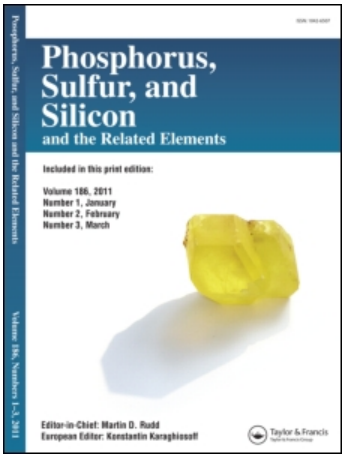

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Polyfunctional Phosphonic Acids, Phosphinoxides and Phosphines

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Polyfunctional Phosphonic Acids, Phosphinoxides and Phosphines

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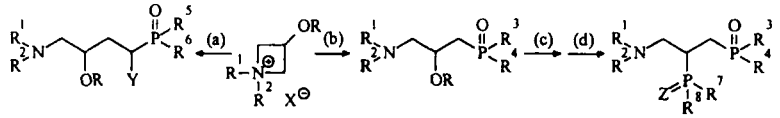
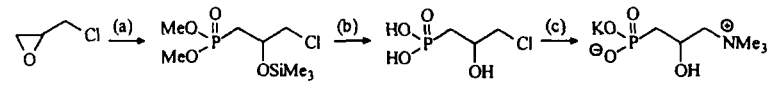
As part of our studies on the synthesis of mono- and bis-phosphonic acids, phosphine oxides and phosphines containing amino and hydroxy groups attached to tricarbon or tetracarbon chains [1], we now report our efforts to find a rational synthesis of compounds **2**, **3** and **4**:



2 **1** **3** **4**

Reagents: (a): $R^3R^6PCH_2Y$, BuLi; (b): $R^3R^4P(O)H$, NaH; (c): 1. Pd/C, H_2, 2.TsCl, Py; (d): 1. Bu^tOK, Bu^tOH, 2. $R^7R^8P(Z)H$, NaH.

The method utilizing azetidinium salts **1** as the key starting material (see above) has some limitations, due to the methylating properties of N,N-dimethyl 3-hydroxy azetidinium halogenides. For this reason we took an alternative approach to the synthesis of phosphocarnitine, taking advantage of the fact that compound **6** can be obtained according to Azuhata and Okamoto [2]:



5 **6** **7** **8**

Reagents: (a): $(MeO)_2POSiMe_3$, $ZnCl_2$; (b): 1. Me_3SiBr, 2. MeOH, H_2O; (c): 1. MeOH aq., 2. K_2CO_3.

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[1] J. Heliński, Z. Skrzypczyński and J. Michalski, *Tetrahedron Letters*, **36**, 9201 (1995).
[2] T. Azuhata and Y. Okamoto, *Synthesis*, 916 (1983).