Phosphole-*N*-phenylmaleimide [4 + 2] cycloadducts as synthetic equivalents of nucleophilic phosphinidenes

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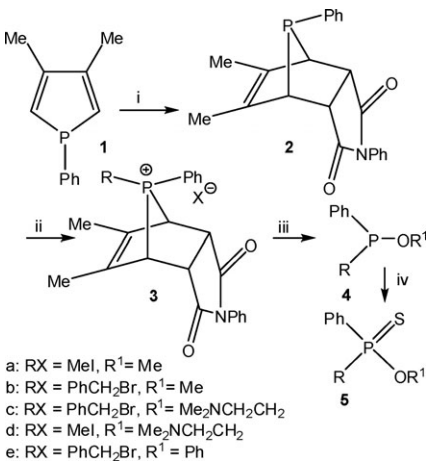
Using 1-R-3,4-dimethylphosphole-*N*-phenylmaleimide cycloadducts as synthetic equivalents of phosphinidenes [R–P], the following sequence has been developed: [R–P] + R^1X → RR^1PX → $RR^1P–OR^2$.

Although there are several methods to generate them,[1] transient free phosphinidenes [R–P] have seen only limited use as synthetic tools in organophosphorus chemistry until now. Among the reasons for this state of affairs, one is certainly that most phosphinidenes have a triplet ground state,[2] favouring oligomerisation and other erratic reactions. In the few cases where the phosphinidene ground state is a singlet, *e.g.* [R_2P–P], an interesting cycloaddition chemistry has been developed; [3] however, of course, its scope is very limited. This is why the carbene-like reactivity of electrophilic singlet terminal phosphinidene complexes has been so extensively studied recently.[4] The drawback to this approach is that the products resulting from this chemistry are formed in the coordination sphere of a metal, whose elimination is often quite difficult. One way to circumvent this problem is to replace the phosphinidene by a synthetic equivalent, RPX_2, displaying normal P(III) behaviour and susceptible to losing X_2 by reductive elimination during the reaction pathway. With this idea in mind, our attention was drawn to the easy reductive elimination that takes place under moderate heating in pentacoordinate phospholenes with the loss of dienes.[5] On this basis, we decided to investigate the possibility of using the [4 + 2] cycloadducts between 1-R-3,4-dimethylphospholes and *N*-phenylmaleimide[6] as synthetic equivalents of [R–P]. Several reasons guided our choice: the strain of the bicyclic structure must favour the collapse of the phosphorus bridge; such structures have already been used to generate [R–P=S] species under UV irradiation.[7] A wide range of R substituents are also easily accessible for phospholes.[8]

Our initial experiments were carried out with the already described cycloadduct of 1-phenyl-3,4-dimethylphosphole, **1**, with the maleimide.[6] Since we tried to devise a practical reaction sequence, neither the adduct nor the subsequent intermediate products were isolated; we simply monitored the reaction medium for completion of the various transformations by ^{31}P NMR. Adduct **2** was quaternised *in situ* by iodomethane or benzyl bromide. Next, the resulting phosphonium salts, **3**, were subjected to alcoholysis in the presence of triethylamine at room temperature. Our reasoning was that the intermediate pentacoordinate species would collapse easily. In fact, we observed the release of the phosphorus bridge at room temperature (Scheme 1). The formation of the expected phosphinites, **4**, was monitored by ^{31}P NMR, and they were fully characterised as their *P*-sulfides, **5**.† The overall yields of pure **5** from **1** were in the range 27.5–55.0%. What we have is a synthetic sequence that is equivalent to the unprecedented oxidative addition of RX to a nucleophilic phenyl-phosphinidene.

It remains to be seen whether this sequence can be transposed to other phosphinidenes. We were not able to duplicate the synthetic sequence with 1,3,4-trimethylphosphole, but we were successful with 1-*n*-pentyl-3,4-dimethylphosphole, prepared *in situ* from **1** (Li in THF, then 1-bromopentane), subjecting it without purification to the same series of reactions as described in Scheme 1. Phosphinite **6** and its sulfide **7** (Scheme 2) were characterized in the usual way. The overall yield of pure **7** from **1** was an acceptable 22.6%.

Similarly, we were able to convert the 1-bithienyl-3,4-dimethylphosphole, prepared as described in the literature,[9] into the corresponding phosphinite, **8**, in a 21.7% overall yield. The synthetic equivalency between phosphinidenes and phosphole-*N*-phenylmaleimide cycloadducts is thus quite general. According to ^{31}P NMR solution monitoring, the phosphorus bridge of phosphonium salts **3** collapses as soon as the



Scheme 1 *Reagents and conditions:* (i) *N*-phenylmaleimide, 100 °C, 3 h, xylene; (ii) RX, from r.t. to 110–120 °C, 4–5 h; (iii) Et_3N, then, after 20 min, R^1OH, 30 min., r.t.; (iv) sulfur, r.t.

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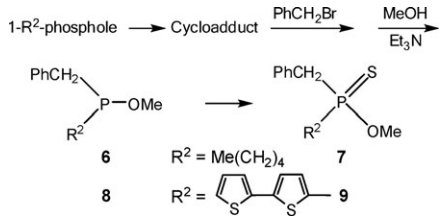

Scheme 2 Synthetic equivalence with phosphinidenes [R^2P].

triethylamine is added to the reaction mixture. In the case of **3e**, we observed a complex series of signals in the range δ −35.4 to +74.7, including an AB system at δ −30.5 and −34.5 (J_{AB} = 223 Hz), which suggests the formation of a dinuclear P(v) intermediate with a P–P bond. Upon adding phenol, all of these signals almost completely disappeared. The mechanism probably involves a nucleophilic attack of the triethylamine onto the positive phosphonium centre, similar to that observed in the reaction of *N*-methylimidazole with 7-phosphanorbornadiene complexes.[10] Finally, it must be stressed that another P–C bond can be easily created from **4** through an Arbuzov reaction. We therefore have at our disposal a new tool that allows *P*-chiral phosphines to be built at will.

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Notes and references

† **4a**: ^{31}P NMR: δ 118.4.

5a: yield 49.2% from **1**; ^{31}P NMR ($CDCl_3$): δ 89.7; ^{1}H NMR ($CDCl_3$): δ 2.01 (d, 3H, $^2J_{HP}$ = 13.8 Hz, Me), 3.56 (d, 3H, $^3J_{HP}$ = 14.1 Hz, OMe), 7.29–7.96 (m, 5H, Ph); ^{13}C NMR ($CDCl_3$): δ 23.65 (d, $^1J_{CP}$ = 83.1 Hz, PMe), 51.02 (d, $^2J_{CP}$ = 6.0 Hz, OMe), 128.53 (d, J_{CP} = 12.8 Hz, Ph-CH), 131.00 (d, J_{CP} = 11.3 Hz, Ph-CH), 132.18 (d, $^4J_{CP}$ = 2.9 Hz, Ph-C$_{para}$), 133.14 (d, $^1J_{CP}$ = 99.4 Hz, Ph-C$_{ipso}$).

4b: ^{31}P NMR: δ 123.3.

5b: yield 55.0% from **1**; ^{31}P NMR ($CDCl_3$): δ 90; ^{1}H NMR ($CDCl_3$): δ 3.51 (unresolved ABX, 2H, CH_2), 3.59 (d, 3H, $^2J_{HP}$ = 13.5 Hz, OMe), 7.00–7.73 (m, 10H, Ph); ^{13}C NMR ($CDCl_3$): δ 44.59 (d, $^1J_{CP}$ = 73.9 Hz, PCH_2), 51.53 (d, $^2J_{CP}$ = 6.6 Hz, OMe), 127.00 (d, J_{CP} = 4.0 Hz, CH_2Ph-C$_{para}$), 128.12 (d, J_{CP} = 3.47 Hz, CH_2Ph-*C*H), 128.28 (d, J_{CP} = 12.7 Hz, Ph-CH), 130.25 (d, J_{CP} = 5.8 Hz, CH_2Ph-*C*H), 131.26 (d, $^2J_{CP}$ = 7.9 Hz, CH_2Ph-C$_{ipso}$), 131.77 (d, J_{CP} = 10.6 Hz, Ph-CH), 131.78 (d, $^1J_{CP}$ = 98.2 Hz, Ph-C$_{ipso}$), 132.15 (d, J_{CP} = 2.9 Hz, Ph-C$_{para}$). Exact mass calc. for $C_{14}H_{16}OPS$: 263.0659 $[M + H]^+$. Found: 263.0656.

4c: ^{31}P NMR: δ 119.6.

5c: yield 36.7% from **1**; ^{31}P NMR ($CDCl_3$): δ 90; ^{1}H NMR ($CDCl_3$): δ 2.29 (s, 6H, NMe), 2.61–2.66 (m, 2H, NCH_2), 3.55 (unresolved ABX, 2H, PCH_2), 3.80–3.91 (m, 1H, OCH_2), 4.13–4.23 (m, 1H, OCH_2), 7.02–7.79 (m, 10H, Ph); ^{13}C NMR ($CDCl_3$): δ 44.55 (d, $^1J_{CP}$ = 73.6 Hz, PCH_2), 45.42 (s, NMe), 58.85 (d, J_{CP} = 7.6 Hz, NCH_2), 62.22 (d, J_{CP} = 6.6 Hz, OCH_2), 127.00 (d, J_{CP} = 4.2 Hz, CH_2Ph-C$_{para}$), 128.07 (d, J_{CP} = 3.5 Hz, CH_2Ph-*C*H), 128.27 (d, J_{CP} = 12.8 Hz, Ph-CH), 130.30 (d, J_{CP} = 5.7 Hz, CH_2Ph-*C*H), 131.13 (d, $^2J_{CP}$ = 7.8 Hz, CH_2Ph-C$_{ipso}$), 131.70 (d, J_{CP} = 10.7 Hz, Ph-CH), 132.17 (d, $^4J_{CP}$ = 2.9 Hz, Ph-C$_{para}$), 132.27 (d, $^1J_{CP}$ = 96.1 Hz, Ph-C$_{ipso}$). Exact mass calc. for $C_{17}H_{23}NOPS$: 320.1238 $[M + H]^+$. Found: 320.1238.

4d: ^{31}P NMR: δ 120.9.

5d: yield 40% from **1**; ^{31}P NMR ($CDCl_3$): δ 92.9; ^{1}H NMR ($CDCl_3$): δ 2.23 (d, 3H, $^2J_{HP}$ = 14.1 Hz, PMe), 2.91 (s, 6H, NMe), 3.47–3.49 (m, 2H, NCH_2), 3.86–3.96 (m, 1H, OCH_2), 4.40–4.49 (m, 1H, OCH_2), 7.50–8.08 (m, 5H, Ph); ^{13}C NMR ($CDCl_3$): δ 22.03 (d, $^1J_{CP}$ = 81.9 Hz, PMe), 41.49 (s, NMe), 54.84 (d, J_{CP} = 8.5 Hz, CH_2), 55.29 (d, J_{CP} = 4.9 Hz, CH_2), 126.72 (d, J_{CP} = 13.0 Hz, Ph-CH), 129.21 (d, J_{CP} = 11.9 Hz, Ph-CH), 129.92 (d, $^1J_{CP}$ = 95.7 Hz, Ph-C$_{ipso}$), 130.73 (d, J_{CP} = 3 Hz, Ph-CH$_{para}$). Exact mass calc. for $C_{11}H_{19}NOPS$: 244.0925 $[M + H]^+$. Found: 244.0925.

4e: ^{31}P NMR: δ 117.4.

5e: yield 27.5% from **1**; ^{31}P NMR ($CDCl_3$): δ 90; ^{1}H NMR ($CDCl_3$): δ 3.72 (unresolved ABX, 2H, CH_2), 6.93–7.89 (m, 15H, Ph); ^{13}C NMR ($CDCl_3$): δ 45.11 (d, $^1J_{CP}$ = 73.8 Hz, PCH_2), 121.43 (d, J_{CP} = 5.1 Hz, PhO-C$_{ortho}$), 124.70 (d, J_{CP} = 1.3 Hz, PhO-C$_{para}$), 127.22 (d, J_{CP} = 4.1 Hz, CH_2Ph-C$_{para}$), 128.22 (d, J_{CP} = 3.5 Hz, CH_2Ph-*C*H), 128.38 (d, J_{CP} = 13.1 Hz, Ph-CH), 129.34 (d, J_{CP} = 0.8 Hz, PhO-C$_{meta}$), 130.46 (d, J_{CP} = 5.9 Hz, CH_2Ph-*C*H), 130.95 (d, $^2J_{CP}$ = 7.8 Hz, CH_2Ph-C$_{ipso}$), 132.01 (d, J_{CP} = 10.9 Hz, Ph-CH), 132.36 (d, $^1J_{CP}$ = 98.6 Hz, Ph-C$_{ipso}$), 132.43 (d, J_{CP} = 3.0 Hz, Ph-C$_{para}$), 150.78 (d, $^2J_{CP}$ = 9.8 Hz, PhO-C$_{ipso}$). Exact mass calc. for $C_{19}H_{18}OPS$: 325.0816 $[M + H]^+$. Found: 325.0815.

6: ^{31}P NMR: δ 136.9.

7: yield 22.6% from **1**; ^{31}P NMR ($CDCl_3$): δ 102.0; ^{1}H NMR ($CDCl_3$): δ 0.88 (t, 3H, Me), 1.30 (m, 4H, CH_2), 1.60 (m, 2H, CH_2), 1.82 (m, 2H, CH_2), 3.36 (unresolved ABX, 2H, $PhCH_2$), 3.60 (d, 3H, $^3J_{HP}$ = 13.2 Hz, OMe), 7.24–7.36 (m, 5H, Ph); ^{13}C NMR ($CDCl_3$): δ 13.85 (s, Me), 22.05 (d, J_{CP} = 3.8 Hz, CH_2), 22.17 (s, CH_2), 32.48 (d, J_{CP} = 6.9 Hz, CH_2), 33.06 (d, $^1J_{CP}$ = 48.7 Hz, PCH_2), 42.40 (d, $^1J_{CP}$ = 63.4 Hz, PCH_2Ph), 51.77 (d, $^2J_{CP}$ = 7.0 Hz, OMe), 127.16 (d, J_{CP} = 3.7 Hz, CH_2Ph-C$_{para}$), 128.55 (d, J_{CP} = 3.0 Hz, CH_2Ph-*C*H), 129.86 (d, J_{CP} = 5.4 Hz, CH_2Ph-C*H*), 131.78 (d, $^2J_{CP}$ = 8.3 Hz, CH_2Ph-C$_{ipso}$). Exact mass calc. for $C_{13}H_{22}OPS$: 257.1129 $[M + H]^+$. Found: 257.1129.

8: ^{31}P NMR: δ 112.3.

9: yield 21.7% from the bithienylphosphole; ^{31}P NMR ($CDCl_3$): δ 80.6; ^{1}H NMR ($CDCl_3$): δ 3.59 (unresolved ABX, 2H, $PhCH_2$), 3.64 (d, 3H, $^3J_{HP}$ = 14.1 Hz, OMe), 7.01–7.29 (m, 10H, Ph-CH and Th-CH); ^{13}C NMR ($CDCl_3$): δ 45.20 (d, $^1J_{CP}$ = 80.7 Hz, PCH_2Ph), 51.70 (d, $^2J_{CP}$ = 7.0 Hz, OMe), 124.51 (d, J_{CP} = 13.7 Hz, CH-Th), 125.19 (s, Th-CH), 126.07 (s, Th-CH), 127.28 (d, J_{CP} = 4.2 Hz, CH_2Ph*C*$_{para}$), 128.16 (s, Th-CH), 128.30 (d, J_{CP} = 3.6 Hz, CH_2Ph*C*H), 130.32 (d, J_{CP} = 6.1 Hz, CH_2Ph-*C*H), 131.03 (d, $^2J_{CP}$ = 8.4 Hz, CH_2Ph-C$_{ipso}$), 131.72 (d, $^1J_{CP}$ = 105.7 Hz, C–P-Th), 135.95 (s, Th-C), 137.83 (d, J_{CP} = 9.7 Hz, Th-C), 146.46 (d, J_{CP} = 5.4 Hz, Th-C). Exact mass calc. for $C_{16}H_{16}OPS_3$: 351.0101 $[M + H]^+$. Found: 351.0138.

1 J. C. Slootweg and K. Lammertsma, *Sci. Synth.*, 2008, **42**, 15.
2 M. T. Nguyen, A. Van Keer and L. G. Vanquickenborne, *J. Org. Chem.*, 1996, **61**, 7077.
3 G. Fritz, T. Vaahs, H. Fleischer and E. Matern, *Angew. Chem., Int. Ed. Engl.*, 1989, **28**, 315.
4 Recent references: R. Waterman, *Dalton Trans.*, 2009, 18; M. Rani, *Synlett*, 2008, 2078; F. Mathey, *Dalton Trans.*, 2007, 1861.
5 P. J. Hammond, J. R. Lloyd and C. D. Hall, *Phosphorus Sulfur Relat. Elem.*, 1981, **10**, 47.
6 F. Mathey and F. Mercier, *Tetrahedron Lett.*, 1981, **22**, 319.
7 S. Holand and F. Mathey, *J. Org. Chem.*, 1981, **46**, 4386.
8 S. Holand and F. Mathey, *Organometallics*, 1988, **7**, 1796.
9 M.-O. Bevierre, F. Mercier, L. Ricard and F. Mathey, *Angew. Chem., Int. Ed. Engl.*, 1990, **29**, 655.
10 I. Kalinina and F. Mathey, *Organometallics*, 2006, **25**, 5031.

