Synthesis of Dihydrophosphepin 1-Oxides by Ring Enlargement†

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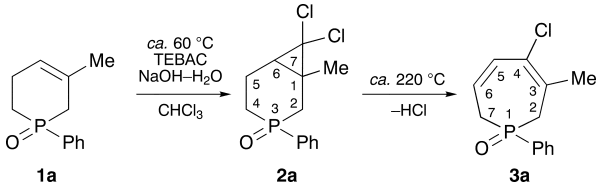
Dihydrophosphepin oxides were prepared by the ring enlargement of 1,2,3,6-tetrahydrophosphinine oxides.

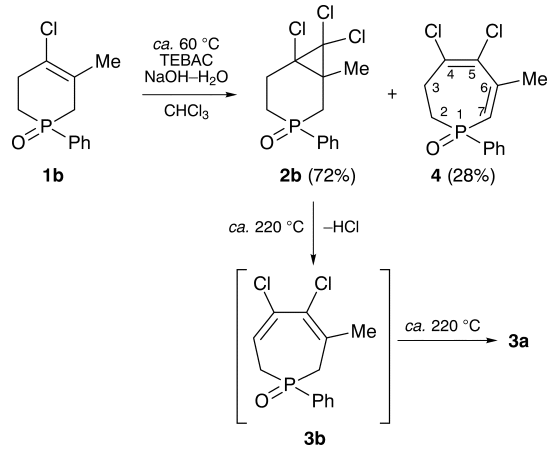
The phosphepin derivatives constitute a representative class of P-heterocycles.[1–3] P-Substituted phosphepin oxides are easily available by the dichlorocarbene ring enlargement of 1,2-dihydrophosphinine oxides.[4] In this paper, the preparation of new dihydrophosphepin oxides from 1,2,3,6-tetrahydrophosphinine oxides is described.

Tetrahydrophosphinine oxide **1a** was reacted with dichlorocarbene generated from chloroform by aqueous sodium hydroxide under phase-transfer catalytic conditions. The work-up procedure, including column chromatography, afforded the expected dichlorocarbene adduct (**2a**) in 71% yield, whose structure was supported by ^{13}P and ^{13}C NMR, as well as MS and HRMS data. The spectral data available do not justify a judgement on the sterostructure of phosphabicycloheptane **2a**.



Scheme 1

Thermal examinations (TG and DTG) showed that adduct **2a** suffered cyclopropane ring opening in the temperature range 220–250 °C. The preparative scale experiment was carried out at 220 °C for 12 min. Column chromatography of the crude product so obtained furnished 2,7-dihydrophosphepin oxide **3a** in 67% yield (Scheme 1). The structure of product **3a** was suggested by the ^{13}C and ^{1}H NMR, as well as the mass spectra. The ^{13}C NMR spectrum revealed all skeletal carbon atoms including two methylene carbons adjacent to the phosphoryl group and four sp^2 carbons of which two were CH═ units. The ^{13}C NMR assignment shown in Table 1 was confirmed by a spectrum obtained by the Attached Proton Test technique. Proton signals of the C^5—H and C^6—H moieties at δ 6.21 and 6.09, respectively, are coupled by 10.3 Hz. The δ_p of 78.7 ($CDCl_3$) for **3a** is the most downfield shift ever recorded for the different derivatives of phosphepine oxides. The δ_p values of partially or fully saturated phosphepin oxides fall in the range δ 26.0–40.7.[2,5]‡ The δ_p of 76.1 obtained in C_6D_6 for **3a** eliminates the possibility of a solvent effect. The exact reason for the anomalous δ_p of **3a** must wait for an explanation.§



Scheme 2

The addition of dichlorocarbene to the double bond of tetrahydrophosphinine oxide **1b** led to the formation of phosphabicyclo[4.1.0]heptane **2b**; partial opening of the cyclopropane ring to a 4,5-dichloromethyl-1-phenyldihydrophosphepin oxide (m/z = 286) also occurred under the conditions of the cyclopropanation as was indicated by the ^{31}P NMR and GC-MS spectra of the mixture. The ^{13}C NMR spectrum of a fraction with *ca.* 85% purity suggested the 2,3-dihydrophosphepin (**4**) structure (Scheme 2). Beside the ^{13}C NMR data (Table 1), product **4** was also characterized by ^{1}H and ^{31}P NMR, as well as mass spectra. This time, the δ_p for the dihydrophosphepine oxide (**4**) is 21.3. In contrast to the mass spectrum of **2a**, that of **2b** did not contain the corresponding molecular ion. We could, however, confirm the molecular weight by the CI-MS technique ($M + H$ = 323). Moreover, the correct elemental composition was supported by CI-HRMS.

In the last experiment a fraction of adduct **2b** with a purity of *ca.* 80% was subjected to thermolysis at 220 °C. Flash chromatography of the crude product resulted in a fraction that contained a species with δ_p 78.6 as the main component.¶ The ^{13}C and ^{1}H NMR data, along with the

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‡The δ_p shift of 78.7 could be in accord with the structure of 7-chloro-1-methyl-3-phenyl-3-phosphabicyclo[3.2.0]hept-6-ene 3-oxide that is isomeric with dihydrophosphepin oxide **3a**; this possibility should, however, be ruled out on the basis of the ^{13}C and ^{1}H NMR data (see Table 1 and Experimental section).

§Deoxygenation of phosphine oxide **3a** by trichlorosilane at room temperature afforded the corresponding phosphine with a downfield δ_p of 45.8 (C_6D_6). Oxidation by a slight excess of 30% hydrogen peroxide at 0 °C regenerated **3a** [δ_p 78.6 ($CDCl_3$)].
¶According to ^{31}P NMR spectroscopy, the thermolysis of adduct **2b** gave the product with δ_p 78.6 quantitatively. The impurity that was essentially dihydrophosphepin oxide **4** remained unchanged during the pyrolysis.

Table 1 ^{31}P and ^{13}C NMR data for the dihydrophosphepin oxides

Compound	δ_P	δ_C (J_{PC})										
		C(2)	C(3)	C(4)	C(5)	C(6)	C(7)	Me	C(1′)[a]	C(2′)[a]	C(3′)[a]	C(4′)[a]
3a	78.7	31.6	125.9[b]	129.4[b]	131.7[c]	126.0[c]	38.1	22.4	132.4	128.7[d]	129.8[d]	132.4
		(63.6)	(6.0)	(9.2)	(4.5)	(10.6)	(65.6)		(86.1)	(10.8)	(8.6)	(2.2)
4	21.3	28.4	29.4	121.2	134.6	153.5	122.8	25.2		128.8[d]	130.3[d]	132.1
		(69.3)	(5.7)	—	(12.1)	—	(93.9)	(11.9)		(12.1)	(10.4)	—

[a]Primed numbers represent the aromatic carbon atoms. [b]C(3) and C(4) may be reversed. [c]C(5) and C(6) may be reversed. [d]C(2′) and C(3′) may be reversed.

mass spectrum justified again the formation of 2,7-dihydrophosphepin oxide **3a** (Scheme 2). A possible explanation is that **3a** may be formed from **3b** by disproportionation at 220 °C. The formation of **3a** was accompanied by that of a polymeric by-product that is of unknown nature.

Experimental

^{31}P, ^{1}H and ^{13}C NMR spectra were obtained on a Bruker DRX-500 spectrometer (at 202.4, 500 and 125.7 MHz, respectively) with 85% phosphoric acid (external) and TMS (internal) standards in $CDCl_3$ solutions. Coupling constants are given in Hz. Mass spectra were recorded on a MS 25-RFA instrument at 70 eV.

Tetrahydrophosphinine oxides **1a** and **1b** were prepared as described earlier.[6,7]

7,7-*Dichloro*-1-*methyl*-3-*phenyl*-3-*phosphabicylo*[4.1.0]*heptane* 3-*Oxide* (**2a**).—The solution of tetrahydrophosphinine **1a** (0.38 g, 1.84 mmol) and triethylbenzylammonium chloride (TEBAC) (0.14 g, 0.615 mmol) in alcohol-free chloroform (25 ml) was treated with a solution of sodium hydroxide (7.5 g, 0.188 mol) in water (7.5 ml) and the mixture stirred at the boiling point for 5 h. After filtration, the organic phase was separated and made up to the original volume. After the addition of TEBAC (0.14 g, 0.615 mmol), the solution was treated with a second portion of 50% sodium hydroxide solution as above. The mixture was filtered and the organic phase concentrated to give 0.38 g (71%) of **2a** after column chromatography (silica gel, 3% methanol in chloroform). δ_p 31.9; δ_c 17.4 [J_{PC} 5.4, C(5)], 23.3 [J_{PC} 71.2, C(2)], 24.9 (Me), 26.3 [J_{PC} 5.9, C(1)], 29.1 [J 66.4, C(4)], 32.0 [J_{PC} 17.0, C(6)], 71.4 [J_{PC} 12.3, C(7)], 128.6 [J_{PC} 11.8, C(2)], 129.6 [J_{PC} 9.4, C(3)], 131.5 [C(4)]; *m*/*z* (rel. int.) 288 (M^+, 6), 253 ($M-Cl$, 100), 225 ($M-28$, 28), 125 [PhP(O)H, 47], 91 (22), 77 (36) (Found: M^+ 288.0195, $C_{13}H_{15}Cl_2OP$ requires M_r 288.0238 for the ^{35}Cl isotope).

4-*Chloro*-3-*methyl*-1-*phenyl*-2,7-*dihydrophosphepin* 1-*Oxide* (**3a**).—A sample of adduct **2a** (0.17 g, 0.588 mmol) was heated at 220 °C for 12 min. The crude product so obtained was purified by column chromatography (as above) to yield 0.10 g (67%) of **3a**. TLC showed no impurity. δ_P and δ_C, Table 1; δ_H 2.1 (s, 3 H, Me), 6.09 [dt-like m, 1 H, C(6)—H], 6.21 [d, $^3J_{HH}$ 10.3, 1 H, C(5)—H], 7.46–7.86 (m, 5 H, Ar); *m*/*z* (rel. int.), 252 (M^+, 88), 217 ($M-Cl$, 100), 125 [PhP(O)H, 40], 91 (39), 77 (51) (Found: M^+, 252.0419, $C_{13}H_{14}ClOP$ requires M_r 252.0471 for the ^{35}Cl isotope).

Reaction of Tetrahydrophosphinin Oxide **1b** *with Dichlorocarbene*.—Compound **1b** was reacted with dichlorocarbene as described above for **1a**. Four portions of 50% sodium hydroxide were used. The crude sample contained 72% of **2b** and 28% of **4**. Column chromatography afforded a fraction consisting of *ca.* 80% of **2b** (36%). Another fraction contained **4** in a 85% purity (15%).

2b. δ_P 30.9; CI-MS, *m*/*z* 323 ($M+H$); CI-HRMS, $M+H$ (Found: 323.0018, $C_{13}H_{15}Cl_3OP$ requires 322.9926 for the ^{35}Cl isotope).

4. δ_P and δ_C, Table 1; δ_H 2.38 (s, Me, 3 H), 5.96 [d, $^2J_{PH}$ 8.7 Hz, C(7)—H]; *m*/*z* (rel. int.) 286 (M^+, 48), 258 ($M-28$, 25), 251 ($M-35$, 100), 125 [PhP(O)H, 28], 91 (37), 77 (39) (Found: M^+ 286.0134, $C_{13}H_{13}Cl_2OP$ requires M_r 286.0081 for the ^{35}Cl isotope).

Thermolysis of Adduct **2b**.—**2b** obtained above (0.16 g, 0.40 mmol, purity *ca.* 80%) was thermolysed as described above for **2a**. Repeated column chromatography (as above) yielded 0.027 g (24%) of **3a** in a purity of 90%.

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