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A novel synthesis of cyclic α-hydrazinophosphonic acid

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Abstract

The first synthesis of 6-membered cyclic α-hydrazinophosphonic acid has been achieved using hetero Diels–Alder adducts.

Keywords: α-hydrazinophosphonic acid; hetero Diels–Alder reaction; phosphonylation.

α-Hydrazinophosphonic acids (type **1** in Fig. 1) and their derivatives are of potential biological importance,[1] several of these compounds show a good safening effect against the phytotoxic action of chloroacetanilide herbicides. A few examples of synthesis of α-hydrazinophosphonic acids have been reported.[2] These methods, however, cannot be directly applicable for the preparation of cyclic α-hydrazinophosphonic acids (type **2**) which have not been synthesized yet.

Herein, we wish to report a novel and convenient method for the synthesis of 6-membered cyclic α-hydrazinophosphonic acid (**8**) via nucleophilic substitution of hetero Diels–Alder (DA) adducts (**5**) by trimethyl phosphite in the presence of Lewis acid, as shown in Scheme 1.

The hetero DA reaction of 1-methoxy-1,3-butadiene (**3**) with dialkyl azodicarboxylates (**4a–c**) was carried out in CH_2Cl_2 at room temperature to give 3-methoxy-1,2,3,6-tetrahydropyridazine derivatives (**5a–c**) in nearly quantitative yields. Conversion of the methoxyl group of the DA adducts into dimethylphosphono group was conducted smoothly by treatment of **5a–c** with trimethyl phosphite in the presence of trimethylsilyl triflate (TMSOTf) or $BF_3 \cdot OEt_2$ (case of **5a**) in CH_2Cl_2 at room temperature to afford the corresponding methyl phosphonates (**6a–c**) in good yields. Catalytic hydrogenation of **6a** using Pd on charcoal in methanol gave the saturated derivative (**7a**) in 89% yield. Finally, the compound **7a** was

1 **2**

Figure 1.

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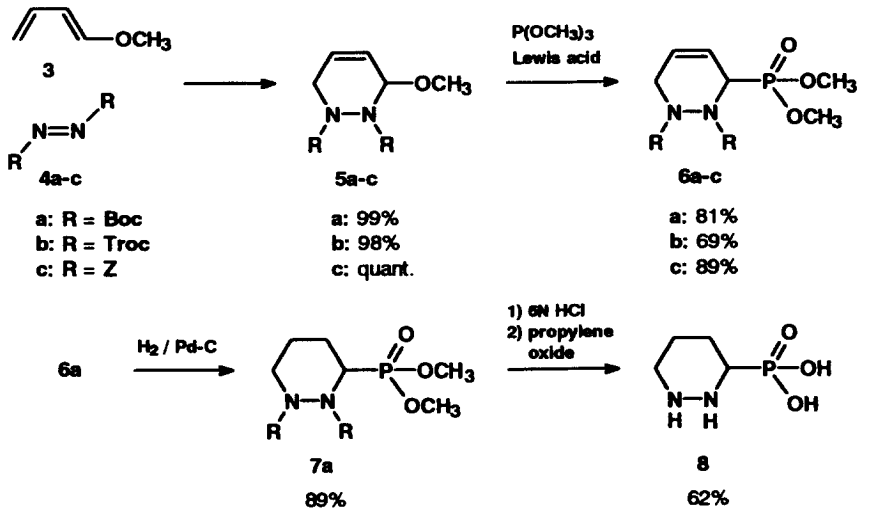

Scheme 1.

hydrolyzed in boiling 6N HCl and then desalted by the method using propylene oxide[3] in methanol to furnish the cyclic α-hydrazinophosphonic acid (**8**) in 62% yield.[4]

The present method is simple and will be applicable to the synthesis of a variety of 6-membered cyclic α-hydrazinophosphonic acids.

References

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4. Compound **8** (hexahydropyridazine-3-phosphonic acid): white powder (mp 158–160°C); ^{1}H NMR (400 MHz, D_2O): 1.56–1.85 (2H, m), 1.90–2.05 (2H, m), 3.02–3.12 (1H, m), 3.16–3.26 (1H, m), 3.30–3.40 (1H, m); HRMS (FAB): require 167.0586 (M^++1), found 167.0586 (M^++1).