

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 phosphine function.

Introduction

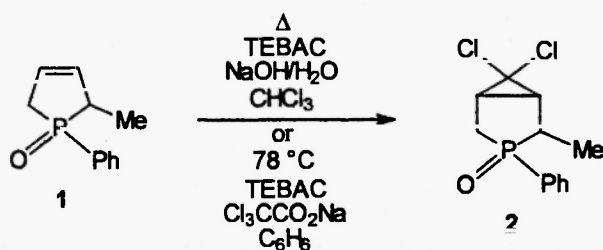
The easily available 3-methyl-2,5-dihydro-1H-phosphole 1-oxides may serve as starting materials for 6- and 7-membered P-heterocycles,¹⁻³ as well as for functionalised derivatives including phosphine-boranes.⁴ We wished to explore, how the 2-methyl-1-phenyl-2,5-dihydro-1H-phosphole 1-oxide can be utilised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

Results and discussion

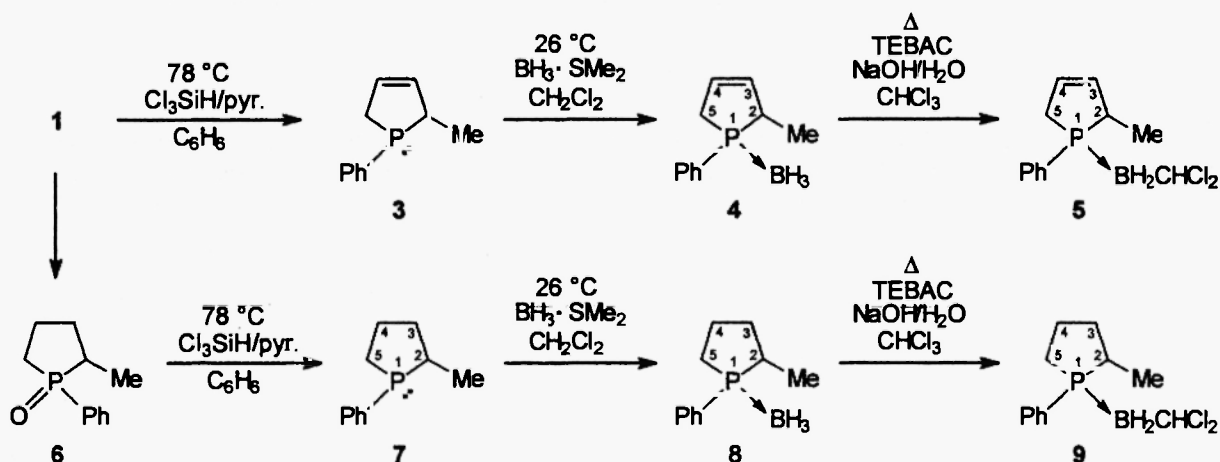
Ring enlargement of dihydro-1H-phosphole oxide **1** was attempted by the „dichlorocarbene” method.^{1,5} According to this, substrate **1** consisting of a 52–48 mixture of two diastereomers was reacted with dichlorocarbene generated from chloroform by aqueous sodium hydroxide under phase transfer catalytic 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 trichloroacetate⁶ 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-phosphole moiety is the consequence of the proximity of the electron-withdrawing P=O function. For this, phosphine oxide **1** was deoxygenated by trichlorosilane 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.

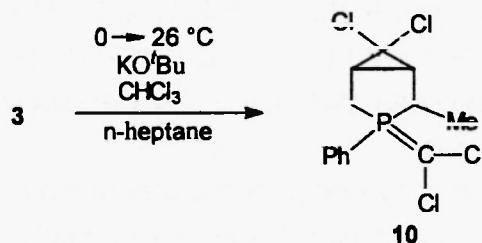
The above transformation was also applied to the tetrahydro-1H-phosphole oxide (**6**) obtained from the dihydro derivative (**1**) by catalytic hydrogenation. Hence, phosphine oxide **6** was deoxygenated, the phosphine (**7**) so obtained converted to the phosphine-borane (**8**) and finally, the borane was reacted with dichlorocarbene. Starting from 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 phosphine ligands. The decomplexation of phosphine-boranes can be realised by treatment with a secondary amine.¹¹ P-ligands including chiral species¹² are widely used in transition metal complexes.

Finally, phosphine **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 optimize the above syntheses and to extend the sphere of the reactions examined.

Experimental

The ³¹P-, ¹¹B-, ¹³C- and ¹H-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% H₃PO₄, F₃B·OEt₂ 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 prepared as described earlier.¹³ (M+H)⁺_{found} = 193.0745, C₁₁H₁₄PO requires 193.0782.

1A: δ_P (CDCl₃) 60.1 (52%); δ_C (CDCl₃) 12.7 (C₂-Me), 32.8 (*J* = 66.1, C₃), 37.4 (*J* = 69.0, C₂), 125.4 (*J* = 11.5, C₃),^a 128.2 (*J* = 11.7, C₃),^b 129.3 (*J* = 9.1, C₂),^b 131.5 (C₄), 133.2 (*J* = 90.0, C₁), 134.8 (*J* = 14.4, C₄)^a; δ_H (CDCl₃) 1.33 (dd, *J*₁ = 7.5, *J*₂ = 7.6, Me).

1B: δ_P (CDCl₃) 69.4 (48%); δ_C (CDCl₃) 12.9 (C₂-Me), 32.4 (*J* = 65.7, C₃), 38.2 (*J* = 68.1, C₂), 125.6 (*J* = 10.1, C₃),^c 128.1 (*J* = 15.9, C₃),^d 129.7 (*J* = 87.1, C₁), 130.2 (*J* = 8.7, C₂),^d 131.7 (C₄), 135.0 (*J* = 17.2, C₄)^c; δ_H (CDCl₃) 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-phosphine oxide (**1**)

The solution of 0.50 g (2.6 mmol) of **1** and 0.50 g (2.2 mmol) of TEBA 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 (CDCl₃) 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 $\text{BH}_3\cdot\text{SMe}_2$ 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; $(\text{M}-1)_{\text{found}}^+ = 189.0693$, $\text{C}_{11}\text{H}_{15}^{11}\text{BP}$ requires 189.1004.

4A: δ_{P} (CDCl_3) 34.8 (m, $^1J_{\text{PB}} = 54.2$); δ_{B} (CDCl_3) -36.7; δ_{C} (CDCl_3) 14.4 ($J = 14.5$, $\text{C}_2\text{-Me}$), 32.2 ($J = 35.7$, C_3), 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, $^1J_{\text{PB}} = 61.7$); δ_{B} (CDCl_3) -38.7; δ_{C} (CDCl_3) 16.3 ($J = 4.9$, $\text{C}_2\text{-Me}$), 33.1 ($J = 35.9$, C_3), 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 TEBAAC 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%); $(\text{M}-1)_{\text{found}}^+ = 271.0382$, $\text{C}_{12}\text{H}_{13}^{11}\text{BP}^{35}\text{Cl}_2$ requires 271.0323.

5A: δ_{P} (CDCl_3) 25.1 ($^1J_{\text{PB}} = 82.1$); δ_{B} (CDCl_3) -4.7; δ_{C} (CDCl_3) 16.1 ($J = 3.9$, $\text{C}_2\text{-Me}$), 31.5 ($J = 36.3$, C_3), 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 ($^1J_{\text{PB}} = 75.6$); δ_{B} (CDCl_3) -8.5; δ_{C} (CDCl_3) 17.5 ($J = 4.3$, $\text{C}_2\text{-Me}$), 29.9 ($J = 32.6$, C_3), 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 ($^1J_{\text{PB}} = 60.6$); δ_{B} (CDCl_3) 0.48; δ_{C} (CDCl_3) 15.1 ($J = 3.5$, $\text{C}_2\text{-Me}$), 30.8 ($J = 35.6$, C_3), 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; $(\text{M}+\text{H})_{\text{found}}^+ = 195.0902$, $\text{C}_{11}\text{H}_{16}\text{PO}$ requires 195.0939.

6A: δ_P (CDCl₃) 59.0; δ_C (CDCl₃) 11.9 ($J = 2.6$, C₂-Me), 22.7 ($J = 5.9$, C₃), ^a 29.7 ($J = 66.2$, C₅), 33.8 (C₄), ^a 36.9 ($J = 67.8$, C₂), 128.6 ($J = 15.6$, C₃), ^b 129.8 ($J = 9.5$, C₂), ^b 131.7 ($J = 2.0$, C₄), 133.2 ($J = 87.3$, C₁); δ_H (CDCl₃) 0.85 (dd, $J_1 = 3.1$, $J_2 = 11.5$, Me).

6B: δ_P (CDCl₃) 64.5; δ_C (CDCl₃) 13.4 (C₂-Me), 23.4 ($J = 6.2$, C₃), ^c 27.3 ($J = 66.2$, C₅), 33.7 ($J = 5.1$, C₄), ^c 35.1 ($J = 67.9$, C₂), 128.4 ($J = 15.6$, C₃), ^d 130.7 ($J = 8.8$, C₂), ^d 130.5 ($J = 89.4$, C₁), 131.6 ($J = 2.1$, C₄); δ_H (CDCl₃) 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, C₁₁H₁₇¹¹BP requires 191.1161.

8A: δ_P (CDCl₃) 34.6 (q, ¹J_{PB} = 52.5); δ_B (CDCl₃) -35.8; δ_C (CDCl₃) 14.5 ($J = 5.4$, C₂-Me), 25.3 (C₄), 29.3 ($J = 41.4$, C₅), 35.0 ($J = 35.9$, C₂), 36.1 (C₃), 128.5 ($J = 9.5$, C₃), ^a 131.2 (C₄), 132.8 ($J = 8.3$, C₂).^a

8B: δ_P (CDCl₃) 33.4 (q, ¹J_{PB} = 60.1); δ_B (CDCl₃) -37.7; δ_C (CDCl₃) 14.1 ($J = 9.6$, C₂-Me), 26.1 (C₄), 26.9 ($J = 38.4$, C₅), 35.2 ($J = 35.4$, C₂), 36.3 ($J = 6.4$, C₃), 128.7 ($J = 9.6$, C₃), ^b 130.9 (C₄), 131.3 ($J = 8.5$, C₂).^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 (CDCl₃) 22.5; δ_B (CDCl₃) -5.4; δ_C (CDCl₃) 14.6 (C₂-Me), ^a 23.4 ($J = 36.3$, C₅), ^b 24.0 (C₄), ^c 35.1 ($J = 29.6$, C₂), ^d 36.0 ($J = 3.3$, C₃), ^e 70.9 (CHCl₂), ^e 120.5 ($J = 47.9$, C₁), ^f 128.9 ($J = 9.4$, C₃), ^g 131.8 ($J = 2.3$, C₄), ^h 133.5 ($J = 7.4$, C₂).^g

9B: δ_P (CDCl₃) 24.5; δ_B (CDCl₃) -9.0; δ_C (CDCl₃) 15.8 (C₂-Me), ^a 23.1 ($J = 34.1$, C₅), ^b 23.7 (C₄), ^c 34.3 ($J = 35.5$, C₂), ^d 34.8 ($J = 5.1$, C₃), ^e 70.9 (CHCl₂), ^e 127.6 ($J = 50.0$, C₁), ^f 128.8 ($J = 9.5$, C₃), ^g 131.3 ($J = 7.5$, C₂), ^g 131.4 ($J = 2.3$, C₄).^h

9C: δ_P (CDCl₃) 26.7; δ_B (CDCl₃) -9.0; δ_C (CDCl₃) 16.3 (C₂-Me), ^a 25.0 ($J = 33.1$, C₅), ^b 24.9 (C₄), ^c 36.7 ($J = 4.4$, C₃), ^e 41.3 ($J = 31.1$, C₂), ^d 70.9 (CHCl₂), ^e 126.9 ($J = 49.1$, C₁), ^f 129.0 ($J = 9.2$, C₃), ^g 131.0 ($J = 2.1$, C₄), ^b 132.0 ($J = 7.3$, C₂).^g

9D: δ_P (CDCl₃) 22.5; δ_B (CDCl₃) -5.4; δ_C (CDCl₃) 14.0 (C₂-Me), 21.8 ($J = 36.1$, C₅), 24.2 (C₄), ⁱ 31.1 (C₃), ⁱ 33.1 ($J = 32.6$, C₂), 70.9 (CHCl₂), ^e 123.2 ($J = 51.9$, C₁), 129.0 ($J = 9.2$, C₃), ^j 131.5 ($J = 2.3$, C₄), 132.5 ($J = 7.3$, C₂).^j

^{a, d, f, j} tentative assignment; ^e broad signal.

Dichlorocarbene addition to 2-methyl-1-phenyl-2,5-dihydro-1H-phosphine (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 (CDCl₃) 27.6; FAB-MS, 341 (M+H).

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