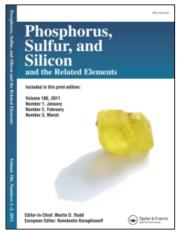
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Polyfunctional Phosphonic Acids, Phosphinoxides and Phosphines

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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:

Reagents: (a): R³R⁶PCH₂Y, BuLi; (b): R³R⁶P(O)H, NaH; (c): 1. Pd/C, H₂, 2.TsCl, Py; (d): 1. Bu¹OK, Bu¹OH, 2. R⁷R⁸P(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]:

$$Cl \xrightarrow{(a)} MeO \xrightarrow{p} OSiMe_3 Cl \xrightarrow{(b)} HO \xrightarrow{p} OH Cl \xrightarrow{(c)} KO \xrightarrow{q} OH NMe_3$$

$$6 7 8$$

Reagents: (a): (MeO)₂POSiMe₃, ZnCl₂; (b): 1. Me₃SiBr, 2. MeOH, H₂O; (c): 1. MeOH aq., 2. K₂CO₃

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