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Regioselective uncatalysed hydrophosphination of alkenes: a facile route to *P*-alkylated phosphine derivatives

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The synthesis of alkylarylphosphines is easily carried out by hydrophosphination of unactivated alkenes under mild thermal activation; gram scale amounts of products can be prepared by this simple methodology.

The search for an ideal catalyst is a never-ending challenge.[1] A large number of reactions can now be carried out in high yields but despite all these existing systems, there remains a need for new catalysts that combine high rates and selectivity, and long lifetimes. The efficiency of a catalyst is dependent on both the nature of the metal and the structure of the ligand. Among the latter, phosphines have proven to be the best for a large variety of reactions.[2] Although many phosphines are commercially available, there is still a search for a method that allows the properties of a phosphine to be fine tuned for a given application. In particular, few methods have been reported for the synthesis of electron-rich alkylarylphosphines. They are mainly prepared by reactions between haloarylphosphines and alkyl-magnesium or -lithium derivatives,[3] but functional groups are not tolerated and extreme care is required to avoid oxidation. A greener way to alkylphosphines is the addition of a P–H bond onto an alkene since no atom loss is observed (the atom economy concept). This reaction is mainly carried out in the presence of radical initiators.[4] A few recent examples reported the use of catalytic activation.[5] Even if some of these reactions can be efficiently carried out, they all involve phosphines which are highly oxidizable compounds and consequently not easy to handle. In our laboratory, we are familiar with phosphine–borane complexes.[6] The borane plays a dual role: it protects the phosphine from oxidation and activates the hydrogen carried by the phosphorus atom.[7] It can then be easily removed under basic[8] or acidic[9] conditions.

We recently showed that phosphine–borane complexes could be advantageously used for the preparation of vinylphosphine derivatives by hydrophosphination of alkynes.[10] Expanding this methodology to unactivated alkenes would give a simple and easy access to alkyl-substituted phosphines. To our knowledge, only one previous article has reported such a reaction with alkenes and the yields obtained were low (7–35%).[11] The present contribution describes a facile gram scale synthesis of alkyldiarylphosphines and aryldialkylphosphines using this hydrophosphination methodology.

We first examined the reaction of diphenylphosphine–borane **1** with a simple alkene (*e.g.* oct-1-ene) as a basis for our initial model reaction. Following the conditions developed for the hydrophosphination of alkynes, the reaction was performed in the absence of catalyst under microwave irradiation. After 30 min at 50 °C, the starting materials had completely disappeared. Analysis of the crude product by ^{1}H NMR indicated that the phosphorus atom has attacked exclusively the terminal carbon atom of octene (anti-Markovnikov addition) as already observed with alkynes.[10] Octyldiphenylphosphine–borane† **3** was isolated by chromatography on silica gel in 68% yield (Scheme 1). Remarkably, no oxidation was observed during the reaction and purification even though inert gas was not used.

The yield obtained in this work, compared to the 35% yield obtained by Imamoto[11] using the same reactants under radical conditions, shows that thermal activation is more reliable for the reaction between secondary phosphine–boranes and unactivated alkenes.

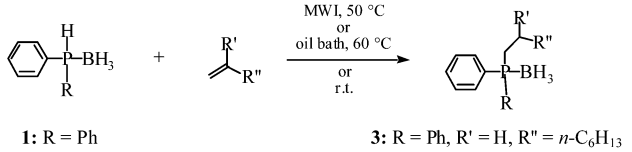
Sterically crowded alkenes (*e.g.* 2,3,3-trimethylbutene) are also suitable precursors for this reaction. The phosphinated product **4** was obtained under the same conditions in good yield (64% after chromatography). Again, only the anti-Markovnikov adduct was formed. These two experiments demonstrate that radical initiators and transition metal catalysts are not necessary to add a phosphine–borane onto an unactivated double bond.

To widen the scope of the process, we performed this reaction in more commonly available oil baths. Among the various solvents investigated, toluene was found to give the best results. Thus, oct-1-ene was reacted with **1** in toluene at 60 °C for 20 h (Scheme 1). The expected anti-Markovnikov adduct **3** was isolated by silica gel chromatography in 52% yield. The other regioisomer could not be detected. Interestingly, the reaction can even be performed at RT due to the strong P–H activation induced by the borane group. However, the reaction was slower (48 h *vs.* 20 h at 60 °C) but the ^{31}P NMR spectrum showed clean product formation. After silica gel chromatography, the phosphine–borane **3** was isolated in pure form in 69% yield. Scaling-up the reaction to 1 gram of **1** did not change the efficiency and yield of the reaction.

Extending the reaction to secondary alkylarylphosphine–boranes could lead to interesting new asymmetric dialkylarylphosphine–boranes. For this purpose, methylphenylphosphine–borane **2** was reacted with oct-1-ene at RT in toluene. The reaction was significantly slower than that involving **1**. Even after one week, only traces of **5** were observed. However, upon thermal activation (60 °C, oil bath), the addition reaction was completed within 60 hours and the hydrophosphination product **5** was obtained in 62% yield after chromatography.

Using a chiral alkene (*e.g.* a terpene) should open the way to the preparation of chiral phosphines, which play a central role in organometallic catalysis. We, thus, reacted **1** with (−)-β-pinene. Heating the mixture neat at 70 °C under microwave irradiation and purification by silica gel chromatography afforded enantiopure phosphine–borane **7**† in 95% yield. Phosphine **9** was never observed (Scheme 2).

The formation of **7** can be explained as follows: homolytic cleavage of the P–H bond could give the phosphinyl radical $H_3B{\cdot}PPh_2{\cdot}$ which upon reaction with the alkene gives a carbon



1: R = Ph
2: R = Me

3: R = Ph, R' = H, R" = *n*-C_6H_{13}
4: R = Ph, R' = Me, R" = *t*-Bu
5: R = Me, R' = H, R" = *n*-C_6H_{13}

Scheme 1 Hydrophosphination reactions of simple alkenes.

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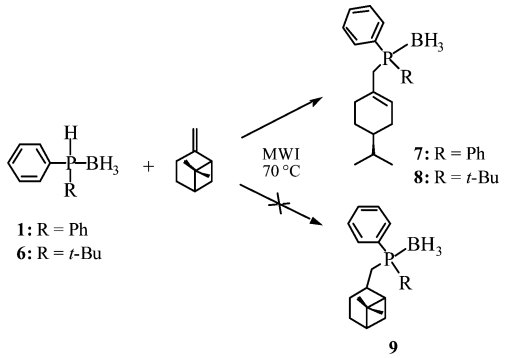

Scheme 2 Hydrophosphination of (−)-β-pinene.

radical. After rearrangement of the radical by bridge opening,[12] the final product **7** would be formed by abstraction of hydrogen from another molecule of **1** (Scheme 3). This ring opening is thermodynamically favoured since it leads to a less strained molecule.

To check the validity of this hypothesis, the reaction was performed with the deuterated diphenylphosphine–borane **10**, this being formed by deprotonation of **1** with NaH and hydrolysis with D_2O. NMR analysis of the hydrophosphination product unambiguously showed the addition of a deuterium atom on radical **12** leading exclusively to **13**.

The hydrophosphination reaction of (−)-β-pinene with a bulky and electron rich secondary phosphine–borane (*e.g. tert*-butylphenylphosphine–borane **6**)[11] gave the same result leading to **8** in 90% yield as a mixture of 2 diastereomers (1 : 1 ratio) due to the chiral phosphorus atom (Scheme 2).

In conclusion, regioselective hydrophosphination of alkenes using secondary phosphine–boranes is a simple process for the synthesis of alkyldiarylphosphines and aryldialkylphosphines. Due to the strong P–H activation induced by the borane, the reactions can be carried out under mild conditions (RT to 60 °C) and can involve various secondary phosphines and many types of alkenes, leading to a wide molecular diversity of achiral or chiral phosphines. Investigation of the reaction mechanism and the origin of the regioselectivity are ongoing in our laboratory.

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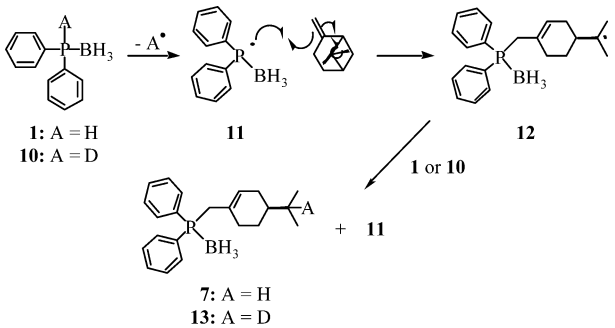

Scheme 3 Possible mechanism for the formation of **7**.

Notes and references

† Experimental procedure for **3**: **1** (1 g, 5 mmol), oct-1-ene (950 μL, 6 mmol) and toluene (15 mL) were placed in a nitrogen flushed Schlenk tube. The reaction was allowed to run for 48 h at RT. The crude product was then purified by silica gel column chromatography with toluene as eluent. Phosphine–borane **3** was obtained as an oil in 69% yield. δ_P (162 MHz, $CDCl_3$): 16.1; δ_H (400 MHz, $CDCl_3$): 7.67 (m, 4H), 7.44 (m, 6H), 2.19 (m, 2H), 1.51 (m, 2H), 1.37 (m, 2H), 1.25 (m, 8H), 1.00 (q, $^1J_{HB}$ 98, 3H), 0.86 (t, $^3J_{HH}$ 6.9, 3H); δ_C (101 MHz, $CDCl_3$): 132.5 (d, $^2J_{CP}$ 8.9, *o*-Ph), 131.5 (d, $^4J_{CP}$ 2.3, *p*-Ph), 130.1 (d, $^1J_{CP}$ 54.7 , *i*-Ph), 129.2 (d, $^3J_{CP}$ 9.8, *m*-Ph), 32.2, 31.6 (d, $^3J_{CP}$ 14.0), 29.5, 29.4, 26.0 (d, $^1J_{CP}$ 37.0), 23.4, 23.0, 14.5; δ_B (128 MHz, $CDCl_3$): −36.7; HRMS calcd for $C_{20}H_{27}P$ ([M − BH_3]$^{+\cdot}$) 298.1850, found 298.1858. Experimental procedure for **7**: **1** (100 mg, 0.5 mmol), (−)-β-pinene (88 μL, 0.55 mmol) and toluene (1 mL) were placed in a quartz reaction vessel. The reactor was submitted to microwave irradiation for 30 min at 70 °C and allowed to cool to RT. The crude product was then purified by silica gel column chromatography with CH_2Cl_2 as eluent. Phosphine–borane **7** was obtained as an oil in 95% yield. δ_P (121 MHz, $CDCl_3$): 15.5; δ_H (300 MHz, $CDCl_3$): 7.60 (m, 4H), 7.30 (m, 6H), 5.15 (m, 1H), 2.85 (dm, $^2J_{HP}$ 12.9, 2H), 1.85 (m, 2H), 1.80 (m, 1H), 1.55 (m, 2H), 1.30 (m, 1H), 1.05 (m, 2H), 1.00 (q, $^1J_{HB}$ 97, 3H), 0.75 (d, $^3J_{HH}$ 6.7, 3H), 0.70 (d, $^3J_{HH}$ 6.7, 3H); δ_C (75 MHz, $CDCl_3$): 132.7 (d, $^2J_{CP}$ 8.6, *o*-Ph), 132.3 (d, $^2J_{CP}$ 8.6, *o*′-Ph), 131.2 (d, $^4J_{CP}$ 1.4, *p*-Ph), 131.0 (d, $^4J_{CP}$ 1.4, *p*′-Ph), 130.1 (d, $^1J_{CP}$ 53.7, *i*-Ph), 129.7 (d, $^1J_{CP}$ 53.7, *i*′-Ph), 128.7 (d, $^2J_{CP}$ 5.6), 128.6 (d, $^3J_{CP}$ 9.7, *m*-Ph), 128.3 (d, $^3J_{CP}$ 9.7, *m*′-Ph), 127.7 (d, $^3J_{CP}$ 9.6), 39.8, 35.4 (d, $^1J_{CP}$ 32.9), 32.3, 31.4 (d, $^3J_{CP}$ 1.7), 29.6, 26.7, 20.4, 20.1; δ_B (96 MHz, $CDCl_3$): −38.8; ν(KBr)/cm^{-1}: 2358 (ν_{BH}), 2340 (ν_{BH}); HRMS calcd for $C_{22}H_{30}BP$ ([M]$^{+\cdot}$) 336.2172, found 336.2179.

1 J. A. Gladysz, *Pure Appl. Chem.*, 2001, **73**, 1319.
2 (*a*) R. Noyori, in *Asymmetric Catalysis in Organic Synthesis*, J. Wiley & Sons Ltd, New York, 1994; (*b*) J. M. Brunel and G. Buono, *Top. Curr. Chem.*, 2002, 79.
3 D. G. Gilheany and C. M. Mitchell, in *The Chemistry of Organophosphorus Compounds*, **vol. 1**, ed. F. R. Hartley, J. Wiley & Sons Ltd, New York, 1990, pp. 151–190.
4 (*a*) D. L. Dubois, W. H. Myers and D. W. Meek, *J. Chem. Soc., Dalton Trans.*, 1975, 1011; (*b*) P. F. Brandt, D. M. Schubert and A. D. Norman, *Inorg. Chem.*, 1997, **36**, 1728; (*c*) A. Robertson, C. Bradaric, C. S. Frampton, J. McNulty and A. Capretta, *Tetrahedron Lett.*, 2001, **42**, 2609; (*d*) L. Ropartz, R. E. Morris, D. F. Foster and D. J. Cole-Hamilton, *J. Mol. Catal. A: Chem.*, 2002, **182–183**, 99.
5 (*a*) M. R. Douglass and T. J. Marks, *J. Am. Chem. Soc.*, 2000, **122**, 1824; (*b*) M. R. Douglass, C. L. Stern and T. J. Marks, *J. Am. Chem. Soc.*, 2001, **123**, 10221; (*c*) M. O. Shulyupin, M. A. Kazankova and I. P. Beletskaya, *Org. Lett.*, 2002, **4**, 761.
6 See for examples: (*a*) A.-C. Gaumont, M. B. Hursthouse, S. J. Coles and J. M. Brown, *Chem. Commun.*, 1999, 63; (*b*) K. Bourumeau, A.-C. Gaumont and J. M. Denis, *J. Organomet. Chem.*, 1997, **529**, 205; (*c*) J. M. Denis, H. Forintos, H. Szelke, L. Toupet, T. N. Pham, P. J. Madec and A.-C. Gaumont, *Chem. Commun.*, 2003, 54.
7 T. Imamoto, T. Kusumoto, N. Suzuki and K. Sato, *J. Am. Chem. Soc.*, 1985, **107**, 5301.
8 H. Brisset, Y. Gourdel, P. Pellon and M. Le Corre, *Tetrahedron Lett.*, 1993, **34**, 4523.
9 (*a*) L. McKinstry and T. Livinghouse, *Tetrahedron Lett.*, 1995, **36**, 9319; (*b*) L. McKinstry and T. Livinghouse, *Tetrahedron*, 1995, **51**, 7655.
10 D. Mimeau and A.-C. Gaumont, *J. Org. Chem.*, 2003, **68**, 7016.
11 T. Imamoto, T. Oshiki, T. Onozawa, T. Kusumoto and K. Sato, *J. Am. Chem. Soc.*, 1990, **112**, 5244.
12 F. Bellesia, L. Forti, F. Ghelfi and U. M. Pagnoni, *Synth. Commun.*, 1997, **27**, 961.