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Study on Reactivity of Five-Coordinate Bicycloazastannoxides. IV. Michael Addition with Acrylonitrile

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ABSTRACT: *Michael addition of α-carbanions formed from the α-amino acids in five-coordinate bicycloazastannoxides* **(1–6)** *with acrylonitrile was investigated. Four novel organotin (IV) complexes* **(7–10)** *and one new five-membered α-amino acid* **(11)** *were synthesized, and their structures were characterized by IR, ^{1}H NMR spectroscopy, MS, and elemental analyses. It has been found that the Michael addition takes place by two paths, 1,2-addition (path A) and cycloaddition (path B), and the α- and γ-carbanion intermediates are involved.*© 1999 John Wiley & Sons, Inc. Heteroatom Chem 10: 319–323, 1999

INTRODUCTION

With regard to the large number of known vitamin B_6 related enzymes, one of the important features of the mechanism of these reactions is the formation of an α-carbanion in the presence of a base catalyst [1,2]. The most widely used type of these reactions consists of the conversion of a suitable derivative into a carbanion, followed by reaction with an electrophile. For five-coordinate bicycloazastannoxides, the coordination between a metal Sn atom and a Schiff base ligand increases the αCH acidity and stabilizes the incipient carbanion [4]. But their reactions with electrophiles at the α-position have received less attention [3].

In our earlier studies, we have noticed that the structures of five-coordinate bicycloazastannoxides with Schiff bases derived from amino acids are similar to those of the metal vitamin B_6 chelates, as demarcated by the X-ray method [5]. Recently, we investigated the condensation of five-coordinate bicycloazastannoxides with aldehydes [3] and the hydrolysis of the related condensation products using 10% HCl [11]. As a result, the β-hydroxy-α-amino acids are obtained, and this represents a new method for preparing β-hydroxy-α-amino acids. The mechanism for the hydrolysis of the organotin (IV) complexes was discussed, and the related yields were also determined by the HPLC method. The whole process, from the condensation of organotin (IV) complexes with aldehydes to the hydrolysis, imitates the chemical reaction in vivo that is catalyzed by pyridoxal phosphate coenzyme derivatives. In addition, the thermodynamic α-CH acidities (pKa values) of five-coordinate bicycloazastannoxides by the accurate spectrophotometeric method for relative equilibrium acidities of weak carbon acids in dimethyl sulfoxide were first determined [4]. The bulkiness of the amino acid moieties affects the α-CH acidity directly, and the effect of the bulkiness of the amino acid moieties on their α-CH acidities was also interpreted by the Taft equation. It has been found that

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the effect of α-CH acidity and stability of the α carbanions on condensation are important.

In this article, we describe the Michael addition of five-coordinate bicycloazastannoxides **(1–6)** with acrylonitrile in the presence of MeONa. The structures of products **7–11** are characterized by ^{1}H NMR, IR, elemental analysis, and MS. The results show that two kinds of products are formed: 1,2-addition and cycloaddition products. The reaction mechanisms are discussed, including, among them, the fact that α- and γ-carbanion intermediaters are involved. Two paths for reactions of organotin (IV) complexes with acrylonitrile, 1,2-addition and cycloaddition are suggested (Scheme 1).

EXPERIMENTAL

General

A series of α-amino acids (Gly, Ala, Leu, Phe, and Met) were purchased from Bejing Chemical Reagent Company. Acrylonitrile was purchased from Merck-Schuchardt Company, and this was purified by the general method before use. Sodium methoxide was prepared by dissolution of metallic Na into methyl alcohol under argon with cooling. The five-coordinate bicycloazastannoxides (1–6) with Schiff bases derived from α-amino acids (Gly, Ala, Leu, Phe, and Met) and a salicylicaldehyde were synthesized as described previously [5]. Characterization data are given in Table 1.

Melting points were determined by use of a PHMK melting-point stage and are presented without corrections. Elemental analyses were carried out on a CHN corder M73 apparatus. ^{1}H NMR spectra were recorded on a BRUKER Ac-P 200 spectrograph. The chemical shifts were reported as δ values with respect to $SiMe_4$ as an internal reference. All runs were carried out on homogeneous systems. The mass spectra were obtained on a VG-7070E-HF instrument with electron bombardment of 70 eV. The IR spectra were recorded on a Nicolet FI-IR 50X spectrometer. Thin-layer and preparative-layer plates were made by use of silica gel GF_{254}.

General Synthetic Procedure for Complexes **(7–10)** *by the Michael Addition of Five-coordinate Bicycloazastannoxides* **(2–5)**, *respectively, to Acrylonitrile*

The acrylonitrile (1.5 mmol) in absolute methanol (2 mL) was added under Ar with stirring to a solution of complex **2** (1 mmol) in 10 mL of 1.0 N CH_3ONa methanol solution at 25°C. The course of reaction was monitored with TLC using neutralized samples (SiO_2, $CHCl_3$-acetone, 5:1). Each sample was treated with 6% aqueous acetic acid, and the mixture of the complexes was extracted with $CHCl_3$ before being applied to the plate. After complex **2** had disappeared in the reaction mixture, the latter was poured into a stirred mixture of $CHCl_3$ (50 mL) and 6% aqueous acetic acid (50 mL). The chloroform layer was separated and the solvent removed in vacuo. The residue was separated on a preparative-layer plate in CH_2Cl_2-acetone (8:1). Complex **7** was obtained.

Yield of complex **7**: 54%, mp 137–139°C; ^{1}H NMR ($CDCl_3$) δ 6.8–8.0 (15H, m, Ar, -CH=N-), δ 1.6–2.5 (4H, m, $-CH_2CH_2CN$), δ 1.6 (3H, s, $-CH_3$); IR (KCl) $\nu_{(C=O)}$ 1663, $\nu_{(CN)}$ 2261, $\nu_{(C=N)}$ 1614, $\nu_{(Sn-O)}$ 530, $\nu_{(Sn-N)}$ 451. Anal. calcd for $C_{25}H_{22}O_3N_2Sn$: C, 58.03; H, 4.20; N, 5.42. Found: C, 57.71; H, 4.07; N, 5.36. MS spectrum: 517 (M^+, 4.71%).

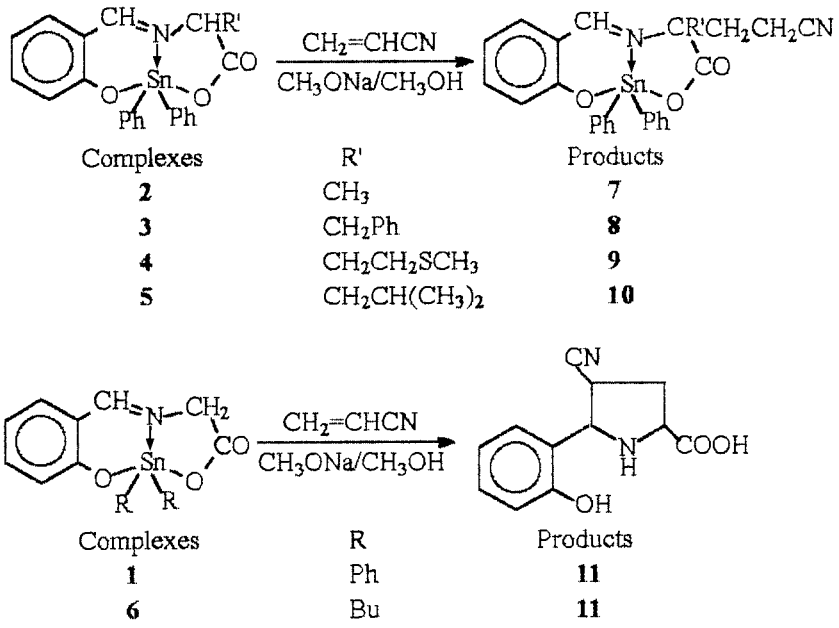
Product **8** was obtained by the Michael addition of complex **3** to acrylonitrile according to the same procedure with a yield of 57%, mp 188–189°C; ^{1}H NMR ($CDCl_3$) δ 6.8–8.0 (15H, m, Ar, -CH=N-), δ 1.8–3.0 (4H, m, $-CH_2CH_2CN$), δ 2.95–3.5 and 6.8–8.0 (7H, m, $-CH_2Ph$); IR (KCl) $\nu_{(C=O)}$ 1681, $\nu_{(CN)}$ 2262, $\nu_{(C=N)}$ 1614, $\nu_{(Sn-O)}$ 547, $\nu_{(Sn-N)}$ 449. Anal. calcd for $C_{31}H_{26}O_3N_2Sn$: C, 62.73; H, 4.38; N, 4.72. Found: C, 62.48; H, 4.12; N, 4.68.

Product **9** was obtained by the Michael addition of complex **4** to acrylonitrile according to the same procedure with a yield of 60%, mp 169–170°C; ^{1}H NMR ($CDCl_3$) δ 6.9–8.2 (15H, m, Ar, -CH=N-), δ 1.9–2.6 (4H, m, $-CH_2CH_2CN$), δ 1.6–2.6 (7H, m, $-CH_2CH_2SCH_3$); IR (KCl) $\nu_{(C=O)}$ 1668, $\nu_{(CN)}$ 2262, $\nu_{(C=N)}$ 1614, $\nu_{(Sn-O)}$ 539, $\nu_{(Sn-N)}$ 449. Anal. calcd for $C_{27}H_{26}O_3N_2SSn$: C, 56.15; H, 4.51; N, 4.85. Found: C, 55.67; H, 4.47; N, 4.56. MS spectrum: 577 (M^+, 12.36%).

Product **10** was obtained by the Michael addition of complex **5** to acrylonitrile according to the same procedure with a yield of 59%, mp 145–147°C; ^{1}H NMR ($CDCl_3$) δ 7.0–8.2 (15H, m, Ar, -CH=N-), δ 1.6–2.4 (4H, m, $-CH_2CH_2CN$), δ 0.9–1.8 [9H, m, $-CH_2CH(CH_3)_2$]; IR (KCl) $\nu_{(C=O)}$ 1670, $\nu_{(CN)}$ 2263, $\nu_{(C=N)}$ 1614, $\nu_{(Sn-O)}$ 540, $\nu_{(Sn-N)}$ 449. Anal. calcd for $C_{28}H_{29}O_3N_2Sn$: C, 60.11; H, 5.01; N, 5.01. Found: C, 59.87; H, 4.90; N, 4.72.

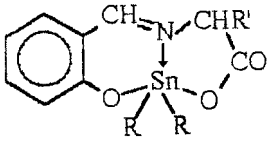
Synthetic Procedure for Complex **11** *by Michael Addition of Five-Coordinate Bicycloazastannoxides (***1** *or* **6***) to Acrylonitrile*

Product **11** was prepared by the Michael addition of complex **1** or **6**, respectively, to acrylonitrile according to the foregoing procedure. The chloroform layer was concentrated and placed on a Dowex-50 column



SCHEME 1

TABLE 1 Characterization Data for Bicycloazastannoxides **1–6**



Complexes	*R*	*R'*	*Mp* (°*C*)	*Yield* (%)	δ (*α-CH*)
1	Ph	H	191–192	65	4.35
2	Ph	Me	205	70	4.20
3	Ph	CH_2Ph	202	75	4.30
4	Ph	$CH_2CH_2SCH_3$	115–117	87	4.33
5	Ph	CH_2Pr^i	207–208	67	4.20
6	Bu	H	123.5	80	4.40

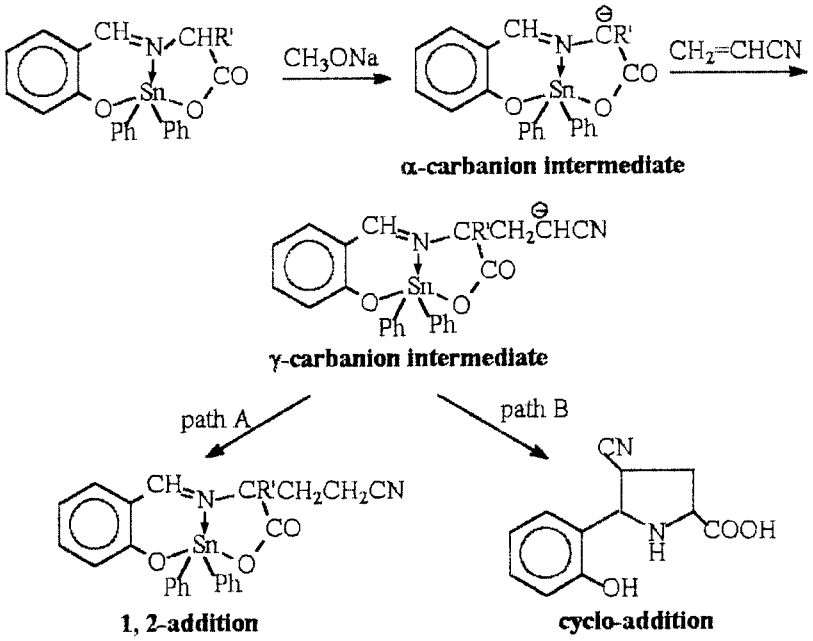
(H^+ form). The column was washed with water and then with 5% aqueous ammonia. The eluant was chromatographed on a Dowex-50 column (a weak form) again. Product **11** mixtures were obtained with a yield of 62% or 55%, mp 139–141°C; ^{1}H NMR (D_2O) δ 6.6–7.4 (4H, m, Ar), δ 4.3 (1H, d, -CH), δ 3.9 (1H, m, -CH), δ 2.4–3.3 (3H, m, -CH, and CH_2); IR (KCl) $\nu_{(C=O)}$ 1792, $\nu_{(CN)}$ 2263. Anal. calcd for $C_{12}H_{12}O_3N_2$: C, 62.07; H, 5.17; N, 12.07. Found: C, 62.39; H, 5.21; N, 12.38.

RESULTS

The IR spectra of products **7–10** are similar. The 2262 cm^{-1} absorption is assigned to be the stretching modes of the -CN group. Other absorptions ($\nu_{C=O}$, $\nu_{C=N}$, ν_{Ph-O}, ν_{Sn-O}, and ν_{Sn-N}) are similar with their reactants (**2–5**), respectively. These results show there is the similar molecular skeleton between the reactants and the products.

^{1}H NMR spectroscopy is significant in identification of the structures of products **7–10**. Comparison with the related reactants shows that αCH peaks of products **7–10** disappear completely, and there is appearance of new peaks at δ 1.6–3.0, and the ratio of their protons is 2:2 in the products. Obviously, the new peaks are assigned to the -CH_2CH_2CN group. The ^{1}H NMR and IR data indicate that 1,2-addition products are formed, and the Michael addition via path A of reactants **2–5** takes place.

It has been noticed that the structure of product **11** is different from that of other products (**7–10**). ^{1}H NMR spectra of **11** indicate that the proton resonance of the -CH=N group disappears, and there are appearances of a series of new peaks near δ 2.4–3.9, and the ratio of their protons is 1:1:2, respectively. In addition, there is still the peak of the -Ar group, but the number of protons is decreased from 15 to 4. Its IR data also show that there are no absorptions that are assigned to the Sn–O, Sn–N, and C=N bonds, but there is the absorption near 1729 cm^{-1}, which is assigned to the -COOH group. As a result, the five-membered structure of **11** is determined, and these facts indicate that the reaction of reactants **1** and **6** with acrylonitrile takes place by cyclo-addition (path B). The ratio of diastereomers was 31.5:25.7:



SCHEME 2

22.7:20.1 according to 500 MHz ^{1}H NMR data taker in D_2O.

DISCUSSION

The results show that two kinds of products are formed: 1,2-addition and cycloaddition products. Therefore, the following paths for these reactions are suggested, among them, the α, and γ-carbanion intermediates are involved (Scheme 2).

A probable mechanism for the Michael addition includes attack of the α carbanion from the α-amino acid fragments at the activated olefin double bond with the formation of a further intermediate γ carbanion (see Scheme 1). This γ-carbanion intermediater can attack at the imine carbon by intramolecular addition to the -CH=N bond, leading to cyclization (path B), or accept a proton from the solution, resulting in the usual 1,2-addition product (path A).

As we know, all attempts to carry out the addition of transition metal Schiff base glycine complexes to activated olefins have led to either cyclization products [6,7,10] (nonaqueous solutions) or to a low yield of 1,2-addition compounds [8]. In the case of acrylonitrile (aqueous solution), only the product of the addition of two molecules of acrylonitrile to one molecule of glycine was formed [9]. As might be expected, the reactions of organotin (IV) complexes with Ala, Leu, Phe, and Met **(2–5)** take place by path A in a protic solvent system, and 1,2-addition products are formed. However, the reactions of organotin (IV) complexes with glycine (**1** or **6**) follow path B, cycloaddition. Cyclization via path B for complexes **1** or **6** perhaps undergo the following process: the γ carbanion attacks at the imine carbon of the C=N bond, which is changed into a C–N single bond. Concomitantly, the coordinate N→Sn bond and O–Sn bonds break. As a result, the organotin (IV) complex is completely decomposed and cycloaddition products **11** are formed. In the foregoing process, the presence of an α proton in the γ-carbanion intermediate may be important for the cyclization to form **11**.

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