First insights into the synthesis of carbo-phospholane and carbo-phospholene oxides

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Fifteen-membered ring carbo-mers of five-membered rings are considered in the heterocyclic series of the phosphole oxide and less unsaturated parents. The synthesis of the first carbo-phospholane oxides is achieved by a [14+1] two-step/one-pot macrocyclization route with 86 % yield. Reduction of the latter phosphora-[5]pericyclyne with SnCl2 allowed consistent 1H and 31P NMR characterization of the corresponding carbo-phospholene, produced with 11 % yield. The ultimate carbo-phosphole oxide could not be isolated, but preliminary results on alternative strategies towards this 14 ππ-electron Hückel carbo-aromatic are reported.

Introduction

While carbo-mers [1] of six-membered carbon rings have been largely exemplified since 1995 [2], their five-membered counterparts have been much less studied. To the best of our knowledge, since the early reports by L. T. Scott et al. on the synthesis of peralkylated ring carbo-mers of cyclopentane, for which the term “[5]pericyclynes” was coined [3], only one experimental report on functional carbo-cyclopentane derivatives has been published [4]. Nevertheless, expanded [5]pericyclynes [5] and full hetero-[5]pericyclynes (pericyclynes of second generation, corresponding to the carbo2-mer series), in particular sila- and germa-representatives 1, have been described [2a,6] (Figure 1). Perphospha-[3], -[4], and -[6]pericyclynes of first and second generations were also exemplified [2a,7], but pentaphospha-[5]pericyclyne derivatives are still missing to the best of our knowledge. Mixed hetero/carbo-pericyclynes were also considered [2a,8], at both the experimental and theoretical levels in the case of the carbo-silolane 2 [9] which was envisaged as synthesis precursor of the
unknown *carbo*-silole 3a (Figure 1). Carbo-mer-heterocycles with 
X = O, NH, S and PHX, are 3b-e, of stoichiometry C_{12}H_{14}X, which are 
antiaromatic according to the Hückel rule (with a 16 π-electron count), were indeed calculated to exhibit positive Nucleus Independent Chemical Shift (NICS) values [8]. Only the **carbo**-phosphole oxide 3f presents a negative NICS value of \(-4.9 \text{ ppm}\), which is comparable to that of phosphole (NICS = \(-5.3 \text{ ppm}\)): this is consistent with the Hückel rule for a strongly semipolar P\(^{\text{+}}\)-O\(^{-}\) bond (vs P=O), giving a formal 14 π-electron count over the macrocycle. This makes 3f a relevant *carbo*-aromatic target [2h].

**Figure 1.** Full hetero-[5]pericyclines 1 and mixed hetero/carbo-[5]pericyclines 2 (top), and *carbo*-mers of cyclically π-conjugated five-membered heterocycles 3a-f (bottom).

**Results and discussion**

The phosphora-[5]pericyclinic precursor 4 was readily obtained from the previously described pentayne 7 [11] by treatment of the dimagnesium salt of the latter with one equivalent of dichlorophenylphosphine oxide (Scheme 1). The two-step/one-pot [14+1] cyclization reaction occurred with a 86 % yield, a quite high yield for such a macrocyclization process in the absence of template. The formation of the side-product 8 however required a purification by silica gel chromatography. The ethyl alkynylphosphinate 8 likely resulted from a contamination of the commercial ethylmagnesium bromide solution used with ethoxymagnesium bromide.

The *carbo*-phospholane oxide 4 was isolated as a mixture of its nine diastereoisomers, five of them being chiral. In \(^{31}\text{P}\) NMR spectroscopy, the mixture of isomers gives a massif at \(-20 \text{ ppm}\), in the characteristic range for the ≡C-P(O)(Ph)-C≡ environment. The *carbo*-phosphole oxide 5 was then targeted
by reductive acidic treatment of 4 with SnCl$_2$/HCl, which is classically used for the synthesis of carbo-benzenes from hexapody-[6]pericyclic precursors [2,12] (Scheme 2).


The procedure did not lead to the aromatic macrocycle 5, but afforded the diol 9 as a main product, resulting from the cleavage of the two silylether groups of 4. A side product was also identified as the carbo-phospholene oxide 6 resulting from a partial reduction of 4 (see below). The formation of another less polar side product was also revealed by a pink spot on silica gel TLC plates of the reaction mixture. The corresponding trace product can be tentatively assigned to the targeted carbo-phosphole oxide 5, the strongly chromophoric nature of which being indeed consistent with a π-conjugation extent including a nearly planar dibutatrieny lacetylene (DBA) moiety [12c,13]. Nevertheless, the very small amount formed prevented any characterization of the putative product 5.

The carbo-phospholene oxide 6 was also obtained in small amount, but it could be isolated as a yellow solid and partly characterized. The $^{31}$P and $^1$H NMR spectra are fully consistent with the proposed structure. With respect to 4, the simplification of the spectra of 6 is indeed in accordance with the reduction of the number of isomers. The two remaining asymmetric carbon atoms of 6 thus generate four stereoisomers (two of them containing a pseudo-asymmetric P atom) which are found to be formed in statistically equal amounts. This mixture gives rise to two $^{31}$P NMR signals (at –19.89 and –20.32 ppm) and four $^1$H NMR signals for the non-equivalent methoxy groups of 6 (Figure 2).
The first examples of carbo-phospholane oxides have been described, and a carbo-phospholene oxide has also been identified. The target carbo-phosphole oxide could however not be isolated by the classical reductive elimination process. An alternative isohypsic elimination process could thus be envisaged for the synthesis of carbo-phosphole oxides from the tetraoxy-carbo-phospholane containing two secondary carbinol vertices.
As summarized in Scheme 4, a [5+10] cyclization route from the triyne 16 and the diyne 17 was envisaged but failed to produce 15 [15]. The same target could however be envisaged through an alternative [8+7] strategy from the triyne 18 [2h,11,17] and the unknown C7P bisynal 19 (Scheme 4). Advances in this sense for the synthesis of carbo-phosphole oxides will be communicated in due course.

**Experimental section**

**General.** All reagents were used as commercially available from Acros Organics, Avocado, Aldrich, Lancaster, Strem. THF and diethylether were dried and distilled on sodium/benzophenone, pentane and dichloromethane on P2O5. Commercial solutions of EtMgBr were 3 M in diethylether. Commercial solutions of n-BuLi were 1.6 or 2.5 M in hexane. The HCl solutions were 2M in diethylether. Previously described procedures were used for the preparation of 7 [11, 15]. All the reactions were carried out under nitrogen or argon atmosphere, using Schlenk tubes and vacuum line techniques. Column chromatographies were carried out with SDS silicagel (60 Å C.C. 70–200 mm). Thin layer chromatography (TLC) plates were purchased from SDS (60F254, 0.25 mm) and revealed by treatment with an ethanolic solution of phosphomolybdic acid (20 %). The following analytical instruments were used. IR: 0.1 mm CaF2 cell, Perkin-Elmer GX FT-IR. ¹H and ¹³C NMR: Brucker AC 200, WM 250, DPX 300 or AMX 400. Mass spectrometry: Quadrupolar Nermag R10-10H. All IR and NMR spectra were recorded in CDCl3 solutions. IR absorption frequencies ν are in cm⁻¹. NMR chemical shifts δ are in ppm, with positive values to high frequency relative to the tetramethylsilane reference; coupling constants J are in Hz.
4,13-Dimethoxy-1,4,7,10,13-pentaphenyl-7,10-bis[(trimethylsilyloxy)-1,2^2-phosphacyclopentadeca-2,5,8,11,14-pentayn-1-one (4). EtMgBr (0.093 mL, 0.28 mmol) was added dropwise to a stirred solution of 7 (0.100 g, 0.14 mmol) in THF (5 mL) at 0 °C. The resulting mixture was stirred for 15 min at the same temperature before addition of dichlorophenylphosphine oxide (0.027 mL, 0.14 mmol). The temperature was allowed to warm up slowly, and the reaction mixture was stirred for 3 h at rt. The solution was diluted with diethylether (15 mL) and washed with a saturated aqueous NH₄Cl solution (2 x 25 mL). The combined organic layers were dried over MgSO₄ and evaporated under reduced pressure. The crude residue was purified by silica gel chromatography (heptane/acetone 8:2) to give 4 as a pale yellow oil in 86 % yield (100 mg, 0.12 mmol).

TLC: Rf (heptane/acetone 8/2) = 0.24.

MS (DCI/NH₃): m/z = 858 [M+NH₄]^+, 751 [M-OSiMe₃]^+

^1H NMR (CDCl₃): δ = -0.07 – 0.35 (m, 18 H, -OSi(CH₃)₃), 3.28 – 3.70 (m, 6 H, -OCH₃), 7.29 – 7.43 and 7.59 – 7.76 (m, 23 H, o-, m-, p-C₆H₅ and m-, p-C₆H₅-PO), 7.76 – 8.09 (m, 2 H, o-C₆H₅-PO).

^13C[^1H] NMR (CDCl₃): δ = 95.95, 1.26 and 1.47 (OSi(CH₃)₃), 53.43 – 54.15 (-OCH₃), 65.75 (=C-C(OSiMe₃)Ph-C=), 72.23 (=C-C(OMe)Ph-C=), 79.74 – 88.72 (C=C), 99.95 (d, ^1JPC = 37 Hz, =C-PO), 125.93 – 129.84 (o-, m-, p-C₆H₅ and m-C₆H₅-PO), 130.52 (d, ^2JPC = 13 Hz, o-C₆H₅-PO), 133.12 (p-C₆H₅-PO), 137.84 (d, ^1JPC = 39 Hz, ipso-C₆H₅-PO), 141.75 (ipso-C₆H₅-C-OMe), 142.12 (ipso-C₆H₅-C-OSiMe₃)

^31P[^1H] NMR (CDCl₃): δ = -20.6 – 19.8

IR (CDCl₃): ν = 3066 – 2935 (s, Csp^3-H), 2829 (m, OCH₃), 2246 and 2196 (s, C=O-P), 1955 (w, C=C), 1591, 1490 and 1450 (m, C=C Ph), 1439 (m, P-C₆H₅), 1253 (s, C-Si), 1178 (m, P=O), 1116 (s, Si-O-C), 1069 (s, C-O).

Ethyl {3,12-dimethoxy-3,6,9,12-tetraphenyl-6,9-bis{(trimethylsilyloxy)tetradeca-1,4,7,10,13-pentayn-1-yl}(phenyl)phosphinate (8). Side-product isolated by silica gel chromatography from the reaction mixture obtained during the synthesis of 4.

TLC: Rf (heptane/acetone 8/2) = 0.19.

MS (DCI/NH₃): m/z = 904 [M+NH₄]^+, 888 [M+H]^+, 797 [M-OSiMe₃]^+

^1H NMR (CDCl₃): δ = -0.09 – 0.32 (m, 18 H, -OSi(CH₃)₃), 1.35 (q, 3 H, -OCH₂CH₃), 2.76 (s, 1 H, =C-H), 3.32 – 3.59 (m, 6 H, -OCH₃), 4.12 – 4.21 (m, 2 H, -OCH₂CH₃), 7.29 – 7.45 and 7.52 – 8.09 (m, 25 H, o-, m-, p-C₆H₅ and o-, m-, p-C₆H₅-PO).

^13C[^1H] NMR (CDCl₃): δ = 1.32 (OSi(CH₃)₃), 16.31 (-OCH₂CH₃), 53.23 – 53.94 (-OCH₃), 62.35 (-OCH₂CH₃), 65.74 (=C-C(OSiMe₃)Ph-C=), 71.62 (=C-C(OMe)Ph-C=), 75.43 (=C-H), 80.54 – 89.12 (C=C), 100.94 (d, ^1JPC = 33 Hz, =C-PO), 125.92 – 129.82 (o-, m-, p-C₆H₅ and m-C₆H₅-PO), 130.54 (d, ^2JPC = 13 Hz, o-C₆H₅-PO), 133.12 (p-C₆H₅-PO), 137.84 (d, ^1JPC = 40 Hz).
Hz, ipso-C₆H₅-PO), 141.72 (ipso-C₆H₅-C-OMe), 142.14 (ipso-C₆H₅-C-OSiMe₃)).

3¹P{¹H} NMR (CDCl₃): δ = 8.7 – 8.8

IR (CDCl₃): ν = 3306 (w, ≡C-H), 3064 – 2905 (m, Csp³-H), 2826 (w, OCH₃), 2248 and 2167 (s, C≡C-P), 1952 (w, ≡C), 1600, 1490 and 1450 (m, C≡C), 1253 (vs, C-Si), 1176 (m, P=O), 1069 (s, C-O).

7,10-Dihydroxy-4,13-dimethoxy-1,4,7,10,13-pentaphenyl-1-2³-phosphacyclopentadeca-2,5,8,11,14-pentayn-1-one (9). To a solution of 4 (0.070 g, 0.08 mmol) in diethylether (3 mL) under stirring at -50 °C were added SnCl₂ (0.180 g, 0.80 mmol) and HCl (6 mL, 12 mmol). The resulting mixture was stirred 5 h between -50 °C and -10 °C before dilution with diethylether (15 mL). The solution was washed with a saturated aqueous NH₄Cl solution (2 x 10 mL) and the combined organic layers were dried over MgSO₄ and evaporated under reduced pressure. The residue was purified by silica gel chromatography (heptane/aceton 7:3) to give the diol 9 as a pale yellow oil in 75 % yield (0.042 g, 0.06 mmol).

TLC: Rf (heptane/aceton 8/2) = 0.17.


¹H NMR (CDCl₃): δ = 3.27 – 3.65 (m, 6 H, OCH₃), 7.30 – 8.09 (m, 25 H, o-, m-, p-C₆H₅ and o-, m-, p-C₆H₅-PO).

¹³C{¹H} NMR (CDCl₃): δ = 53.81 – 54.45 (OCH₃), 65.33 – 65.45 (≡C-C(OH)Ph-C≡), 72.42 (=C-C(OMe)Ph-C≡), 79.85 – 83.83 (C≡C), 100.11 (d, 1/²p-C = 33 Hz, ≡C-PO), 125.89 – 129.83 (o-, m-, p-C₆H₅ and m-C₆H₅-PO), 130.52 (d, 1/²p-C = 13 Hz, o-C₆H₅-PO), 133.54 (p-C₆H₅-PO), 137.86 (d, 1/²p-C = 40 Hz, ipso-C₆H₅-PO), 140.58 (ipso-C₆H₅-C-OMe), 140.62 (ipso-C₆H₅-C-OH).

3¹P{¹H} NMR (CDCl₃): δ = -20.7 – -19.8.

4,13-Dimethoxy-1,4,7,10,13-pentaphenyl-1-2³-phosphacyclopentadeca-2,5,8,11,14-pentayn-1-one (10). Isolated by silica gel chromatography from the reaction mixture of the reductive elimination from 4, in 11 % yield (5 mg).

TLC: Rf (heptane/acetone 7/3) = 0.38.

¹H NMR (CDCl₃): δ = 3.46, 3.50, 3.69 and 3.72 (4s, 6 H, -OCH₃), 7.36 – 8.12 (m, 25 H, o-, m-, p-C₆H₅ and o-, m-, p-C₆H₅-PO).

3¹P{¹H} NMR (CDCl₃): δ = -20.3, -19.9 (2s).

{η²(7,10-dihydroxy-4,13-dimethoxy-1,4,7,10,13-pentaphenyl-1-2³-phosphacyclopentadeca-2,5,8,11,14-pentayn-1-one)dicobalthexacarbonyl (11). Dicobalt-octacarbonyl (0.038 g, 0.11 mmol) were added to a degassed solution of 9 (0.070 g, 0.10 mmol) in diethylether (5 mL) under stirring at 0 °C. After 1.5 h, the solvent was removed under reduced pressure and the red residue was purified by silica gel chromatography (heptane/acetone 8/2) to give 11 as a red oil in 20 % yield (0.016 g, 0.02 mmol).

TLC: Rf (heptane/acetone 8/2) = 0.29.
The residue was dehydrated over MgSO₄ and combined. The organic layers were washed with brine, and the organic layer was separated and extracted twice with Et₂O. The combined organic layers were washed with brine, dried over MgSO₄, filtered, and concentrated under reduced pressure. The residue was subjected to silica gel chromatography (heptane/EtOAc 5/5) to give 17 in 73% yield as a white solid (380 mg). TLC (heptane/EtOAc 5/5): Rf ≈ 0.21.

MS (DCI/NH₃): m/z = 192 [M+NH₄]⁺, 175 [M+H]⁺.

**Diethynylphenylphosphine oxide (17, diethynlyphosphoryl)benzene.** In a Schlenk tube at -50°C, a solution of ethynylmagnesium bromide (30 mL, 0.015 mol) is added dropwise to PhP(O)Cl₂ (426 µL; 0.003 mol). After stirring for 15 min at -50°C, then for 17 h at 0°C, the mixture is treated with a saturated aqueous solution of NH₄Cl. The aqueous layer is separated and extracted twice with Et₂O. The combined organic layers are washed with brine, dried over MgSO₄, filtered, and concentrated under reduced pressure. The residue was submitted to silica gel chromatography (heptane/EtOAc 5/5) to give 17 in 73% yield as a white solid (380 mg).

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**References**

explored. Ultimate efforts should however focus on the dimagnesium salt, and no reaction with the precipitation of the corresponding dilithium or PhP(O)Cl been actually been prepared in 73% yield directly from with diethynylphosp...