenyl)phosphine oxide (6), which would show evidence for 4-fluorophenyl radical cleavage.

It is expected that the substitution of a *tert*-butylphenyl radical to TFP, a peak in similar chemical shift would appear at a higher frequency than -8.51 ppm. The shifts of triarylphosphine peaks are additive[7] and though we see a peak at -8.56 ppm it is not likely to be that of compound 5. In addition there were no peaks observed at approximately -80 ppm (Ph_5P) and it can be concluded that the reported disproportionation of $Ph_4P^{\bullet}$ (eq 8) does not actually occur.

Also, no evidence for the formation of 5 and 6 were seen in the GC-MS. Instead we saw a peak at 5.6 min with M+ at m/z = 135 and is 4-deuterio-1-*tert*-

butylbenzene. The m/z value is consistent with D abstraction by *tert*-butylphenyl radicals. Peaks at 6.1 min (M+ at m/z = 134), 5.6 min, 15.9 min (M+ at m/z = 186), 20 min (M+ at m/z = 316), and 22.7 min (M+ at m/z =331) are *tert*-butylbenzene isomer, unreacted BPAIN, unreacted TFP, and tris(4-fluorophenyl)phosphine oxide respectively.

Figure 4. ^{31}P NMR of TFP and BPAIN in $CDCl_3$ under visible illumination.

Conclusion

No evidence for phenyl radical cleavage from TPPRs generated in these reactions could be found. This does not rule out the possibility that the phenyl radical additions are reversible because it may be that the phenyl radical just added is the only one that cleaves. It appears that tetraphenylphosphoranyl radicals only do bimolecular reactions. However, we could also find no evidence of disproportionation to form pentaphenylphosphorane (eq 8) as speculated by previous workers.[5] Computational studies of these TPPRs may reveal reactions for this behavior.

Experimental

General Procedure

Phenyl radical reactions were run in $CDCl_3$ in an NMR tube under a 65-W CFL light. Analysis was performed using a 300 MHz NMR spectrometer. All other reagents except BPAIN was purchased from commercial sources and used as received.

4-*tert*-Butylphenylhydrazinoisobutyronitrile. 4-*tert*-Butylphenylhydrazine hydrochloride (5 g, 0.025 mol, Apollo Scientific) was suspended in water with excess NaOH. The mixture was tested with litmus paper to confirm basicity. The mixture was transferred to a separatory funnel and extracted with diethyl ether, and dried over Na_2SO_4. The decanted solution was added to an r.b.f. with acetone cyanohydrin (2.27 mL) and the solvent evaporated *in vacuo* (30 min). The solution was set aside until crystal formation (8 days). Excess liquid was pipetted off the

crystals which were washed with ether. ^{1}H NMR (300MHz, $CDCl_3$) δ 7.25 (2H, m), 6.85 (2H, m), 5.35 (1H, s), 3.80 (1H, s), 1.50 (6H, s), 1.28 (9H, s) ppm.

4-tert-butylphenylazoisobutyronitrile (BPAIN). The hydrazino compound was added to chloroform in a separatory funnel and washed repeatedly with a Br_2 saturated 15% KBr(aq) solution until the aqueous layer retained the red Br_2 color. The organic layer was then washed with aqueous 5% sodium bisulfite, 2N Na_2CO_3, and water and dried over Na_2SO_4 and the solvent evaporated *in vacuo.* The flask was removed and stored in a refrigerator until crystals formed, which were washed with cold pentane. Recrystallization from dichloromethane to successfully remove the ring-brominated impurity shown at 7.35 (d, J=1.0 Hz), 1.77 (s), and 1.33 (s) ppm (see discussion) giving a final yield of 26%. ^{1}H NMR (300MHz, $CDCl_3$) δ 7.72 (2H, m) , 7.51 (2H, m), 1.77 (6H, s), 1.34 (9H, s), ppm.

Testing for Phenyl Radical Cleavage

Equimolar amounts of BPAIN (0.001 mol) and triphenylphosphine (PPh_3) or tris(4-fluorophenyl)phosphine (TFP) were allowed to react together in $CDCl_3$ (1 mL) in an NMR tube. This solution was illuminated with a 65-W compact fluorescent lamp. ^{31}P and ^{1}H NMR spectra were obtained at varying intervals at t = 0, 60, and 720 min.

PPh_3: ^{31}P NMR δ 23.00, -5.19 ppm.

TFP: ^{31}P NMR δ 27.52, 21.97, -8.51, -8.56, ppm

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Appendix