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Synthesis of N-*t*-Butyl-N′-Aminocarbonyl-N-(Substituted) Benzoylhydrazine Containing α-Aminoalkylphosphonate Groups

Qing Min WANG, Run Qiu HUANG*, Zai Guo LI, Rui Lian SHAO

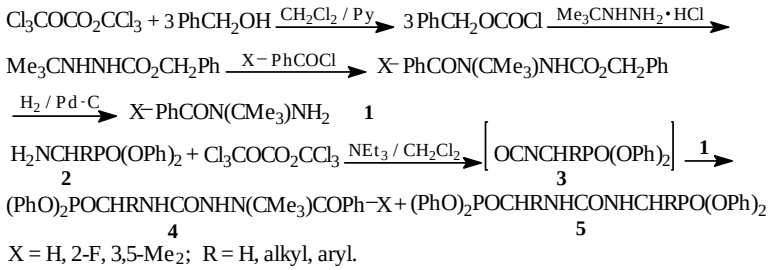
Research Institute and State Key Laboratory of Elemento-Organic Chemistry, Nankai University, Tianjin 300071

Abstract: A variety of novel N-*t*-butyl-N′-aminocarbonyl-N-(substituted)benzoylhydrazines containing α-aminoalkylphosphonate groups were synthesized by the addition of N-*t*-butyl-N-(substituted)benzoylhydrazines to α-isocyanatoalkylphosphonates, which were synthesized by the reaction of α-aminoalkylphosphonates with triphosgene in good yields. The structures of products including by-products were confirmed by ^{1}H NMR, ^{31}P NMR, IR, mass spectroscopy, and elemental analysis.

Keywords: Diacylhydrazines, α-aminoalkylphosphonates, triphosgene.

The 1,2-diacyl-1-*tert*-butylhydrazines has been found to mimic the action of 20-hydroxyecdysone. It can activate the ecdysone receptor, leading to lethal premature molting[1-4]. In addition, α-aminophosphonic acid derivatives are considerably important isosteres of aminocarboxylic acids[5,6]. Corresponding compounds also can serve in agrochemistry as antifungal agents, herbicides, plant regulators and plant virucides[7,8]. Considering the wide application of these kinds of compounds, we decided to introduce the α-aminoalkylphosphonate groups into the structures of acylhydrazines, and designed, synthesized a series of the title compounds as shown in **Scheme 1**.

Scheme 1



We found that benzyl chloroformate can be obtained in good yield when benzyl alcohol was treated with triphosgene. This method can avoid the use of toxic phosgene

gas. Benzyl chloroformate was condensed with *t*-butylhydrazine hydrochloride to give N-*t*-butyl-N′-benzyloxycarbonylhydrazine, and subsequent acylation with appropriately substituted benzoyl chloride yielded N-*t*-butyl-N′-benzyloxycarbonyl-N-substituted-benzoylhydrazine. After deprotection of amino-group using 5% Pd-C as a catalyst N-*t*-butyl-N-substitutedbenzoylhydrazine was obtained in good yield.

We found that triphosgene also can be used to convert diphenyl α-aminoalkylphosphonates **2** to diphenyl α-isocyanatoalkylphosphonates **3** under mild condition in the presence of triethylamine. The intermediate **3** shows a very strong IR band at approximately 2240cm^{-1}, indicating the presence of the cumulative double bond of N=C=O. **3** without isolating reacts with nucleophiles to give compound **4**. The triphosgene-mediated reaction for the synthesis of α-isocyanatoalkylphosphonates has following advantages: mild reaction condition, good yield, safety, and simplicity. This efficient method is expected to have wide synthetic utility for other α-isocyanatoalkylphosphonates.

In some cases, a small amount of symmetrical ureas **5** were isolated as by-products when **3** reacted with **2**. The formation of **5** can be retarded by lower reaction temperature and slower drop rate of **2**.

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9. **4a** (X=H, R=4-Cl-C_6H_4): mp 199-201°C, IR cm^{-1}: 3343.0, 1707.1, 1682.5, 1588.0, 1533.7, 1486.4, 1360.5, 1241.7, 1197.6, 1155.1, 955.8, 759.8, 721.7, 685.5, 655.2. ^{1}H-NMR (200 MHz, $CDCl_3$): δ(ppm) 1.20 (s), 1.28 (s) (9H, Bu^t), 5.50 (dq, 1H, CHPO, $^2J_{PH}$=22.9Hz, $^3J_{HH}$=10.4Hz, J=6.3Hz), 6.57-7.40 (m, 19H, Ph). Anal. Calcd. for $C_{31}H_{31}ClN_3O_5P$(%):C, 62.89; H, 5.28; N, 7.10. Found: C, 62.97; H, 5.12; N, 7.10. **5a** (R=4-Cl-C_6H_4): mp 174-175°C, ^{1}H-NMR (200 MHz, $CDCl_3$): δ(ppm) 5.78 (dd, 1H, CHPO, $^2J_{PH}$=22.9Hz, $^3J_{HH}$=10.4Hz), 6.80-7.30 (m, 28H, Ph). Anal. Calcd. for $C_{39}H_{32}Cl_2N_2O_7P_2$(%):C, 60.56; H, 4.17; N, 3.62. Found: C, 60.55; H, 3.93; N, 3.59.

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