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1-PHOSPHA-2-AZANORBORNENE AS PRECURSOR FOR 1-PHOSPHA-BICYCLO[3.2.1]OCTA-2,5-DIENE*

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ABSTRACT. 1-Phospha-2-azanorbornenes, the cycloaddition products of 2*H*-phospholes with a sulfonyl imine, can be converted to 1-phospha-bicyclo[3.2.1]octa-2,5-dienes by a reductive rearrangement. This reaction is, however, dependent on the substituent R in a-position. While a clean reaction is observed for R = H or Ph, the 2-pyridyl derivative leads to a complex product mixtures.

Keywords: *P-heterocycles, phosphanes, reduction, ring expansion, sulfonamides*

INTRODUCTION

Phospholes are versatile starting materials for the production of phosphorus heterocycles. The intermediate 2*H*-phospholes, which are accessible *in situ* by sigmatropic rearrangements from 1*H*-phospholes, represent a highly reactive and versatile class of substances with an sp^2-hybridised phosphorus atom [1]. In particular, as diene components in Diels-Alder reactions, they provide access to a range of bicyclic phosphorus heterocycles through cycloaddition reaction with a wide variety of dienophiles. In addition to Diels-Alder reactions with carbon dienophiles [2,3,4,5], selected reactions with heteroatom dienophiles such as aldehydes [6] or additional

* See also Supporting information.

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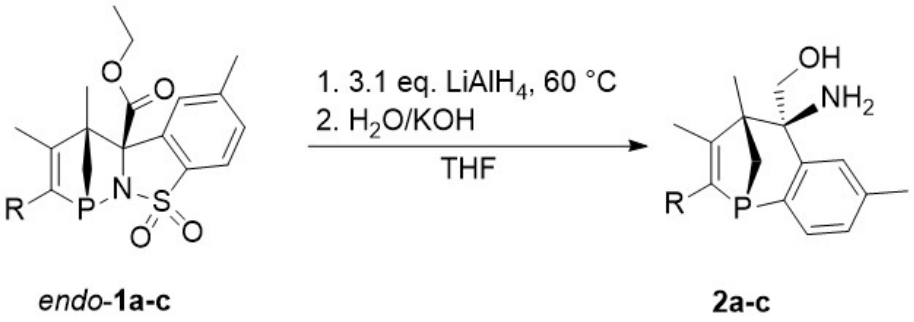
2*H*-phospholes (dimerisation of 2*H*-phospholes) [1] have also been reported. Furthermore, the stereoselective phospha-aza Diels-Alder reaction between 2*H*-phospholes or P-substituted 2*H*-phospholes and *N*-sulfonyl-α-iminoester affords diastereomeric (α-substituted) 1-phospha-2-azanorbornenes (PANs) [7]. The straightforward preparation of PANs and their reactive P–N bond allows numerous derivatisations and therefore access to P-stereogenic compounds with multiple stereocentres [8]. Thus, the P–N bond of PANs can be cleaved by achiral or chiral nucleophiles to give 2,3-dihydrophosphole derivatives as a racemic mixture [7]. Furthermore, we have already shown that reduction of the diastereomerically pure *endo*-5-phenyl-1-phospha-2-azanorbornene (R_P/S_P)-*endo*-**1a** with lithium aluminium hydride yielded a seven-membered P-heterocycle, 1-phospha-bicyclo-[3.2.1]octa-2,5-diene, under ring extension (**2a**, Scheme 1) [9]. Only a few synthetic pathways to bridged seven-membered phosphorus heterocycles have been reported until now [10,11,12,13]. We here report our attempts to extend this concept, reductive cleavage of the P–N bond and additional functional groups for the synthesis of 7-membered phosphorus heterocycles, to other (α-substituted) 1-phospha-2-azanorbornenes.

RESULTS AND DISCUSSION

We have investigated the possibility of converting other PAN derivatives into 1-phospha-bicyclo[3.2.1]octa-2,5-dienes. In an analogous reaction employed for the conversion of *endo*-**1a** to **2a** [9], the two PANs *endo*-**1b** and *endo*-**1c** were reacted with an excess of lithium aluminium hydride in THF, followed by aqueous workup (Scheme 1). The compound *endo*-**1b** could be converted to **2b** in a mostly selective reaction, but the isolated yield was only 29% due to losses during recrystallisation. Therefore, the air stable corresponding phosphane sulfide was prepared, but subsequent column chromatographic workup failed and only unspecified decomposition products could be isolated. A potential mechanism for the formation of **2a** was reported previously [9]. Apparently, the ester group has been reduced besides the expected cleavage of the P–N bond via nucleophilic attack of a hydride anion.

Crystals of compound **2b** were obtained from isopropanol at −30 °C. The molecular structure of **2b** is shown in Figure 1 (top). The bonding geometry of the P atom is distorted trigonal pyramidal. In the solid state, dimers are formed via intermolecular OH···N hydrogen donor-acceptor bonds (Figure 1 bottom and Table S6, Supporting Information). Of the nitrogen bonded hydrogen atoms, only H1N is interacting with the π system of an adjacent phenyl ring whereas for the remaining H2N no interactions are detectable at all.



endo-**1a-c** **2a-c**

Scheme 1. Reductive ring extension of the PANs *endo*-**1a-c**.
All chiral compounds presented here are racemic mixtures.
For clarity, always only one enantiomer of each compound is shown.

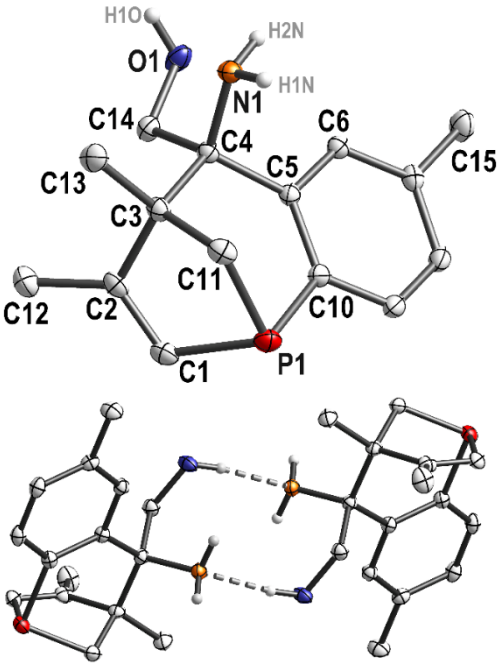


Figure 1. Molecular structure of **2b**. Ellipsoids at 50 % probability, hydrogen atoms other than NH and OH have been omitted for clarity. Selected bond lengths [pm] and angles [°]: P1–C1 182.9(1), P1–C10 182.6(1), P1–C11 183.6(2); C1–P1–C10 98.55(5), C1–P1–C11 88.15(6), C10–P1–C11 95.32(5), P1-C11-C3 105.77(8).

In the case of *endo*-**1c**, the reduction resulted in a complex mixture of P-containing substances in similar ratios. Beside an unsymmetrical diphosphane [$^{31}P\{^{1}H\}$ NMR ($CDCl_3$) δ = 8.8 (d, $^{1}J_{P\text{-}P}$ = 194.6 Hz), −40.7 (d, $^{1}J_{P\text{-}P}$ = 194.6 Hz) ppm], a primary phosphane [^{31}P NMR ($CDCl_3$) δ = −140.9 (t, $^{1}J_{P\text{-}H}$ = 194.2 Hz) ppm] and several minor secondary and tertiary phosphanes were observed. In the shift range in which the product **2c** was expected, only a very small singlet [$^{31}P\{^{1}H\}$ NMR ($CDCl_3$) δ = −46.2 (s) ppm] could be found. No products could be isolated, even after sulfurisation of the mixture followed by chromatography.

Phosphorus-containing cage compounds have also attracted much attention since earlier reports by Regitz and coworkers [14]. A tricyclic compound that is related to **2a,b** featuring a seven-membered diphospha ring has been peviously reported by Tian and Duan in a three-component reaction between different 3,4-dimethyl-1-aryl-phospholes, various ketones (R^1R^2CO) and pyrrolidine at 170 °C and 5 mol % iron(II) chloride as catalyst (Figure 2) [15].

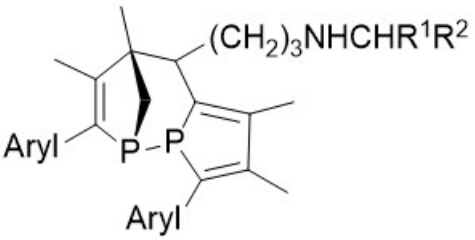


Figure 2. Related seven-membered diphospha ring obtained in a three-component reaction between different 3,4-dimethyl-1-aryl-phospholes, various ketones (R^1R^2CO) and pyrrolidine [15].

CONCLUSIONS

We have shown that the reductive rearrangement of *endo*-6-phenyl-PAN reported by us previously [9] can be partially extended to other *endo*-PAN derivatives. While **2c** was not accessible, **2b** could be obtained and structurally characterised.

The 7-membered phosphorus heterocycle has gained attention for its potential applications, e.g. in optoelectronics [16] or in chiral ligands [17]. Thus, synthetic approaches to these types of compounds are very valuable.

EXPERIMENTAL SECTION

General: All reactions were carried out with standard Schlenk techniques in an atmosphere of dry high purity nitrogen. THF was degassed and distilled from potassium. Hexanes (mixture of isomers) were dried and degassed with the solvent purification system SPS-800 series from MBRAUN. Isopropanol was degassed and used without further drying. The NMR spectra were recorded with a Bruker Avance DRX 400 spectrometer (^{1}H NMR 400.13 MHz, ^{13}C NMR 100.63 MHz, ^{31}P NMR 161.98 MHz) or a Bruker Ascend 400 spectrometer (^{1}H NMR 400.16 MHz, ^{13}C NMR 100.63 MHz, ^{31}P NMR 161.99 MHz). For ^{1}H NMR and ^{13}C NMR spectra, $SiMe_4$ (TMS) was used as internal standard. The ^{31}P NMR spectra were referenced to TMS using the Ξ scale [18]. Assignment of the configurations and chemical shifts was done using HSQC, HMQC, HMBC, and COSY techniques. The high-resolution mass spectrum (HRMS; ESI) was measured with a Bruker Daltonics APEX II FT-ICR spectrometer. The IR spectrum was recorded on a Thermo Scientific Nicolet iS5 with a diamond ATR (400–4000 cm^{-1}). The melting point was determined in a glass capillary sealed under vacuum using a Gallenkamp apparatus and is uncorrected. $LiAlH_4$ was commercially available; *endo*-**1b** and *endo*-**1c** were prepared according to literature procedures [7].

1-Phosphabicyclo[3.2.1]octa-2,5-diene (**2b**): A solution of 2.169 g (5.94 mmol, 1.0 eq.) *endo*-**1b** in 60 mL THF was added to 0.697 g (18.37 mmol, 3.1 eq.) lithium aluminum hydride at 0 °C. After 5 min, the cooling bath was removed, and the suspension was stirred at 60 °C for 21 h. Subsequently, excess hydride species were quenched at 0 °C by adding 1.5 mL of degassed 10% (w/w) aqueous potassium hydroxide solution, resulting in hydrogen evolution. The slurry was heated to 60 °C for 15 min to agglomerate the precipitate. The precipitate was removed using a Schlenk frit and washed four times with 5 mL THF each. The filtrate was concentrated under reduced pressure. The yellowish residue was washed with 20 mL of hexanes and dissolved in 30 mL of boiling isopropanol. The solution was stored at −30 °C overnight and the formed crystals were separated from the mother liquor using a filter cannula and washed with 10 mL of hexanes. Solvent traces were removed under reduced pressure at 60 °C. **2b** was obtained as white crystals (0.447 g, 1.71 mmol, 29%). Mp: 179 °C. ^{1}H NMR ($CDCl_3$): δ = 7.50 (s, 1H), 7.33 – 7.23 (m, 1H), 6.96 (d, $^{3}J_{H\text{-}H}$ = 7.4 Hz, 1H), 6.15 (d, $^{2}J_{H\text{-}P}$ = 47.4 Hz, 1H), 3.84 – 3.70 (m, 2H), 2.59 – 2.52 (m, 1H), 2.32 (s, 3H), 2.20 (dd, $^{2}J_{H\text{-}H}$ = 13.0 Hz, $^{2}J_{H\text{-}P}$ = 6.6 Hz, 1H), 1.94 (dd, $^{2}J_{H\text{-}H}$ = 13.0 Hz, $^{2}J_{H\text{-}P}$ = 9.1 Hz, 1H), 1.91 (s, 3H), 1.64 (s, 2H), 1.42 (s, 3H) ppm. ^{13}C{^{1}H} NMR ($CDCl_3$) δ = 159.0 (d, $^{2}J_{C\text{-}P}$ = 4.1 Hz), 145.7 (d, $^{2}J_{C\text{-}P}$ = 3.8 Hz), 140.0 (s), 133.8 (d, $^{2}J_{C\text{-}P}$ = 42.6 Hz), 133.4 (d, $^{1}J_{C\text{-}P}$ = 12.2 Hz), 131.3 (d, $^{1}J_{C\text{-}P}$ = 13.9 Hz), 130.2 (s), 127.1 (d, $^{3}J_{C\text{-}P}$ =

13.5 Hz), 68.3 (s), 57.2 (s), 55.0 (d, $^{2}J_{C\text{-}P}$ = 4.0 Hz), 41.8 (s), 22.8 (d, $^{3}J_{C\text{-}P}$ = 3.5 Hz), 21.6 (s), 18.6 (d, $^{3}J_{C\text{-}P}$ = 3.4 Hz) ppm. $^{31}P\{^{1}H\}$ NMR ($CDCl_3$) δ = −46.2 (s) ppm. ^{31}P NMR ($CDCl_3$) δ = −45.8 to −46.5 (virtual quartet) ppm. HRMS (ESI, THF, pos. mode): m/z calcd. for $C_{15}H_{20}NOP+H^+$: 262.136 $[M+H]^+$; found: 262.138. FT-IR: $\tilde{\nu}$ = 3356 (m), 3294 (m), 3178 (m), 3046 (w), 2957 (w), 2945 (w), 2924 (w), 2870 (w), 1596 (m), 1561 (w), 1469 (m), 1437 (w), 1372 (m), 1262 (m), 1225 (w), 1172 (w), 1154 (w), 1064 (s), 959 (m), 940 (s), 917 (w), 903 (w), 871 (w), 814 (s), 754 (w), 722 (w), 634 (w), 620 (w), 536 (w), 513 (w), 504 (w), 474 (w) cm^{-1}.

X-ray crystallography data

The data for **2b** were collected on a Gemini diffractometer (Rigaku Oxford Diffraction) using Mo-Kα radiation (λ = 71.073 pm) and ω-scan rotation. Data reduction was performed with CrysAlis Pro [19], including the program SCALE3 ABSPACK for empirical absorption correction. The structure was solved by dual-space methods with SHELXT-2018 [20] and the refinement was performed with SHELXL-2018 [21]. All non-hydrogen atoms were refined with anisotropic displacement parameters. Detailed structure parameters are given in Tables S1 to S6, Supporting Information. CCDC 2490394 contains the supplementary crystallographic data for this paper. The data is accessible free of charge from the Cambridge Crystallographic Data Centre via: https://www.ccdc.cam.ac.uk/structures/

$C_{15}H_{20}NOP$, M = 261.29 g/mol, T = 130(2) K, Triclinic crystal system, space group $P\bar{1}$, a = 812.02(4) pm, b = 995.95(4) pm, c = 1002.79(4) pm, a = 103.699(4)°, b = 111.168(4)°, g = 108.539(4)°, V = 0.65787(6) nm^3, Z = 2, r calcd = 1.319 g/cm^3, m= 0.197 mm^{-1}, crystal size = 0.36 x 0.26 x 0.18 mm^3, q range for data collection = 2.351 to 32.390°, reflections collected = 13522, independent reflections = 4381 [R(int) = 0.0305], completeness to q: 30.510° = 100.0 %, 243 parameters, 0 restraints, R indices (all data): R1 = 0.0525, wR2 = 0.1044, Final R indices [I>2s (I)]: R1 = 0.0413, wR2 = 0.0977. All H atoms were located on difference Fourier maps calculated at the final stage of the structure refinement.

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