ORGANIC LETTERS

2002
Vol. 4, No. 8
1245−1247

Synthesis of Phosphole-2,5-dicarboxylic Acids via a [1,5]-Shift of Carbon Dioxide around the Phosphole Nucleus

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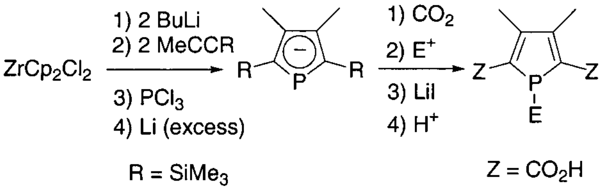
Received December 10, 2001

ABSTRACT



A new methodology for the synthesis of 1-*P*-functionalized phosphole-2,5-dicarboxylic acids is described. The carboxylic group is introduced through a two-step sequence which involves a preliminary attack of the phospholide unit onto CO_2 followed by a [1,5]-shift reaction of the CO_2Li group around the phosphole nucleus. This approach was extended to the preparation of a new type of bidentate ligands.

Phospholes are probably one of the most important classes of phosphorus heterocycles with regard to their numerous applications in organophosphorus chemistry and catalysis.[1] Over the past few years, a great deal of effort has been devoted to functionalization of the ring. In this respect, the synthesis of 2- and 2,5-dilithiophospholes[2] and the use of the 1,5-shift reaction of P-substituents around the ring constituted important advances.[3] Though several 2,5-disubstituted phospholes are now available, only a few routes toward their corresponding phospholide anions have been devised so far. Here we report a simple methodology which allows, in one step, both the functionalization of the phosphorus atom with electrophiles and the carboxylation of the two α-carbon atoms.

Two years ago, we and others reported a simple access toward 2,5-disilyl-substituted phospholide anions such as **1**.[4,5] In some respects, if we take into account the polarization of the C−Si bond, these anions can be considered as synthetic equivalents of 1-*P*-metalla-2,5-dimetalla phospholes. Thus, by exploring the reactivity of **1** toward diverse electrophiles, we found a quite unexpected result involving carbon dioxide. When a solution of **1** in THF is treated with carbon dioxide in excess, a significant downfield shift of the ^{31}P NMR signal is observed (from 142.0 to 165.0 ppm). On the basis of mass spectroscopy and NMR data, we found that the insertion of two CO_2 groups had taken place at the adjacent positions at phosphorus (C_2 and C_5), yielding the 2,5-bis(trimethylsilyloxycarbonyl) phospholide anion **5** (Scheme 1).

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[1] (a) Quin, L. D.; Quin, G., S. In *Phosphorus−Carbon Heterocyclic Chemistry: The rise of a New Domain*; Mathey, F., Ed.; Pergamon: Amsterdam, 2001; Chapter 4.2.2, p 307. (b) Dillon, K. B.; Mathey, F.; Nixon, J. F. *Phosphorus: The Carbon Copy*; Wiley: Chichester, 1998; p 203. (c) Quin, L. D. In *Comprehensive Heterocyclic Chemistry*; Katritzky, A. R., Rees, C. W., Scriven, E. F. V., Eds; Elsevier: Oxford, 1996; Vol. 2, p 757. (d) Mathey, F. In *Science of Synthesis*; Maas, G., Ed.; Thieme: Stuttgart, 2001; Chapter 14, p 553.

[2] (a) Deschamps, E.; Mathey, F. *Bull. Soc. Chim. Fr.* **1992**, *129*, 486. (b) Deschamps, E.; Ricard, L.; Mathey, F. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 1158. (c) Deschamps, E.; Mathey, F. *C. R. Acad. Sci., Paris, Ser. IIc* **1998**, 715.

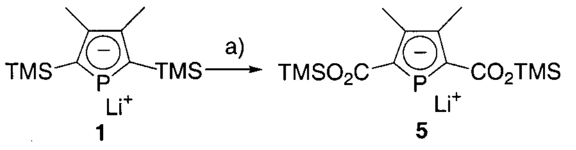
[3] (a) Holand, S.; Jeanjean, M.; Mathey, F. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 98. (b) Deschamps, B.; Mathey, F. *Bull. Soc. Chim. Fr.* **1996**, *133*, 541. (c) Holand, S.; Maigrot, N.; Charrier, C.; Mathey, F. *Organometallics* **1998**, *17*, 2996. (d) Toullec, P.; Mathey, F. *Synlett* **2001**, 1977.

[4] (a) Sava, X.; Maigrot, N.; Mézailles, N.; Ricard, L.; Mathey, F.; Le Floch, P. *Organometallics* **1999**, *18*, 4205. (b) Westerhausen, M.; Digeser, M. H.; Gücjel, C.; Nöth, H.; Knizek, J.; Ponkwar, W. *Organometallics* **1999**, *18*, 2491.

[5] Anion **1** was synthesized using a two-step sequence which involves a preliminary oxidative coupling of 1-trimethylsilylpropyne using zirconocene. For a general reference, see: Fagan, P. J.; Nugent, W. A. *J. Am. Chem. Soc.* **1988**, *110*, 7239.

10.1021/ol0102895 CCC: $22.00

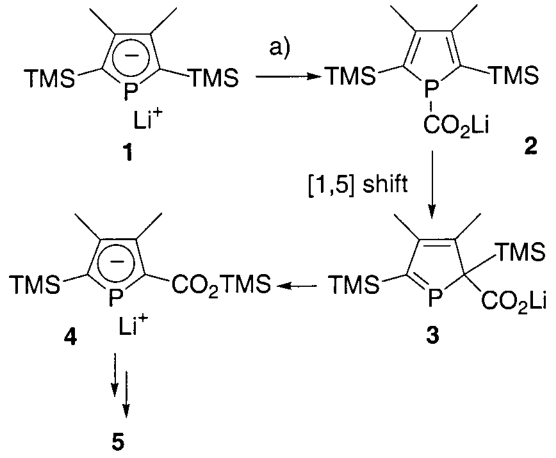
Scheme 1. Reaction of Anion **1** with Carbon Dioxide[a]



[a] Reagents and conditions: (a) CO_2 (excess), THF, rt (2 min).

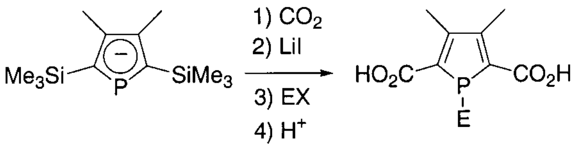
Apparently, these insertions take place successively. Thus, in the presence of a stoichiometric equivalent of carbon dioxide (1 equiv), the 2-(trimethylsilyloxycarbonyl)-5-trimethylsilyl phospholide anion **4** is formed. Though no intermediates could be detected in ^{31}P NMR during these experiments, a mechanism can be tentatively proposed. This transformation is very likely promoted by a preliminary attack of the nucleophilic phosphorus atom onto CO_2 to yield the 1-*P*-carboxylate-phosphole **2**.[6] In a second step, the carboxylate group undergoes a [1,5]-sigmatropic shift around the ring to yield the transient 2*H*-phosphole **3**. Though [1,5]-shift reactions of phosphorus substituents often require drastic conditions, it has already been shown that a carboxylate group can migrate around 25 °C. Finally, the last step of the mechanism involves a [1,3]-shift reaction of the silyl group from the Cα carbon atom to one oxygen atom of the carboxylate to give **4** (Scheme 2). The formation of **5** follows the same scheme starting from **4** which is still sufficiently reactive to attack a second molecule of carbon dioxide.

Scheme 2. Proposed Mechanism for the Formation of Phospholides **4** and **5**[a]



[a] Reagents and conditions: (a) CO_2, (1 equiv), THF, rt (2 min).

Table 1. Synthesis of *P*-Substituted Phosphole 2,5-Dicarboxylic Acids



entry	EX	product	yield/%
1	$BrCH_2Ph$	**6**	80
2	$BrCH_2CO_2Et$	**7**	78
3	$BrCH_2CH_2CO_2Et$	**8**	81
4	$BrCH_2CH_2CN$	**9**	82
5	1/2 *o*-$C_6H_4(CH_2Br)_2$	**10**	73
6	1/2 *m*-$C_6H_4(CH_2Br)_2$	**11**	72

Having this new phospholide anion **5** at hand we then explored the nucleophilicity of the phosphorus atom toward electrophiles. Though **5** proved to be poorly reactive toward chloro derivatives, good conversion yields were obtained with bromo compounds. In all cases, nucleophilic substitutions proceeded in THF at room temperature to yield the corresponding phospholes. Since trimethylsilylcarboxylate derivatives are relatively sensitive toward hydrolysis, all these new phospholes were converted into the corresponding dicarboxylic acid upon treatment with LiI followed by acidic hydrolysis.[7] Using this procedure, phospholes **6**−**9** were thus obtained in moderate to good yields as can be seen from Table 1. To demonstrate the generality of our approach, we also explored the synthesis of bidentate ligands. Reaction of **5** with *o*-α,α′-dibromo- and *m*-α,α′-dibromoxylene followed by acidic treatment yielded compounds **10** and **11** in good yields. A definitive evidence ascertaining the formulation of **10** was given by an X-ray crystallographic study (Figure 1).

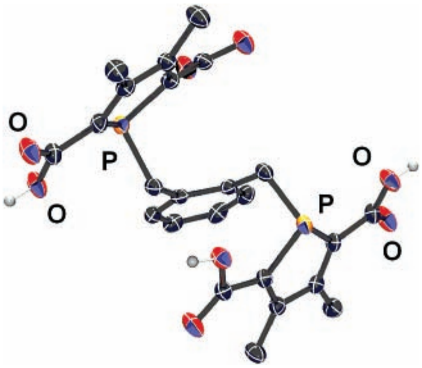


Figure 1. ORTEP drawing of **10** (50% probability thermal ellipsoids; CCDC 178852).

In conclusion, we have developed a novel and extremely simple "one-pot" procedure toward a 2,5-di(carboxylate) phospholide anion and its corresponding 1-*P*-functionalized dicarboxylic acid derivatives. Extension of this chemistry as well as the study of the coordinative properties of bidentate

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(6) Though phospholide anions are strongly delocalized, a significant amount of the negative charge resides at the P atom and electrophilic attacks always take place at this site. No example of attack at the α-carbon atoms has previously been reported in the literature.

ligands **10** and **11** is currently under investigation in our laboratories.

Acknowledgment. The authors thank the CNRS and the Ecole Polytechnique for financial support of this work.

Supporting Information Available: Experimental procedures and analytical data for all new compounds and X-ray data for compound **10**. This material is available free of charge via the Internet at http://pubs.acs.org.

OL0102895

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(7) **Typical experimental procedure:** Carbon dioxide was bubbled into a solution of 2,5-bis(trimethylsilyl) lithium phospholide **1** (6.0 mmol) in THF (50 mL) at room temperature for 2 min. After checking the formation of anion **5** by ^{31}P NMR, the electrophile (6.0 or 3.0 mmol for the synthesis of **10** and **11**) was added. After 30 min of stirring, the reaction was completed and LiI (100 mmol) was added. After 12 h of stirring at room temperature, the solvent was evaporated and methanol (40 mL) and then TMSCl (18.0 mmol) were added. The resulting solution was stirred for 5 min, and Celite (2 g) was added. After evaporation of the solvent, the coated silica gel was dropped onto the top of a silica gel packed column for chromatography and the phosphole was eluted with methanol as eluent.