THE REACTION OF DICHLOROCARBENE WITH PHOSPHINE DERIVATIVES RELATED ON THE 2-METHYL-1-PHENYL-2,5-DIHYDRO AND 2,3,4,5-TETRAHYDRO-1H-PHOSPHOLE MOIETY

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Abstract: The reaction of 2,5-dihydro- and 2,3,4,5-tetrahydro-1H-phosphole derivatives including oxide **1**, phosphine-boranes **4** and **8** and phosphine **3** with dichlorocarbene was studied. It was found that the phosphine-borane moiety is more reactive towards the dichlorocarbene than the double-bond or the phopshine function.

Introduction

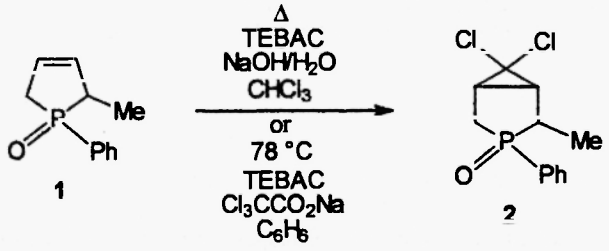
The easily available 3-methyl-2,5-dihydro-1H-phosphole 1-oxides may serve as starting materials for 6- and 7-membered P-heterocycles,[1-3] as well as for functionalised derivatives including phosphine-boranes.[4] We wished to explore, how the 2-methyl-1-phenyl-2,5-dihydro-1H-phosphole 1-oxide can be utilised in ring expansion and in functionalisations.

Results and discussion

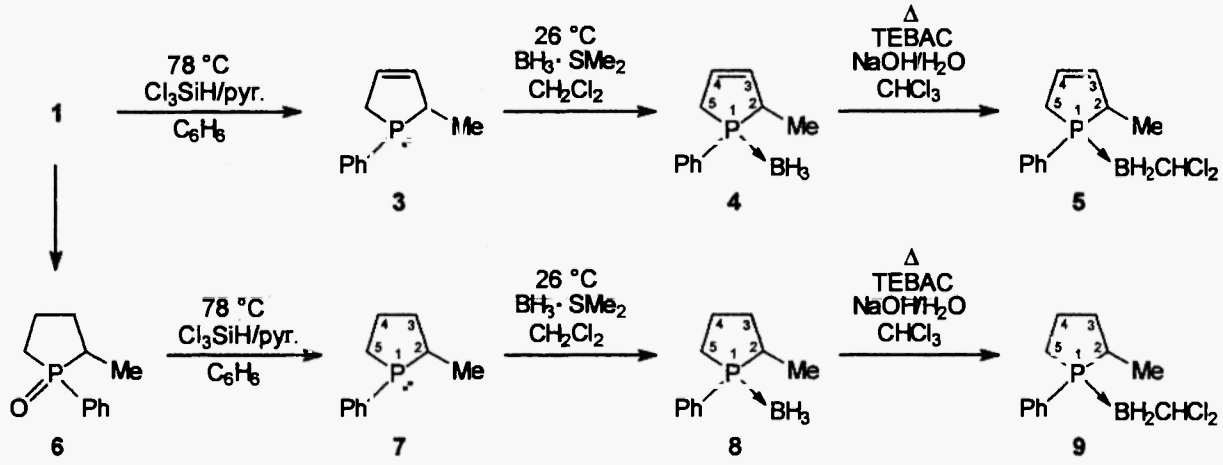
Ring enlargement of dihydro-1H-phosphole oxide **1** was attempted by the „dichlorocarbene" method.[1,5] According to this, substrate **1** consisting of a 52–48 mixture of two diastereomers was reacted with dichlorocarbene generated from chloroform by aqueous sodium hydroxyde under phase transfer catalytic conditions. The expected phosphabicyclo[3.1.0]hexane (**2**) was formed only in a low conversion, no matter if the dichlorocarbene was applied in a 80-fold excess. Due to the unreactivity of the double-bond in **1**, the use of another carbene precursor, sodium trichloroacetate[6] was also not useful in increasing the efficiency (Scheme 1). It is known that the reactivity of the double-bond towards the electrophilic dichlorocarbene is highly influenced by the presence of methyl group(s) on the carbon atom(s) of the double-bond.[7]

We thought that the unreactivity of the double-bond of the 2,5-dihydro-1H-phopshole moiety is the consequence of the proximity of the electron-withdrawing P=O function. For this, phosphine oxide **1** was deoxygenated by trichlorosylane to give the phosphine (**2**) and then the phosphine function was protected as a borane complex (**4**). Phosphine-boranes can be regarded to be activated phosphines.[8] The reaction of phosphine-borane **4** with

dichlorocarbene generated as above did not lead to ring expansion, rather dichloromethylboryl derivative **5** was formed (Scheme 2).



Scheme 1



Scheme 2

Due to the isomeric composition of the starting material (**1**), both the phosphine-borane intermediate (**4**) and the dichloromethyl derivative (**5**) was obtained as the mixture of two diastereomers. Moreover, both diastereomers of product **5** consisted of two rotamers due to the hindered rotation of the $CHCl_2$ group around the B–C bond. After chromatography a 45–32–22% mixture of three species (**5A**, **5B** and **5C**) was obtained and characterised by spectroscopy.

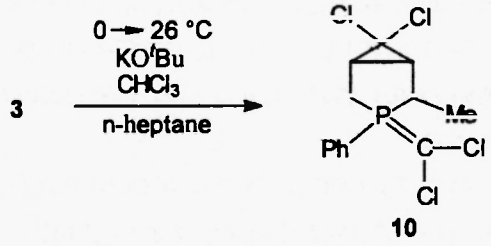
The above transformation was also applied to the tetrahydro-1H-phopshole oxide (**6**) obtained from the dihydro derivative (**1**) by catalytic hydrogenation. Hence, phosphine oxide **6** was deoxygenated, the phosphine (**7**) so obtained converted to the phosphine-borane (**8**) and finally, the borane was reacted with dichlorocarbene. Starting form the two diastereomers of **6**, the dichloromethylboranes (**9**) were formed as a 28–25–24 – 23% mixture of four isomers (**9A**, **9B**, **9C** and **9D**) (Scheme 2).

During the preparation of substituted phosphine-boranes, the hindered rotation around the B–C axis has never been observed before.[9,10]

Boranes **4** and **8**, as well as dichloromethylboranes **5** and **9** were characterised by ^{31}P, ^{11}B and ^{13}C NMR, as well as by mass spectroscopy. The borane complexes **4**, **5**, **8** and **9** can be regarded to be precursors of phosphines that are

useful as phopshine ligands. The decomplexation of phosphine-boranes can be realised by treatment with a secondary amine.[11] P-ligands including chiral species[12] are widely used in transition metal complexes.

Finally, phopshine **3** itself was reacted with dichlorocarbene generated from chloroform by potassium *tert*-butoxide. The reaction was not too efficient, but the P-dichloromethylene dichlorophosphabicyclo[3.1.0]hexane (**10**) formed by reaction with two units of dichlorocarbene was the main component (Scheme 3).



Scheme 3

Efforts will be done to try to optimalize the above syntheses and to extend the sphere of the reactions examined.

Experimental

The ^{31}P-, ^{11}B-, ^{13}C- and ^{1}H-NMR spectra were taken on a Bruker DRX-500 spectrometer operating at 202.4, 160.4 125.7, and 500 MHz, respectively. Chemical shifts are downfield relative to 85% H_3PO_4, $F_3B{\cdot}OEt_2$ or TMS. The couplings are given in Hz. EI and FAB mass spectrometry was performed on a ZAB-2SEQ instrument. The 2-methyl-1-phenyl-2,5-dihydro-1H-phosphole oxide (**1**) was preparated as described earlier.[13] $(M+H)^+_{found}$ = 193.0745, $C_{11}H_{14}PO$ requires 193.0782.

1A: δ_P ($CDCl_3$) 60.1 (52%); δ_C ($CDCl_3$) 12.7 (C_2–Me), 32.8 (J = 66.1, C_5), 37.4 (J = 69.0, C_2), 125.4 (J = 11.5, C_3),[a] 128.2 (J = 11.7, C_3),[b] 129.3 (J = 9.1, $C_{2'}$),[b] 131.5 (C_4), 133.2 (J = 90.0, $C_{1'}$), 134.8 (J = 14.4, C_4)[a]; δ_H ($CDCl_3$) 1.33 (dd, J_1 = 7.5, J_2 = 7.6, Me).

1B: δ_P ($CDCl_3$) 69.4 (48%); δ_C ($CDCl_3$) 12.9 (C_2-Me), 32.4 (J = 65.7, C_5), 38.2 (J = 68.1, C_2), 125.6 (J = 10.1, C_3),[c] 128.1 (J = 15.9, C_3),[d] 129.7 (J = 87.1, $C_{1'}$), 130.2 (J = 8.7, C_2),[d] 131.7 (C_4), 135.0 (J = 17.2, C_4)[c]; δ_H ($CDCl_3$) 0.88 (dd, J_1 = 7.5, J_2 = 9.5, Me).

[a-d] tentative assignment

Dichlorocarbene addition to 2-methyl-1-phenyl-2,5-dihydro-1H-phopshine oxide (1)

The solution of 0.50 g (2.6 mmol) of **1** and 0.50 g (2.2 mmol) of TEBAC in 30 ml of chloroform was treated with 50% aqueous sodium hydroxide containing of 8.2 g (0.21 mol) of sodium hydroxide under vigorous stirring. The temperature rose to reflux. After 5 h of stirring, the mixture was filtered and the filtrate evaporated. The mixture (0.41 g) obtained after column chromatography (silica gel, 3% of methanol in chloroform) contained the desired product (**2**) in 16%; Yield 9 %. δ_P ($CDCl_3$) 80.4; FAB-MS, 275 (M+H).

2-Methyl-1-phenyl-2,5-dihydro-1H-phosphole-borane (4)

To the solution of 0.51 g (2.7 mmol) of oxide **1** and 0.80 ml (9.8 mmol) of pyridine in 15 ml of benzene was added 0.70 ml (6.9 mmol) of trichlorosilane under nitrogen. The mixture was stirred at 78 °C for 20 h. The volatile components were removed *in vacuo* to give 0.46 g of phosphine **3**. To the 20 ml dichloromethane solution of phosphine **3** was added 1.7 ml (3.4 mmol) of 2M tetrahydrofuran solution of $BH_3 \cdot SMe_2$ at room temperature under nitrogen and the mixture was stirred for 24 h. Filtration and evaporation of the volatile components of the filtrate led to 0.45 g (90%) of **4** as a mixture of **4A** (55%) and **4B** (45%) isomers; $(M-1)^+_{found}$ = 189.0693, $C_{11}H_{15}{}^{11}BP$ requires 189.1004.

4A: δ_P ($CDCl_3$) 34.8 (m, $^1J_{PB}$ = 54.2); δ_B ($CDCl_3$) –36.7; δ_C ($CDCl_3$) 14.4 (J = 14.5, C_2–Me), 32.2 (J = 35.7, C_5), 39.0 (J = 34.6, C_2), 126.9 (C_4), 128.5 (J = 9.3, C_3),[b] 131.6 (J = 2.1, C_3), 132.4 (J = 8.5, C_2),[b] 135.8 (J = 3.3, C_4); δ_H ($CDCl_3$) 0.96 (dd, J_1 = 7.5, J_2 = 14.6, Me).

4B: δ_P ($CDCl_3$) 32.4 (m, $^1J_{PB}$ = 61.7); δ_B ($CDCl_3$) –38.7; δ_C ($CDCl_3$) 16.3 (J = 4.9, C_2–Me), 33.1 (J = 35.9, C_5), 39.9 (J = 35.0, C_2), 126.7 (C_4), 128.8 (J = 9.7, C_3),[a] 131.0 (J = 8.8, C_2),[a] 131.3 (J = 2.1, C_3), 135.9 (J = 4.8, C_4); δ_H ($CDCl_3$) 1.38 (dd, J_1 = 7.5, J_2 = 16.8, Me).

[a,b] tentative assignment

2-Methyl-1-phenyl-2,5-dihydro-1H-phosphole-dichloromethylborane (5)

The solution of 0.45 g (2.4 mmol) of **4** and 0.25 g (1.1 mmol) of TEBAC in 20 ml of chloroform was treated with 12.0 g of 50% aqueous sodium hydroxide solution on stirring. The stirring was continued, upon which the temperature rose to reflux. After 4 h, the mixture was filtered and the solvent of the filtrate evaporated. Purification of the crude product by column chromatography (silica gel, 3% methanol in chloroform) afforded 0.27 g (42%) of **5** as a mixture of **5A** (45%), **5B** (33%) and **5C** (22%); $(M-1)^+_{found}$ = 271.0382, $C_{12}H_{15}{}^{11}BP^{35}Cl_2$ requires 271.0323.

5A: δ_P ($CDCl_3$) 25.1 ($^1J_{PB}$ = 82.1); δ_B ($CDCl_3$) –4.7; δ_C ($CDCl_3$) 16.1 (J = 3.9, C_2–Me)), 31.5 (J = 36.3, C_5), 39.8 (J = 30.3, C_2), 71.3 ($CHCl_2$),[a] 120.6 (J = 51.1, $C_{1'}$), 126.0 (C_4), 129.5 (J = 10.5, C_3),[b] 132.7 (J = 2.3, C_3), 133.8 (J = 7.5, $C_{2'}$),[b] 135.6 (J = 4.7, C_4); δ_H ($CDCl_3$) 1.19 (dd, J_1 = 7.4, J_2 = 8.6, 3H, Me).

5B: δ_P ($CDCl_3$) 26.0 ($^1J_{PB}$ = 75.6); δ_B ($CDCl_3$) –8.5; δ_C ($CDCl_3$) 17.5 (J = 4.3, C_2–Me), 29.9 (J = 32.6, C_5), 39.1 (J = 36.1, C_2), 71.3 ($CHCl_2$),[a] 126.4 (C_4), 126.5 (J = 50.9, $C_{1'}$), 129.3 (J = 10.0, C_3),[c] 131.9 (J = 2.2, C_3), 132.0 (J = 8.3, $C_{2'}$),[c] 135.7 (J = 4.7, C_4); δ_H ($CDCl_3$) 1.56 (dd, J_1 = 7.3, J_2 = 9.2, Me).

5C: δ_P ($CDCl_3$) 23.4 ($^1J_{PB}$ = 60.6); δ_B ($CDCl_3$) 0.48; δ_C ($CDCl_3$) 15.1 (J = 3.5, C_2–Me), 30.8 (J = 35.6, C_5), 37.6 (J = 31.6, C_2), 71.3 ($CHCl_2$),[a] 123.4 (J = 52.9, $C_{1'}$), 126.2 (C_4), 129.4 (J = 10.4, C_3),[d] 132.5 (J = 2.2, C_3), 133.1 (J = 7.9, C_2),[d] 135.8 (J = 4.4, $C_{4'}$); δ_H ($CDCl_3$) 0.97 (dd, J_1 = 7.4, J_2 = 8.5, Me).

[a] broad signal; [b–d] tentative assignment

2-Methyl-1-phenyl-2,3,4,5-tetrahydro-1H-phosphole 1-oxide (6)

A mixture of 3.4 g (17.5 mmol) of **1**, 2.0 g of (10%) Pd/C in 40 ml of methanol was hydrogenated at 60–63 °C and at 10–12 bar for 13 h. The mixture was filtered and the solvent of the filtrate evaporated. The oil so obtained was purified by column chromatography (silica gel, 3% methanol in chloroform) to give 2.2 g (67%) of **6** as a mixture of **6A** (53%) and **6B** (47%) isomers; $(M+H)^+_{found}$ = 195.0902, $C_{11}H_{16}PO$ requires 195.0939.

6A: δ_P ($CDCl_3$) 59.0; δ_C ($CDCl_3$) 11.9 (J = 2.6, C_2–Me), 22.7 (J = 5.9, C_3),[a] 29.7 (J = 66.2, C_5), 33.8 (C_4),[a] 36.9 (J = 67.8, C_2), 128.6 (J = 15.6, C_3),[b] 129.8 (J = 9.5, C_2),[b] 131.7 (J = 2.0, C_4), 133.2 (J = 87.3, C_1); δ_H ($CDCl_3$) 0.85 (dd, J_1 = 3.1, J_2 = 11.5, Me).

6B: δ_P ($CDCl_3$) 64.5; δ_C ($CDCl_3$) 13.4 (C_2–Me), 23.4 (J = 6.2, C_3),[c] 27.3 (J = 66.2, C_5), 33.7 (J = 5.1, C_4),[c] 35.1 (J = 67.9, C_2), 128.4 (J = 15.6, C_3),[d] 130.7 (J = 8.8, C_2),[d] 130.5 (J = 89.4, C_1), 131.6 (J = 2.1, C_4); δ_H ($CDCl_3$) 1.22 (dd, J_1 = 7.0, J_2 = 16.5, Me).

[a-d] tentative assignment

2-Methyl-1-phenyl-2,3,4,5-tetrahydro-1H-phosphole-borane (8)

Phosphine-borane 8 was prepared from phosphine oxide **6**, as described for the **1** → 4 transformation. Yield: 93% as a mixture of **8A** (58%) and **8B** (42%) isomers; $(M-1)^+_{found}$ = 191.1123, $C_{11}H_{17}{}^{11}BP$ requires 191.1161.

8A: δ_P ($CDCl_3$) 34.6 (q, $^1J_{PB}$ = 52.5); δ_B ($CDCl_3$) –35.8; δ_C ($CDCl_3$) 14.5 (J = 5.4, C_2–Me), 25.3 (C_4), 29.3 (J = 41.4, C_5), 35.0 (J = 35.9, C_2), 36.1 (C_3), 128.5 (J = 9.5, C_3),[a] 131.2 (C_4), 132.8 (J = 8.3, C_2).[a]

8B: δ_P ($CDCl_3$) 33.4 (q, $^1J_{PB}$ = 60.1); δ_B ($CDCl_3$) –37.7; δ_C ($CDCl_3$) 14.1 (J = 9.6, C_2–Me), 26.1 (C_4), 26.9 (J = 38.4, C_5), 35.2 (J = 35.4, C_2), 36.3 (J = 6.4, C_3), 128.7 (J = 9.6, C_3),[b] 130.9 (C_4), 131.3 (J = 8.5, C_2).[b]

[a, b] tentative assignment.

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

Dichloromethylborane 9 was prepared from borane 8, as described for the 4 → **5** transformation. Yield: 54% as a mixture of **9A** (28%), **9B** (24%), **9C** (25%), **9D** (23%) isomers.

9A: δ_P ($CDCl_3$) 22.5; δ_B ($CDCl_3$) –5.4; δ_C ($CDCl_3$) 14.6 (C_2–Me),[a] 23.4 (J = 36.3, C_5),[b] 24.0 (C_4),[c] 35.1 (J = 29.6, C_2),[d] 36.0 (J = 3.3, C_3),[c] 70.9 (*C*HCl_2),[e] 120.5 (J = 47.9, C_1),[f] 128.9 (J = 9.4, C_3),[g] 131.8 (J = 2.3, C_4),[h] 133.5 (J = 7.4, C_2).[g]

9B: δ_P ($CDCl_3$) 24.5; δ_B ($CDCl_3$) –9.0; δ_C ($CDCl_3$) 15.8 (C_2–Me),[a] 23.1 (J = 34.1, C_5),[b] 23.7 (C_4),[c] 34.3 (J = 35.5, C_2),[d] 34.8 (J = 5.1, C_3),[c] 70.9 (*C*HCl_2),[e] 127.6 (J = 50.0, C_1),[f] 128.8 (J = 9.5, C_3),[g] 131.3 (J = 7.5, C_2),[g] 131.4 (J = 2.3, C_4).[h]

9C: δ_P ($CDCl_3$) 26.7; δ_B ($CDCl_3$) –9.0; δ_C ($CDCl_3$) 16.3 (C_2–Me),[a] 25.0 (J = 33.1, C_5),[b] 24.9 (C_4),[c] 36.7 (J = 4.4, C_3),[c] 41.3 (J = 31.1, C_2),[d] 70.9 (*C*HCl_2),[e] 126.9 (J = 49.1, C_1),[f] 129.0 (J = 9.2, C_3),[g] 131.0 (J = 2.1, C_4),[h] 132.0 (J = 7.3, C_2).[g]

9D: δ_P ($CDCl_3$) 22.5; δ_B ($CDCl_3$) –5.4; δ_C ($CDCl_3$) 14.0 (C_2–Me), 21.8 (J = 36.1, C_5), 24.2 (C_4),[i] 31.1 (C_3),[i] 33.1 (J = 32.6, C_2), 70.9 (*C*HCl_2),[e] 123.2 (J = 51.9, C_1), 129.0 (J = 9.2, C_3).[j] 131.5 (J = 2.3, C_4), 132.5 (J = 7.3, C_2).[j]

[a-d,f,j] tentative assignment; [e] broad signal.

Dichlorocarbene addition to 2-methyl-1-phenyl-2,5-dihydro-1H-phopshine (3)

To phosphine **3** (3.3 mmol) obtained as above and 1.0 g (8.9 mmol) of potassium *tert*-butoxide in 24 ml of n-heptane was added 8 ml of chloroform in 10 ml of n-heptane at 0 °C, under nitrogen and on intensive stirring. Stirring was continued for 3 h at room temperature. After filtration, the solvent was evaporated and the residue passed through a

short layer of silica gel using 3% methanol in chloroform as the eluant to give 0.31 g of an oil containing **10** in 26 %; Yield:7 %. δ_P ($CDCl_3$) 27.6; FAB-MS, 341 (M+H).

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