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Dilithiated phosphazenes: scaffolds for the synthesis of olefins through a new class of bicyclic 1,2-oxaphosphetanes†

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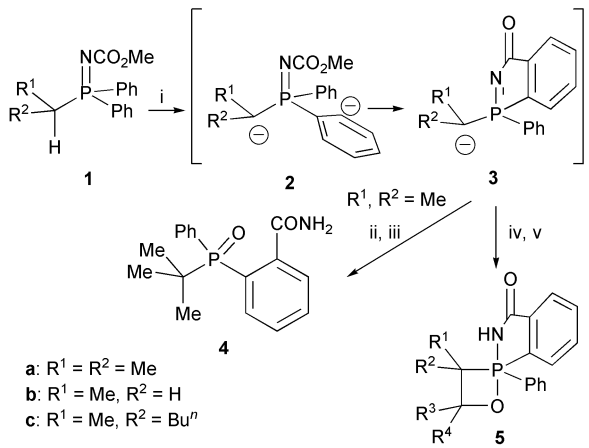
The first examples of the PN-directed dilithiation of (*N*-methoxycarbonyl)phosphazenes in the C_α and C_{ortho} to the phosphorus, and the use of these dianions in the formation of tri- and tetra-substituted olefins through stereospecific thermolysis of a new type of isolable bicyclic 1,2-oxaphosphetanes are described.

The ability of the PN linkage to direct the monometallation of alkyl- and arylphosphazenes to the C_α[1] or the C_{ortho}[2] to the phosphorus has led to a wealth of applications in organic synthesis[3] and organometallic chemistry.[4] α Dilithiation of (*P*-alkyl)phosphazenes proved to be also possible.[5] Moreover, Lappert *et al.* proposed the formation of a α and *ortho* dilithiated species in the reaction of $CH_2(SiMe_3)PPh_2{=}NSiMe_3$ with $LiBu^n$.[6] These precedents suggest that dimetallation of phosphazenes **1** to give the dianionic species **2** should be feasible. Its formation, chemical characterization and application to the synthesis of olefins is described in this paper.

Evidence of the dilithiation of **1** was obtained by conventional metallation-trapping procedures. Sequential treatment of **1a** with 2.2 equiv. of $LiBu^t$ in THF at −35 °C for 30 min, addition of MeI at −95 °C, stirring for 150 min at this temperature, and then hydrolysis with 2M HCl, afforded the amide **4** quantitatively (Scheme 1). The formation of **4** is consistent with the following sequence of reactions: (i) double deprotonation of **1a** at the C_α and C_{ortho} to give the dianion **2**, (ii) cyclocondensation of the metallated phenyl ring with the methoxycarbonyl moiety of the phosphazene leading to **3**, (iii) methylation of the C_α-lithiated phosphazene **3**, and (iv) hydrolysis of the P–N linkage yielding amide **4**. This is the first example of the formation of a dianion of a non-silylated phosphazene.



Scheme 1 *Conditions*: i. $LiBu^t$ 2.2 equiv, THF, −35 °C, 30 min; ii. MeI, −95 °C, 150 min; iii. 2M HCl, 30 min; iv. R^3R^4CO, −95 °C, 150 min; v. H_2O.

When the reaction was carried out using isobutyraldehyde as electrophile 1,2-oxaphosphetanes **5a-*trans*/*cis*** (ratio 49:51) formed in excellent yield (93%).[7] They were separated by column chromatography (ethyl acetate: hexane, 1:1).† Significantly, no traces of 1,3,4-oxazaphosphinin-2-ones, the cycloadducts isolated in the reaction of monolithiated **1a** with aldehydes, were detected.[3c] The oxaphosphetane structure of **5a** was strongly supported by their ^{31}P spectra: δ_P −64.80 and −64.59 for the *cis* and *trans* isomer, respectively. Focusing on **5a-*trans***, the ^1H NMR spectrum showed two doublets for the methyl groups linked to C3 with a very large phosphorus coupling (δ_H 1.35, 28.4 Hz, δ_H 1.39, 26.3 Hz), a double doublet for the methine proton (δ_H 3.25, 10.1 Hz, 3.8 Hz) and two sets of multiplets corresponding to aromatic protons *ortho* to the phosphorus in a ratio 1:2 (δ_H 8.03, 2H°; δ_H 8.15, 1H°). In the ^{13}C NMR spectrum, the carbons bonded to the phosphorus showed large ^{31}P,^{13}C couplings (δ 63.52, ^1J(P,C) = 110.2 Hz; δ 133.3, ^1J(P,C) = 133.7 Hz; δ 137.63, ^1J(P,C) = 154.1 Hz) characteristic of an equatorial arrangement in a trigonal bipyramid.[8] The benzazaphosphole system was characterized based on the correlations observed in the HMBC spectrum between the carbonyl carbon (δ 168.62, ^2J(P,C) = 5.3 Hz) and aromatic protons as well as between the NH and the two C_{ipso} of the benzocondensed ring. The stereochemistry of the molecule was assigned from the NOESY spectrum through the correlation of the methine proton with the *ortho* protons of the *P*-phenyl ring. This is the first isolation and characterization of a 1,2-oxaphosphetane being part of a spirocyclic system containing a benzazaphosphol ring.

The X-ray crystallographic analysis of **5a** reveals a distorted TBP structure (Figure 1) with the oxygen and nitrogen atoms in the apical positions. The bond angle O1–P2–N5 deviates from linearity 13.9(1)°. The oxaphosphetane ring and the five-membered heterocycle are slightly puckered (*cf.* dihedral angles O1–P2–C3–C4 −6.1(1)°; and P2–N5–C6–C7 4.3(2)°).‡

The new oxaphosphetane forming reaction is quite general (Table 1). High yields of spirocyclic phosphoranes **5** were obtained from aliphatic and aromatic aldehydes as well as ketones.[9] All compounds were identified by applying the same spectroscopic analysis outlined for **5a-*trans***. The aliphatic substituent of the phosphazene may be mono- or di-alkylated in the carbon next to the phosphorus. The diastereoselectivity of the process seems to be a combination of steric and electronic effects. Thus, the excellent *trans*:*cis* ratio of 95:5 observed in the formation of **5d** and the higher *dr* obtained in the reaction with pivalaldehyde vs. isobutyraldehyde (entries 1–2) may be ascribed to the minimization of steric interactions. On the contrary, the high *cis* selectivity of the synthesis of **5e** and **5f**, having two phenyl rings on the same face of the oxaphosphetane ring, is assigned to the stabilization derived from π-stacking interactions. This interaction is forced by the per-substitution in the four-membered ring.

Recently, lithiated (*N*-methoxycarbonyl)phosphazenes **1** were added to the armoury of phosphorus-based reagents for the stereoselective synthesis of olefins.[10] Similar to the Wittig and Horner–Wadsworth–Emmons reactions, it was assumed that an

† Electronic supplementary information (ESI) available: experimental and spectroscopic details. See http://www.rsc.org/suppdata/cc/b2/b212708c/

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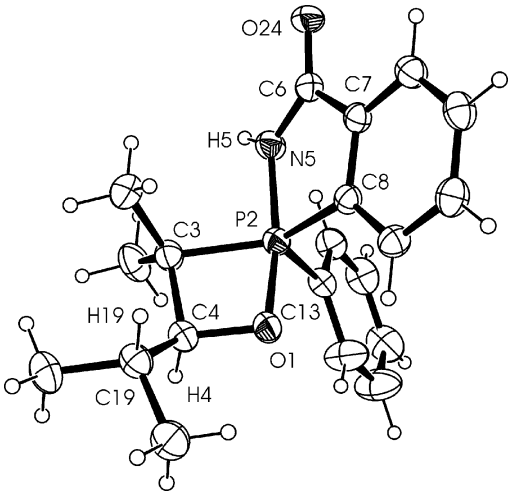


Fig. 1 Crystal structure of **5a-*trans*** (ORTEP). Selected bond lengths (Å) and bond angles (°): P2–O1 1.725(2), P2–N5 1.812(2), P2–C3 1.862(2), P2–C8 1.824(2), P2–C13 1.833(2), C3–C4 1.547(3), O1–C4 1.433(3), O1–P2–N5 166.09(9), O1–P2–C3 77.25(9), P2–C3–C4 87.6(1), O1–C4–C3 97.4(2), C3–P2–C8 132.0(1), C3–P2–C13 115.0(1), C8–P2–C13 112.8(1).

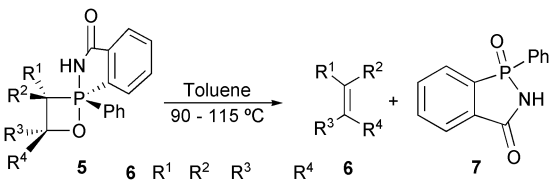
Table 1 Yields (%) and *dr* of the oxaphosphetanes **5** obtained[a]

Comp.	R^1	R^2	R^3	R^4	*Trans*:*cis*	Yield
5a	Me	Me	H	Pr^i	49:51	93
5b	Me	Me	H	Bu^t	23:73	87
5c	Me	Me	H	4-MeO-C_6H_4	40:60	93
5d	Me	H	$(CH_2CH_2CH_2CH_2CH_2)$		95:5	82
5e	Me	Bu^n	Me	Ph	76:24[b]	62
5f	Me	Me	Me	Ph	10:90	89

[a] The diastereoisomers were separated by precipitation in diethyl ether or column chromatography. [b] *Trans*/*cis* descriptors indicate the orientation of the methyl groups, in both stereoisomers the phenyl rings are *cis*.

oxaphosphetane was the required intermediate previous to the carbon–carbon double bond formation step.[11] Several isolable 1,2-oxaphosphetanes have been reported.[12] Those having a bicyclic structure showed increased stability.[13]

Heating oxaphosphetanes **5c–e** to 90–115 °C in toluene-d_8 gave quantitatively olefins **6** and benzazaphosphol **7** (Scheme 2, see electronic supplementary information†). It is worth noting the stereospecific thermolysis of **5e-*cis*** and **5e-*trans*** afforded the olefins **6c** and **6d**, respectively. ^{31}P NMR monitoring of the olefin formation showed a first order kinetic with respect to **5**.[14] The highest rate of decomposition was observed for **5d**, a fact that might be a consequence of the ring strain imposed by the tricyclic system involving the oxaphosphetane moiety. **5e-*trans*** was less resistant than **5e-*cis*** to thermolysis, which suggests that



5 **7**

6	R^1	R^2	R^3	R^4
a	Me	Me	H	4-MeO-C_6H_4
b	Me	H	$(CH_2CH_2CH_2CH_2)$	
c	Me	Bu^n	Me	Ph
d	Bu^n	Me	Me	Ph

Scheme 2 Synthesis of olefins **6** through thermolysis of **5**.

the benzazaphosphol moiety is more sterically demanding than the phenyl ring linked to the phosphorus and the larger steric interaction with the phenyl ring on C4 accelerates the opening of the oxaphosphetane **5e-*trans*** compared to its isomer **5e-*cis***. These results support the participation of oxaphosphetanes in the olefin synthesis through phosphazenes.

In summary, a new type of bicyclic oxaphosphetane system has been obtained and characterized in a tandem process involving the first *ortho* and α dimetallation of *P*-alkyl-*P*,*P*-(diphenyl)(*N*-methoxycarbonyl)phosphazenes and subsequent addition of aldehydes and ketones. When heated in toluene, they afford olefins quantitatively and stereospecifically.

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Notes and references

‡ *Crystal data for* **5a**: Data for the X-ray structure analysis of **5a-*trans***: $C_{20}H_{24}NO_2P$ (*M*r = 341.37); monoclinic, space group *C*2/*c*, *a* = 13.6367(3), *b* = 15.4090(3), *c* = 18.5552(3) Å, *β* = 108.422(1)°, *V* = 3699.2(1) Å^3, *Z* = 8, *D*x = 1.226 Mgm^{-3}, *μ*(Cu Kα) = 1.400 mm^{-1}. Data collection at 200(2) K. A total of 28833 reflections were collected, 3462 unique reflections, *R*int = 0.069. 2486 reflections were observed with I > 2σ(I). Final value of R1 ($F^2 > 2\sigma(F^2)$) = 0.0484, wR2 ($F^2 > 2\sigma(F^2)$) = 0.1199. Residual electron density 0.191/−0.388eÅ^{-3}. CCDC reference number 181221. See http://www.rsc.org/suppdata/cc/b2/b212708c/ for crystallographic files in CIF or other electronic format.

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9 The structure of all compounds was determined by performing the same NMR analysis described for **5a-*trans***.

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14 Rate constants *k*, of the decomposition reactions: **5a**, *k*(115 °C) = 1.27 × 10^{-5} s^{-1}; **5b**, *k*(90 °C) = 7.8 × 10^{-4} s^{-1}; **5c**, *k*(115 °C) = 1.8 × 10^{-5} s^{-1}; **5d**, *k*(115 °C) = 4.22 × 10^{-5} s^{-1} (see electronic supporting information†).