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CONVENIENT METHOD FOR THE REDUCTION OF THE DOUBLE-BOND OF CYCLIC VINYLPHOSPHINE OXIDES USING BORANE

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Abstract: The electronpoor double-bond of cyclic vinylphosphine oxides (**1**, **3** and **4**) is easily reduced by borane in a selective manner to give the corresponding saturated derivatives (**2**, **4** and **5**, respectively) Under forcing conditions, change of the functionality may also take place.

We found that the borane-methyl sulfide complex (BMS) was suitable for the conversion of the phosphine oxide group of 7-phosphanorbornene derivatives to a phosphine-borane function.[1] The ring strain of the bridging P-moiety (the C–P–C angle is 82°) is the indispensable condition of this new type of transformation. It was also observed that the preparation of unsaturated phosphine-boranes from the corresponding phosphine and the BMS was accompanied by reductive side-reactions.[2-4] We wished to evaluate if the reducing

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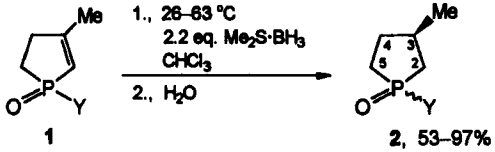
ability of the borane can be utilised in the modification of cyclic vinylphosphine oxides.

Double-bond of the 1-phenyl-dihydrophosphole oxide **1a** was efficiently reduced by treating it with 2.2 equivalents of BMS at 63 °C for 7 h. Completion of the reaction at room temperature required a prolonged reaction time of 24 h, but the yield of the tetrahydrophosphole oxide (**2a**) was in this case nevertheless quantitative after hydrolysis and flash column chromatography (Scheme 1). The double-bond of P-ethoxy dihydrophosphole oxide **1b** could also be reduced at 63 °C; the yield of product **2b** was, however, somewhat lower (53%) (Scheme 1). Due to the stereogenic centre at C_4 of starting compound **1**, the tetrahydro derivatives (**2**) were formed as the mixture of a major- and a minor diastereomer.

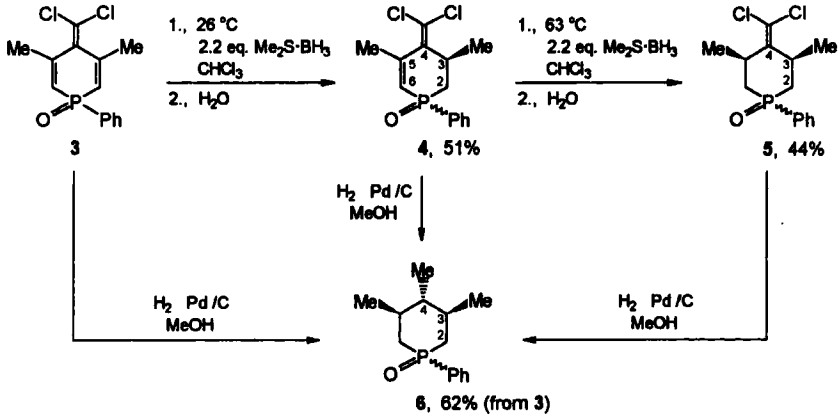


Scheme 1

The products (**2a,b**) were characterised by ^{31}P and ^{13}C NMR, as well as mass spectroscopic data. Our method giving the saturated derivatives (**2**) through hydroboration[5] is a good alternative to the earlier approach involving catalytic hydrogenation of dihydrophosphole oxides.[6]

The above procedure was also useful in the transformation of 1,4-dihydrophosphinine oxide **3** into the corresponding tetrahydro derivative (**4**) (Scheme 2). Working at room temperature for 24 h, the saturation was practically selective leaving the other double-bonds intact. The reaction of

tetrahydrophosphinine oxide **4** with a second portion of the BMS reagent (2.2 equivalents) at 63 °C furnished the symmetrical hexahydrophosphinine oxide (**5**) (Scheme 2). Products **4** and **5** obtained after column chromatography in 51 and 44% yields, respectively, consisted of two diastereomers. The new compounds (**4** and **5**) were characterised by ^{31}P, ^{13}C and ^{1}H NMR, as well as mass spectroscopic data. The **3** → **4** and **4** → **5** transformations shown in Scheme 2 are of importance, as catalytic hydrogenation of the starting material (**3**), or that of intermediate **4** applying 1.2 equivalent of hydrogen was observed not to be selective at all. The complete hydrogenation of compound **3** using 5 equivalents of hydrogen, or that of any of the intermediates (**4** and **5**) led to the diastereomers of hexahydrophosphinine oxide **6** (Scheme 2).



Scheme 2

Single crystal X-ray analysis of the major isomer separated by recrystallization was useful in evaluating its stereostructure. As could also be seen from the ^{13}C and ^{1}H NMR spectra, the isomer having in hand is symmetrical and the axial phenyl group and the equatorial 3- and 5-methyl substituents are in the trans

disposition of the chair conformation. The situation may obviously be similar for the major isomer of dichloromethylene derivative **5**. The 4-methyl group in the major isomer of **6** is in the apical position. In previously described hexahydrophosphinine oxides the 4-substituent was in the equatorial position.[7,8] The bond lengths, bond angles together with the torsion angles for the major isomer of **6** were in the expected region (Fig. 1).

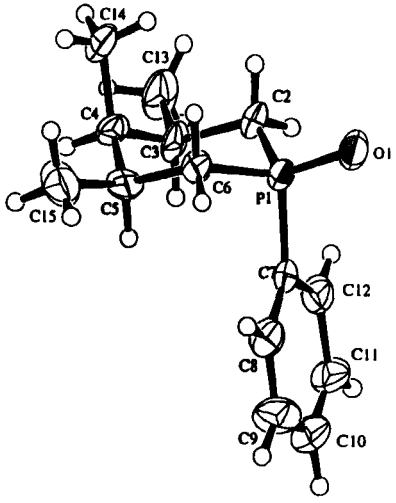
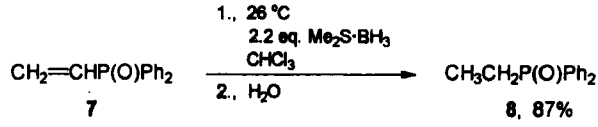


Fig. 1 X-ray structure for the major diastereomer of hexahydrophosphinine oxide 6 [P(1)–O(1) 1.489(4) Å, P(1)–C(2) 1.790(7) Å, P(1)–C(7) 1.805(5) Å, O(1)–P(1)–C(2) 114.6(6)°, O(1)–P(1)–C(7) 111.6(2)°, C(2)–P(1)–C(7) 106.7(6)°, C(2)–P(1)–C(6) 101.8(3)°, P(1)–C(2)–C(3)–C(4) 58.8(12)°, P(1)–C(2)–C(3)–C(13) 174.7(10)°, C(2)–P(1)–C(7)–C(8) 145.7(8)°, P(1)–C(7)–C(8)–C(9) 174.0(10)°.]

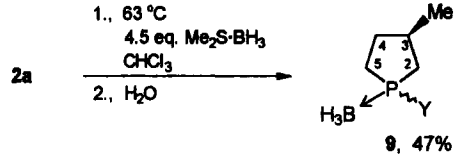
The reducing ability of the BMS reagent seems to be of more general value, as the double-bond of diphenyl-vinylphosphine oxide (**7**) could also be saturated by borane (Scheme 3). The structure of product **8** obtained in 87% yield after flash column chromatography was identified by ^{31}P NMR and FAB.



Scheme 3

Further attention is directed on the possible extension of the reduction to the double-bond of the –HC=CHP(O)< and the –HC=CHC(O)– type of compounds by borane.

Finally, we recall that the P=O moiety of 7-phosphanorbornenes could be transformed to a phosphine-borane function by reaction with two equivalents of the BMS reagent.[1,2] We wished to evaluate if this kind of change in the functionality can also be achieved with other P-heterocycles. It was found that under forcing conditions using 4.5 equivalents of the BMS reagent at 63 °C for 3 days, tetrahydrophosphole oxide **2a** could be converted to phosphine-borane **9** in 47% yield after chromatography. Starting from the diastereomeric mixture of **2a**, the borane complex (**9**) was also formed as the mixture of isomers (Scheme 4).



Scheme 4

The structure of the isomers of product **9** was confirmed by ^{31}P, ^{11}B, ^{13}C and ^{1}H NMR, as well as mass spectroscopy. As earlier,[1] the phosphine oxide (**2a**) is deoxygenated by borane in the first step. The tetrahydrophosphole so obtained reacts fast with the excess of the borane to give product **9**. The above observation is indeed of synthetic potential, as this is the first case that the functional group of

a "common or garden variety" cyclic phosphine oxide is converted to a phosphine-borane moiety by borane in a one-flask experiment. The scope and limitations of this attractive synthetic approach will be explored soon.

The conclusion of our recent research is that the BMS reagent may be of wider applicability. It can be used in the selective reduction of electronpoor double-bonds. On the other hand, in certain cases, the borane seems to be suitable for the conversion of the P=O group to a $P \rightarrow BH_3$ function.

Experimental

The ^{31}P, ^{13}C, ^{1}H and ^{11}B NMR spectra were obtained on a Brüker DRX-500 spectrometer at 202.4, 125.7, 500 and 160.4 MHz, respectively. The coupling constants are given in Hz. The mass spectra were registrated on a ZAB-2SEQ instrument at 70 eV. Dihydrophosphinine oxide **3** was prepared as described earlier.[9] Purity of the products was established by GC or TLC, as well as NMR spectra.

General procedure for the saturation of vinylphosphine oxides (1a,b, 3 and 4)

To the solution of vinylphosphine oxides (**1a,b**, **3** and **4**) (2.0 mmol) in chloroform (15 mL) was added 2M borane-dimethyl sulfide in THF (2.2 mL) and the mixture was stirred at 24 °C (in the case of **1a** and **3**, or at 63 °C (in the case of **1b** and **4**) for 24 h. The mixture was hydrolysed by stirring it with water (1 mL) for 5 minutes. The precipitated material was filtered off and the organic phase separated and dried ($MgSO_4$). The crude product obtained after evaporating the solvent was purified by column chromatography (silica gel, 3% MeOH in

chloroform) to give products **2a,b**, **4** and **5**, respectively as the mixture of two diastereomers.

3-Methyl-1-phenyl-2,3,4,5-tetrahydro-1H-phospole 1-oxide (2a)

Isomeric composition: 71–29%; Yield: 97%; ^{31}P NMR ($CDCl_3$) δ 62.2 for the major and 62.5 for the minor isomer; ^{13}C NMR ($CDCl_3$) δ major: 20.9 (J = 13.7, Me), 30.6 (J = 65.9, C_5), 33.5 (J = 8.3, C_3), 33.9 (J = 5.7, C_4), 37.3 (J = 67.6, C_2), 133.8 (J = 89.1, $C_{1'}$) minor: 21.0 (J~9, Me), 29.5 (J = 65.9, C_5), 32.7 (J = 5.6, C_3), 34.6 (J = 9.1, C_4), 37.8 (J ~ 60, C_2) common signals: 128.5 (J = 11.1), 129.7 (J = 9.6) $C_{2'}$ and $C_{3'}$, 131.6 ($C_{4'}$); MS, m/z (rel. int.) 194 (M^+, 100), 193 (86), 179 (26), 125 (48), 77 (24); HRMS, M^+_{found} = 194.0851, $C_{11}H_{15}OP$ requires 194.0861.

1-Methoxy-3-methyl-2,3,4,5-tetrahydro-1H-phosphole 1-oxide (2b)

Isomeric composition: 67–33%; Yield: 53%; ^{31}P NMR ($CDCl_3$) δ 87,5 for the major and 87,4 for the minor isomer; ^{13}C NMR ($CDCl_3$) δ major: 21.6 (J = 16.9, C_3–Me), 25.8 (J = 86.6), 25.9 (J = 86.7), C_2 and C_5, 31.9 (J = 10.8, C_4), 35.2 (J = 12.3, C_3) minor: 21.5 (J = 17.0, C_3–Me), 25.5 (J = 86.7), 25.8 (J = 86.6), C_2 and C_5, 31.8 (J = 10.7, C_4), 35.1 (J = 12.5, C_3) common signal: 51.6 (J = 7.0, MeO); MS, m/z (rel. int.) 148 (M^+, 26), 133 (15), 79 (100); HRMS, M^+_{found} = 148.0650, $C_6H_{13}O_2P$ requires 148.0653.

4-Dichloromethylene-3,5-dimethyl-1-phenyl-1,2,3,4-tetrahydrophosphinine 1-oxide (4)

Isomeric composition: 69–31%; Yield: 51%; ^{31}P NMR ($CDCl_3$) δ 19.3 for the

major and 19.0 for the minor isomer; ^{13}C NMR ($CDCl_3$) δ major: 19.8 (J=2.5, C_3–Me), 35.0 (J=69.0, C_2), 37.4 (J=6.2, C_3), 120.2 (J=2.3, CCl_2), 123.5 (J=93.4, C_6), 133.8 (J=104.0, $C_{1'}$), 138.0 (J=16.9, C_4), 153.6 (C_5) minor: 22.1 (J=7.4, C_3–Me), 31.4 (J=5.0, C_3), 33.3 (J=65.0, C_2), 117.8 (CCl_2), 123.6 (J=92.7, C_6), 139.0 (J=15.5, C_4), 150.5 (C_5) common signals: 25.4 (J=13.6, C_5–Me), 128.9 (J=12.1), 130.2 (10.5) $C_{2'}$ and $C_{3'}$, 132.1 (J=2.0, $C_{4'}$); ^1H NMR ($CDCl_3$) δ 1.18 (d, J=7.0, C_3–Me (major)), 1.39 (d, J=7.2, C_3–Me (minor)), 2.35 (d, J=0.9, C_5–Me), 6.19 (d, J=14.2, C_6–H); FAB, 301 (M+H); HRFAB, M^+_{found}= 301.0310, $C_{14}H_{16}Cl_2OP$ requires 301.0316 for the ^{35}Cl isotopes.

4-Dichloromethylene-3,5-dimethyl-1-phenyl-1,2,3,4,5,6-hexahydrophosphinine 1-oxide (5)

Isomeric composition: 74–26%; Yield: 44%; ^{31}P NMR ($CDCl_3$) δ 31.4 for the major and 29.4 for the minor isomer; ^{13}C NMR ($CDCl_3$) δ major: 22.1 (J=7.6, Me), 31.4 (J=5.2, C_3), 33.4 (J=65.2, C_2), 117.7 (CCl_2), 133.3 (J=97.1, $C_{1'}$), 139.0 (J=15.5, C_4) minor: 21.7 (J=3.1, Me), 32.3 (J=65.6, C_2), 33.2 (J=5.7, C_3), 117.1 (CCl_2), 133.0 (J=97.4, $C_{1'}$), 140.7 (J=11.9, C_4) common signals: 128.8 (J=11.9), 130.2 (J=9.6) $C_{2'}$ and $C_{3'}$, 132.0 (J=2.1, $C_{4'}$); ^1H NMR ($CDCl_3$) δ 1.40 (d, J=7.5, Me (major)), 1.58 (d, J=7.5, Me (minor)); MS, m/z (rel. int.) 302 (M^+, 31), 267 (100), 231 (34), 125 (33), 77 (33); HRMS, M^+_{found}=302.0412, $C_{14}H_{17}Cl_2OP$ requires 302.0394 for the ^{35}Cl isotopes.

Diphenyl-vinylphosphine oxide **7** was reduced according to the general procedure. Yield of phosphine oxide **8**: 87%; ^{31}P NMR ($CDCl_3$) δ 36.3, (^{31}P NMR (EtOH) δ 36.4)[10]; FAB, 231 (M+H).

1-Phenyl-3,4,5-trimethyl-1,2,3,4,5,6-hexahydrophosphinine 1-oxide (6)

The mixture of 1,4-dihydrophosphinine oxide **3** (0.35 g, 1.17 mmol) and 5% Pd on C (0.1 g) in methanol (30 mL) was hydrogenated at 450 kPa at 24 °C and finally at 50 °C until 5 equivalents of hydrogen were absorbed. The suspension was filtered, the solvent of the filtrate evaporated and the residue so obtained purified by flash column chromatography (as above). Recrystallisation of the main fraction containing two diastereomers afforded product **6** as a single diastereomer. Yield: 62%; ^{31}P NMR ($CDCl_3$) δ 35.6; ^{13}C NMR ($CDCl_3$) δ 4.6 (C_4–Me), 21.8 (J=16.8, C_3–Me), 28.9 (J=63.7, C_2), 34.4 (J=1.9, C_3), 39.1 (J=2.1, C_4), 128.9 (J=10.9), 129.6 (J=9.3), $C_{2'}$ and $C_{3'}$, 131.7 (J=2.1, $C_{4'}$), 132.8 (J=93.5, $C_{1'}$); ^1H NMR ($CDCl_3$) δ 0.75 (d, J=7.2, C_4–Me), 0.94 (dd, J^1=6.4, J^2=2.6, C_3–Me); MS, m/z (rel. int.) 236 (M^+, 34), 221 (39), 194 (38), 179 (100), 152 (51), 140 (78), 125 (93), 91 (61), 77 (38); Anal. found for **6**, C, 70.75, H, 8.54, $C_{14}H_{21}OP$ requires C, 71.16, H, 8.96.

Crystal data for the major diasteromer of hexahydrophosphinine oxide 6

Crystal system: monoclinic, space group C2, unit cell dimensions a=16.341(5) Å, b=9.237(5) Å, β=137.88(1)°, c=14.100(5) Å, volume 1427.2(11) $Å^3$, Z=4, density (calcd.)=1.174 g/cm^3, μ=1.614 mm^{-1}, crystal size 0.50×0.30×0.25 mm, index ranges $0 \le h \le 19$, $0 \le k \le 11$, $-17 \le l \le 11$, independent reflections 1521, data/restraints/parameters: 1521/1/162, goodness-of-fit on F^2 1.081, final R indices [I>2sigma(I)] R1=0.074, wR2=0.199, R indices (all data) R1=0.104, wR2=0.235. Data were collected on a Rigaku AFC6S diffractometer using Cu–K_α radiation. The structure was solved using the SHELXS-86[11] direct methods program. The structure was refined with SHELXL-97-2.[12]

3-Methyl-1-phenyl-2,3,4,5-tetrahydro-1H-phosphole-borane (9)

Product **9** was prepared from compound **2a** according to the general procedure, but 4.5 equivalents of the BMS reagent was used and the reaction mixture was kept at 63 °C for 3 days. Isomeric composition: 73–27%; Yield: 47%; ^{31}P NMR ($CDCl_3$) δ 30.8; ^{13}B NMR ($CDCl_3$) δ –34.7; ^{13}C NMR ($CDCl_3$) δ major: 20.5 (J = 11.4, Me), 26.8 (J = 37.5, C_5), 35.0 (J = 36.8, C_2), 36.2 (J = 3.9, C_3), 36.3 (C_4), 131.7 (J = 46.8, $C_{1'}$) minor: 20.6 (J = 9.5, Me), 26.9 (J = 36.2, C_5), 34.6 (J = 37.6, C_2), 35.3 (C_4), 37.2 (C_3) common signals: 129.0 (J = 9.7), 131.6 (J = 9.3) $C_{2'}$ and $C_{3'}$, 131.2 ($C_{4'}$); ^1H NMR ($CDCl_3$) δ 1.21 (d, J = 6.0, Me (major)), 1.20 (d, J = 6.5, Me (minor)); FAB, 193 (M+H, 6), 179 (M–BH_3, 100); Anal. found for **9**, C, 68.31, H, 9.06, $C_{11}H_{18}BP$ requires C, 68.70, H, 9.45.

Acknowledgements

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