NOVEL BRIDGED P-HETEROCYCLES: THE FIRST 2,3,5-DIAZAPHOSPHABICYCLO[2.2.2]OCT-7-ENE 5-OXIDES

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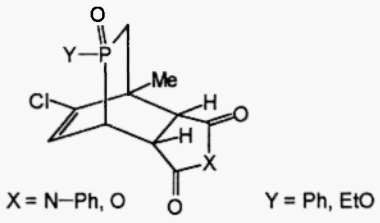
Abstract: The Diels-Alder reaction of 1,2-dihydrophosphinine oxides **3A** and **3B** with 4-phenyl-1,2,4-triazoline-3,5-dione furnished the title compounds **4A** and **4B**, members of a new P-heterocyclic family.

Introduction

The bridged P-heterocycles, such as 2-phosphabicyclo[2.2.2]oct-5-ene 2-oxides (**1**) and 2-phosphabicyclo-[2.2.2]octa-5,7-diene 2-oxides (**2**) are of importance, as precursors of low-coordinate P-fragments, methylenephosphine oxides ($YP(O)CH_2$, Y = Ph, EtO) that are useful in the phosphorylation of alcohols, phenols and amines.[1–9] The fragmentation can be achieved either by thermolysis, or by photolysis.



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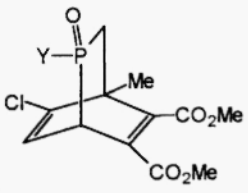

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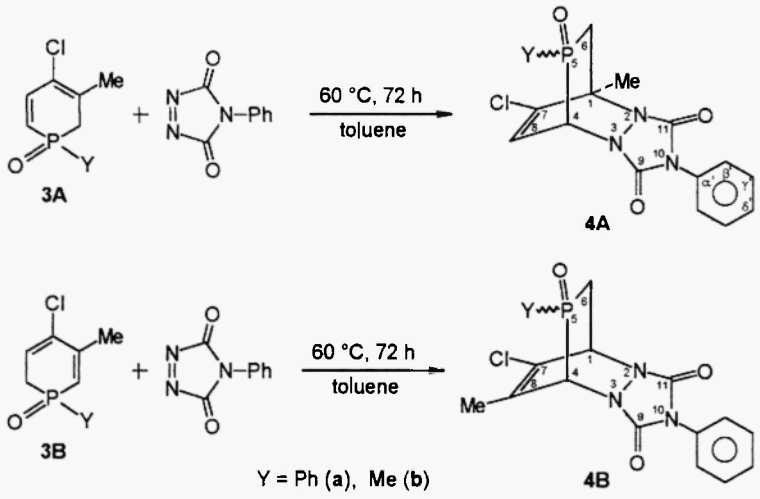
Recently, we have found that the UV light-mediated fragmentation of the phosphabicyclooctenes (**1**) may also take place according to a novel addition–elimination mechanism involving an intermediate with a pentavalent pentacoordinated phosphorus atom.[6,8,10] It was a challenge for us to find new type of phosphabicyclooctenes suitable in thermo- or photoinduced phosphorylations. On one hand, phosphabicyclooctenes with sterically demanding substituents (e.g. **1**, X=N–Ph, Y=2,4,6-trimethylphenyl) have been synthesised to enable us to study the role of steric effects in the mechanism,[11] while on the other hand, we wished to incorporate heteroatoms, such as nitrogen into the phosphabicyclooctene ring to modify

the fragmentation properties of the parent ring system. In this communication, we give an account of our results on the synthesis of diazaphosphabicyclooctene oxides.

Results and Discussion

The 75–25% mixture of the double-bond isomers (**A** and **B**) of 1-phenyl-1,2-dihydrophosphinine oxide **3a**[12] was reacted with 4-phenyl-1,2,4-triazoline-3,5-dione at 60 °C in toluene. After a 72 h's reaction time, the cycloaddition was found to be complete. The ^{31}P NMR spectrum of the crude mixture revealed that the 2,3,5-diazaphosphabicyclo[2.2.2]oct-7-ene (**4a**) had been formed as a 49–31–13–7% mixture of four isomers. The ^{13}C NMR spectrum of a refined sample obtained in a 84% yield suggested that both isomer **4Aa** and isomer **4Ba**, derived from the double-bond isomers (**A** and **B**) of the starting material (**3a**), consisted of two configurational isomers (**4Aa$_1$**–**4Aa$_2$** and **4Ba$_1$**–**4Ba$_2$**, respectively) due to the stereogenic phosphorus atom (Scheme 1).



Scheme 1

Utilising repeated column chromatography (silica gel, 3% methanol in chloroform), isomers **4Aa$_1$** and **4Aa$_2$** could be separated from the mixture in a purity of 95%. Beside ^{31}P NMR and FAB-MS data, isomers **4Aa$_1$**, **4Aa$_2$** and **4Ba$_1$** were also characterised by ^{13}C NMR spectral parameters. Based on analogies,[6] the stereospecific $^3J_{PC}$ coupling of 11.9 and 10.3 Hz detected on C_9 of the cycloadducts (**4Aa** and **4Ba**) substantiated the endo fusion of the two hetero rings. The ^1H NMR spectra confirmed the presence of the olefinic proton (C_8–H) in isomers **4Aa$_1$** and **4Aa$_2$**. The elemental composition of **4Aa** was confirmed by HR-FAB mass spectrometry.

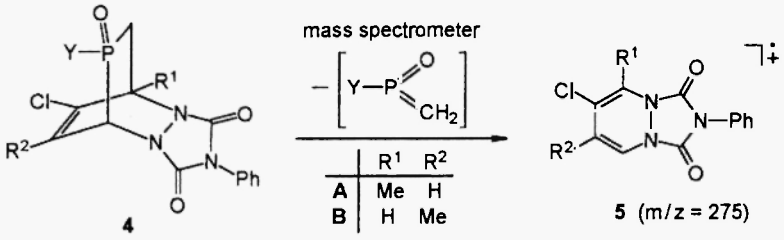
A similar reaction of isomeric 1-methyl-dihydrophosphinine oxides **3Ab**[12] and **3Bb**[12] with the triazolinedione led to diazaphosphabicyclooctenes **4Ab** and **4Bb** (Scheme 1) – this occasion – practically as

single configurational isomers. The isomers (**4Ab** and **4Bb**) were characterised by ^{31}P and ^{13}C NMR, as well as EI-MS data.

The diazaphosphabicyclooctenes (**4Aa,b** and **4Ba,b**) described are the first examples of bridged 8-membered P-heterocycles with two nitrogen atoms in the ring.

Thermal examinations, such as thermal gravimetric (TG), differential thermal gravimetric (DTG) and differential scanning calorimetry (DSC) revealed that diazaphosphabicyclooctene **4Aa** is less stable than phosphabicyclooctene **1** (X = N–Ph, Y = Ph); compound **4Aa** underwent fragmentation in the range of 228–315 °C, while species **1** lost the bridging moiety in the range of 320–450 °C.[7] Hence, the diaza derivative (**4Aa**) seems to be a promising precursor of methylenephosphine oxides under thermal conditions.

It is noteworthy that the fragment due to the loss of the bridging P-moiety ($YP(O)CH_2$) was significant (with a relative intensity of ca 21%) in the EI mass spectrum of the diazaphosphabicyclooctenes (**4**) (Scheme 2).



Conclusion

These preliminary results show that the members of a new P-heterocyclic family, 2,3,5-diazaphosphabicyclo[2.2.2]oct-7-ene 5-oxides synthesised might serve as suitable precursors of low-coordinate P-fragments, especially in thermo-induced fragmentation related phosphorylations.

Experimental part

General procedure for the preparation of 2,3,5-diazaphosphabicclo[2.2.2]oct-7-ene 5-oxides (4a and 4b)

The solution of 4.20 mmol of the ~75:25 isomeric mixture (**A** and **B**) of dihydrophosphinine oxide **3a** or **3b** and 0.77 g (4.40 mmol) of 4-phenyl-1,2,4-triazoline-3,5-dione in 40 ml of toluene was stirred at 60 °C for 72 h. The solvent was evaporated and the crude product so obtained purified by column chromatography (silica gel, 3% methanol in chloroform) to give cycloadducts **4a** and **4b** as a mixture of isomers (see below).

Cycloadduct **4a** was obtained as a 49–31–13–7% mixture of four isomers in a yield of 84%. Isomers $\mathbf{4Aa_1}$ and $\mathbf{4Aa_2}$ could be separated from the mixture as a semicrystalline product in a purity of 95%.

$\mathbf{4Aa_1}$: δ_P ($CDCl_3$) 28.40 (49%); δ_C ($CDCl_3$) 64.1 ($^2J_{PC}$=7.0, C_1), 51.9 ($^1J_{PC}$=78.1, C_4), 39.4 ($^1J_{PC}$=62.5, C_6), 138.8 ($^3J_{PC}$=7.8, C_7), 122.4 ($^2J_{PC}$=2.2, C_8), 152.7 ($^3J_{PC}$=11.9, C_9), 151.8 (C_{11}), 22.7 ($^3J_{PC}$=9.7, CH_3), 126.7 ($^1J_{PC}$=100.4, C_α), 128.9 (J_{PC}=12.5, C_β),[a] 131.7 (J_{PC}=9.4, C_γ),[a] 133.3 ($^4J_{PC}$=2.5, C_δ), 131.0 ($C_{\alpha'}$), 125.5 ($C_{\beta'}$),[b]

129.1 (C_γ),[b] 128.5 ($C_{\delta'}$), [a,b]may be reversed; δ_H ($CDCl_3$) 2.23 (s, 3H, CH_3), 6.78 (dd, $^3J_{PH}$=$^3J_{HH}$=7.1, 1H, C_8–H); FAB-MS, 414 (M+H); M^+_{found}=414.0750, $C_{20}H_{18}N_3O_3PCl$ requires 414.0774 for the ^{35}Cl isotope.

4Aa$_2$: δ_P ($CDCl_3$) 28.68 (31%); δ_C ($CDCl_3$) 64.1 ($^2J_{PC}$ 7.5, C_1), 53.6 ($^1J_{PC}$=70.4, C_4), 36.4 ($^1J_{PC}$=63.9, C_6), 140.1 ($^3J_{PC}$=7.7, C_7), 122.8 (C_8), 152.7 ($^3J_{PC}$ 10.3, C_9), 151.5 (C_{11}), 22.6 ($^3J_{PC}$=10.6, CH_3); δ_H ($CDCl_3$) 2.22 (s, 3H, CH_3), 6.40 (dd, $^3J_{PH}$=$^3J_{HH}$=8.0, 1H, C_8–H); FAB-MS, 414 (M+H).

4Ba$_1$. δ_P ($CDCl_3$) 28.46 (13%); δ_C ($CDCl_3$) 57.7 ($^2J_{PC}$=7.7, C_1), 56.6 ($^1J_{PC}$=75.6, C_4), 31.3 ($^1J_{PC}$=64.9, C_6), 130.7 (C_7), 130.7 ($^2J_{PC}$=3.2, C_8), 154.9 ($^3J_{PC}$=13.2, C_9), 154.5 (C_{11}), 18.3 ($^3J_{PC}$=1.8, CH_3); FAB-MS, 414 (M+H).

4Ba$_2$: δ_P ($CDCl_3$) 28.53 (7%); FAB-MS, 414 (M+H).

Product **4b** was obtained as a 60–40% mixture of isomers **4Ab** and **4Bb** in a yield of 68%.

4Ab: δ_P ($CDCl_3$) 38.65 (60%); δ_C ($CDCl_3$) 63.4 ($^2J_{PC}$=6.7, C_1), 51.2 ($^1J_{PC}$=76.9, C_4), 39.8 ($^1J_{PC}$=60.9, C_6), 138.1 ($^3J_{PC}$=7.7, C_7), 121.4 ($^2J_{PC}$=2.7, C_8), 152.7 ($^3J_{PC}$=11.5, C_9), 151.2 (C_{11}), 12.4 ($^1J_{PC}$=69.5, P–CH_3), 22.3 ($^3J_{PC}$=9.2, C_1–CH_3), 125.7.0 (C_α), 125.4 (C_β),[a] 128.8 (C_γ),[a] 128.3 (C_δ), [a]may be reversed; MS, m/z 316 (M^+).

4Bb: δ_P ($CDCl_3$) 38.76 (40%%); δ_C ($CDCl_3$) 56.9 ($^2J_{PC}$=7.7, C_1), 55.6 ($^1J_{PC}$=74.5, C_4), 31.4 ($^1J_{PC}$=61.1, C_6), 131.0 ($^3J_{PC}$=2.7, C_7), 130.6 (C_8), 154.5 ($^3J_{PC}$=13.0, C_9), 153.8 (C_{11}), 13.1 ($^1J_{PC}$=68.0, P–CH_3), 17.9 (C_8–CH_3); MS, m/z 316 (M^+).

Acknowledgements

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