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Study on Reactivity of Pentacoordinate Bicycloazastannoxides. I. Aldol Condensation with Aldehydes

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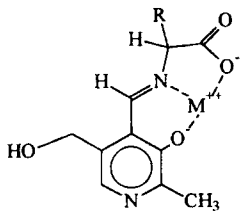
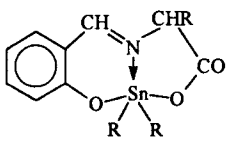
ABSTRACT

The condensation of α-carbanions formed from pentacoordinate bicycloazastannoxides with aldehydes was investigated. Nine novel organotin(IV) complexes with β-hydroxy-α-amino acids were synthesized. Their structures were determined by IR, ^1H NMR, ^{119}Sn NMR spectroscopy, MS, and elemental analyses. The reaction mechanism is discussed. © 1996 John Wiley & Sons, Inc.

Organotin complexes show a spectrum of biological effects [1]. Their chemotherapeutic properties, including antitumor activity, have been extensively investigated. Recently, our group has successfully prepared a variety of pentacoordinate organotin(IV) complexes [2–4], which are designated as pentacoordinate bicycloazastannoxides. The single-crystal structure was identified to be triclinic. We have noticed that the structures of pentacoordinate organotin(IV) complexes with Schiff bases derived from amino acids are similar to those of the metal chelates advanced by Martell [5].



Metal Chelate



Bicycloazastannoxide

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We have also observed that the chelation between organotin(IV) and a Schiff based ligand enhances the α-CH acidity of the amino acid fragment in such complexes [6]. The carbanions formed from the organotin(IV) complexes are stabilized by resonance. It is interesting and significant with regard to aldol condensations to investigate the nucleophilic properties of the carbanions of complexes [7].

In this article, we report on the condensation of α-carbanions formed from dibutyltin(IV) complexes (**1–3**) with aldehydes. The new organotin(IV) complexes (**4–11**) were synthesized. Their structures were determined by IR, ^1H NMR, ^{119}Sn NMR spectroscopy, MS, and elemental analyses (Scheme 1).

EXPERIMENTAL

General. Glycine, alanine, and phenylalanine were purchased from Beijing Chemical Reagent Company. *o*-Anisaldehyde, *p*-anisaldehyde, 2-methylbenzaldehyde, and 4-methylbenzaldehyde were purchased from Merk-Schuchardt Company. Salicylic aldehyde and benzaldehyde were purchased from Beijing Chemical Reagent Company. These compounds were purified before use. Dibutyltin dichloride was prepared (mp = 40°C) [8]. Sodium methoxide was prepared by adding metallic Na to methyl alcohol under argon, with cooling.

Melting points were determined on a PHMK melting point stage and are listed without corrections. Elemental analyses were carried out on a CHN corder M73 apparatus. ^1H NMR spectra were recorded on a JNMPMX 90 MHz NMR instrument using $Me_3SiOSiMe_3$ as an internal reference. ^{119}Sn NMR spectra were obtained on a BRUKER Ac-P 200 MHz NMR instrument using $Me_3SiOSiMe_3$ as an in-

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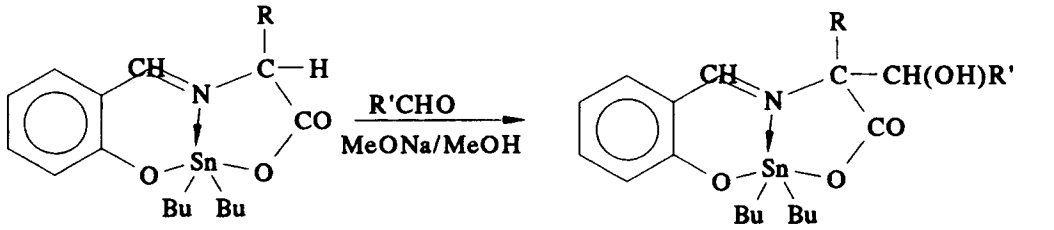


1: R=H; 4: R=CH2OH, R'=H; 5: R=CH_3, R'=H;

2: R=CH_3; 6: R=CH_2Ph, R'=H; 7: R=H; R'=Ph;

3: R=CH_2Ph; 8: R=H, R'=o-CH_3OPh; 9: R=H, R'=p-CH_3OPh;

10: R=H, R'=2-CH_3Ph; 11: R=H, R'=4-CH_3Ph;

SCHEME 1

ternal reference. The MS spectra were obtained on a VG-7070E-HF meter with electron bombardment of 70 eV. The IR spectra were recorded on a Nicolet FI-IR 50X spectrometer. The UV-vis spectra were obtained on a Specord UV-vis spectrophotometer. Thin-layer and preparative-layer plates were made by use of silica gel GF_{254}.

SYNTHESIS OF DIBUTYLTIN(IV) COMPLEXES (1–3) [9]

Dibutyltin(IV) complex I was prepared from dibutyltin dichloride and Schiff bases derived from glycine; complexes 2 and 3 were prepared from alanine and phenylalanine, respectively.

CONDENSATION OF 1, 2, AND 3 WITH FORMALDEHYDE

To 1 mmole of 1 in 15 mL of methyl alcohol were added 0.55 mL of trimethylamine and 0.3225 g (10.75 mmole) of paraformaldehyde. The reaction mixture was stirred at 50°C under argon. The reaction was monitored by thin-layer chromatography (TLC) with neutralized samples (SiO_2, $CHCl_3$-acetone, 5:1). When the content of the reaction mixture ceased to change on the plate, it was neutralized with acetic acid. Methyl alcohol solvent was evaporated in vacuo. The yellow residue was separated on a preparative-layer plate in $CHCl_3$-acetone (5:1). Product 4 was obtained by recrystallization from CH_2Cl_2-ligroin (60–90°C)-acetone solution.

Yield of Product 4: 56%, mp 110°C; UV-vis (CH_3OH) λ (log ε) 377.7 (2.31), 283.4 nm (2.69); ^1H NMR ($CDCl_3$), δ 6.7–8.0 (5H, m, Ar, CH=N), δ 4.05 (4H, s, CH_2OH), δ 0.6–1.8 (18H, m, $2CH_2CH_2CH_2CH_3$); ^{119}Sn NMR ($CDCl_3$) δ 197.815; IR (KCl): $\nu_{(C=O)}$1647, $\nu_{(C=N)}$1614, $\nu_{(ph-O)}$1310, $\nu_{(Sn-O)}$531, $\nu_{(Sn-N)}$450; anal. calcd for $C_{29}H_{29}O_5NSn$: C, 47.50; H, 6.17; N, 2.98. Found: C, 47.84; H, 6.04; N, 3.02.

Product 5 was synthesized from 2 with paraformaldehyde according to a previous procedure with a yield of 66%, mp 110–112°C UV-vis (CH_3OH) λ (log ε) 385.3 (2.49), 282.9 nm (2.89); ^1H NMR ($CDCl_3$) δ 8.3 (1H, s, CH=N), δ 7.2 (4H, m, Ar), δ 3.8–4.0 (2H, t, CH_2OH), δ 1.34 (3H, s, CH_3), δ 0.79–1.6 (18H, m, $2CH_2CH_2CH_2CH_3$); ^{119}Sn NMR ($CDCl_3$) δ 208.231; IR (KCl) $\nu_{C=O}$1642, $\nu_{(C=N)}$1614, $\nu_{(ph-O)}$1309, $\nu_{(Sn-O)}$530, $\nu_{(Sn-N)}$449; anal. calcd for $C_{29}H_{29}O_4NSn$: C, 60.63; H, 5.05; N, 2.44. Found: C, 60.56; H, 4.91; N, 2.29. MS spectrum: 398 (47.97%), 354 (59, 30%), 312 (100%, M^+-2Bu-CHO), 310 (86.44%, M^+-2Bu-CH_2OH) 225 (42.49%), 192 (54.74%), 120 (68.41%), 29 (61.13%).

Product 6 was synthesized from 3 according to the same procedure. Yield of 6: 58.9%, mp 95–97°C. UV-vis (CH_3OH) λ (log ε) 384.7 (2.53), 282.0 nm (2.77); ^1H NMR ($CDCl_3$) δ 6.5–8.1 (10H, m, Ar, CH=N), δ 2.9–3.6 (2H, t, CH_2Ph), δ 3.8–4.2 (2H, d, CH_2OH), δ 0.6–1.8 (18H, m, $2CH_2CH_2CH_2CH_3$); ^{119}Sn NMR ($CDCl_3$): −205.513; IR (KCl) $\nu_{(C=O)}$1639, $\nu_{(C=N)}$1614, $\nu_{(ph-O)}$1311, $\nu_{(Sn-O)}$535, $\nu_{(Sn-N)}$447; anal. calcd for $C_{35}H_{33}O_4NSn$: C, 64.62; H, 5.08; N, 2.15. Found: C, 64.37; H, 4.88; N, 2.21.

CONDENSATION OF 1 WITH THE OTHER ALDEHYDES

To 1 mmole of 1 in 5 mL of 1.5N CH_3ONa methyl alcohol solution was added 3 mmole of benzaldehyde, and the mixture was stirred at 25°C under argon. The reaction was monitored by TLC using neutralized samples (SiO_2, $CHCl_3$-acetone, 5:1). When the composition of the reaction mixture ceased to change, it was neutralized with acetic acid to pH = 7. Methyl alcohol solvent was evaporated in vacuo. The yellow solid was washed with acetone until it became white. Acetone solvent was evaporated in vacuo. The residue was separated on a preparative-

layer plate in $CHCl_3$-acetone (5:1) and further purification with THF-C_6H_6 (1:1). Product 7 was obtained by recrystallization from CH_2Cl_2-ligroin (60–90°C) solution.

Yield of Product 7. 78%, mp 107.5–109°C; UV-vis (CH_3OH) λ (log ε): 382.8 (2.59), 280.0 nm (2.93); ^{1}H NMR ($CDCl_3$) δ 6.6–8.0 (10H, m, Ar, CH=N), δ 4.4 (1H, d, α-CH), δ 4.1 (1H, d, β-CH), δ 0.6–1.8 (18H, m, $2CH_2CH_2CH_2CH_3$); ^{119}Sn NMR ($CDCl_3$) δ = 199.375; IR (KCl) $\nu_{(C=O)}$1638, $\nu_{(C=N)}$1614, $\nu_{(ph-O)}$1310, $\nu_{(Sn-O)}$547, $\nu_{(Sn-N)}$457; anal. calcd for $C_{35}H_{32}O_4NSn$: C, 55.81; H, 6.01; N, 2.71. Found: C, 55.59; H, 5.85, N, 3.02.

Product 8 was synthesized from 1 by condensation with o-anisaldehyde according to the same procedure with a yield of 74.5%; mp 113–115°C; UV-vis (CH_3OH) λ (log ε): 382.5 (2.63), 280.7 nm (3.02); ^{1}H NMR ($CDCl_3$) δ 6.4–7.4 (9H, m, Ar, CH=N), δ 4.25 (1H, d, α-CH), δ 3.8 (1H, d, β-CH), δ 3.6 (3H, s, OCH_3), δ 0.6–1.8 (18H, m, $2CH_2CH_2CH_2CH_3$); ^{119}Sn NMR ($CDCl_3$) δ −200.026; IR (KCl) $\nu_{(C=O)}$1640, $\nu_{(C=N)}$1614, $\nu_{(ph-O)}$1304, $\nu_{(Sn-O)}$531, $\nu_{(Sn-N)}$449; anal. calcd for $C_{36}H_{33}O_5NSn$: C, 54.95; H, 6.04; N, 2.56. Found: C, 54.78; H, 6.20; N, 2.39.

Product 9 was synthesized from 1 with p-anisaldehyde with a yield of 73%; mp 89–91°C; UV-vis (CH_3OH) λ (log ε): 382.9 (2.71), 282.9 nm (3.06); ^{1}H NMR ($CDCl_3$) δ 6.6–7.8 (9H, m, Ar, CH=N), δ 4.5 (1H, d, α-CH), δ 4.05 (1H, d, β-CH), δ 3.81 (3H, s, OCH_3), δ 0.6–1.8 (18H, m, $2CH_2CH_2CH_2CH_3$); ^{119}Sn NMR ($CDCl_3$): δ −200.120; IR (KCl) $\nu_{(C=O)}$1643, $\nu_{(C=N)}$1614, $\nu_{(ph-O)}$1302, $\nu_{(Sn-O)}$531, $\nu_{(Sn-N)}$450; anal. calcd for $C_{36}H_{33}O_5NSn$: C, 54.95; H, 6.04; N, 2.56. Found: C, 54.39, H, 6.18; N, 249.

Product 10 was synthesized from 1 with 2-methylbenzaldehyde with a yield of 70%, mp 109–110°C; UV-vis (CH_3OH) λ (log ε) 383.1 (2.67), 282.1 (3.02); ^{1}H NMR ($CDCl_3$) δ 6.4–7.4 (9H, m, Ar, CH=N), δ 4.20 (1H, d, α-CH), δ 3.9 (1H, d, β-CH), δ 2.4 (3H, s, CH_3), δ 0.6–1.8 (18H, m, $2CH_2CH_2CH_2CH_3$); ^{119}Sn NMR ($CDCl_3$) −198.302. IR (KCl) $\nu_{(C=O)}$1640, $\nu_{(C=N)}$1614, $\nu_{(ph-O)}$1308, $\nu_{(Sn-O)}$547, $\nu_{(Sn-N)}$451; anal. calcd for $C_{36}H_{33}O_4NSn$: C, 56.60, H, 6.23; N, 2.64. Found: C, 56.71; H, 5.93; N, 2.29.

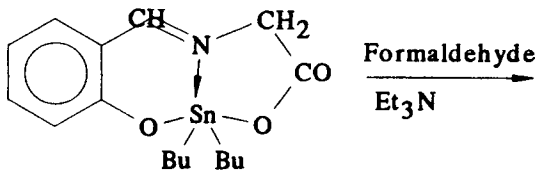
Product 11 was synthesized from 1 with 4-methylbenzaldehyde with a yield of 75%, mp 107–109°C; UV-vis (CH_3OH) λ (log ε) 383.7 (2.605), 282.3 (3.00); ^{1}H NMR ($CDCl_3$) δ 7.0–7.4 (9H, m, Ar, CH=N), δ 4.3 (1H, d, α-CH), δ 3.8 (1H, d, β-CH), δ 2.3 (3H, s, CH_3), gd 0.7–1.6 (18H, m, $2CH_2CH_2CH_2CH_3$); ^{119}Sn NMR ($CDCl_3$) δ −198.112; IR (KCl) $\nu_{(C=O)}$1639, $\nu_{(C=N)}$1614, $\nu_{(ph-O)}$1310, $\nu_{(Sn-O)}$523, $\nu_{(Sn-N)}$450; anal. calcd for $C_{36}H_{33}O_4NSn$: C, 56.60; H, 6.23; N, 2.64. Found: C, 56.57; H, 6.15; N, 2.51. MS spectrum: 367 (1.22%), 354 (1.19%), 254 (14.47%), 225 (5.01%), 119 (100%, CH_3PhCO^+), 91 (95.10%, CH_3Ph^{-+}), 65 (22.41%).

RESULTS

The IR spectra of all products (4–11) are similar. The 1640 cm^{-1} absorptions are assigned to be the stretching modes of coordinated carboxylates. The 1614 cm^{-1} absorptions may be attributed to the presence of the C=N bond in the complexes. The weak absorption at 1302 cm^{-1} may be attributed to the Ph–O bond stretching, and 547 and 449 cm^{-1}, to the Sn–O and Sn–N bond stretchings, respectively.

All the products are yellow. Their electronic spectra are virtually identical. The electronic spectra in the region at about 383 nm correspond to a π-π^* transition of the C=N bond, which is retained in the complex.

^{1}H NMR spectra of all products (4–11) are significant in identification of their structures. Besides the variation of the αCH values in the reactants (1–3), there is the appearance of a new peak near δ 3.8 that is assigned to the β-CH resonance in products (4–11). This indicates that the aldol condensations of complexes (1–3) with aldehydes take place. The data of complex 4 show that the double addition product of complex 1 with formaldehyde is formed at the expense of two α-hydrogens.



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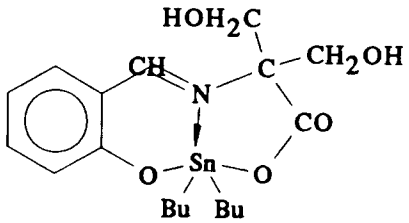

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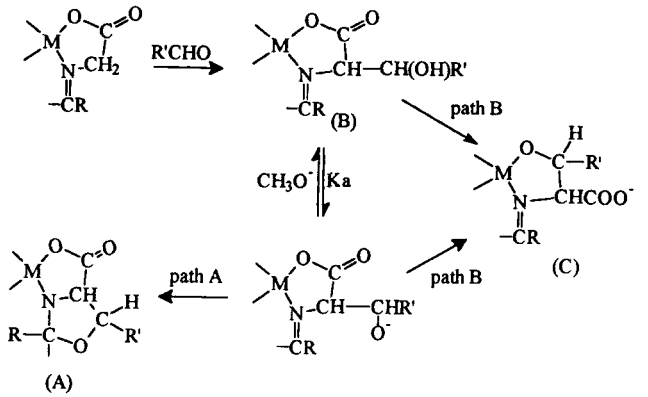
Unlike the foregoing 1 reaction, all condensations of complex 1 with the other aldehydes resulted in monoaddition products (7–11).

^{119}Sn NMR spectra of all the complexes are identical (δ = −200 in $CDCl_3$). The data prove that the central metal Sn atom in the complexes is pentacoordinate.

DISCUSSION

Since the pK_a value of complex 1 in DMSO is 17.43 [6], its α-CH acidity is greater than that of fluorene



SCHEME 2

(pK_a = 22.6) [10] and the Ni^{++} chelate with the Schiff base derived from glycine (pK_a = 18.8) [11] and it approaches that of mononitro compounds (pK_a = 17) [10]. Because of the relatively high thermodynamic acidity and great kinetic stability, the carbanion formed from complex 1 is able to condense, not only under strongly basic conditions, such as with use of 1.5N CH_3ONa, but also in the presence of the weak base Et_3N.

The mechanism of the aldol condensation of complexes (1–3) with aldehydes seems to be of the generally accepted type. It is known that the condensation of amino acid metal complexes with aldehydes consists of the removal of an α-proton from the amino acid fragment followed by the addition of the resulting α-carbanion to a carbonyl group. By analogy with the above mechanism, Belokon et al. [12] have advanced the suggestion of the mechanism shown in (Scheme 2).

Belokon et al. think that there are two possible paths of condensation resulting in different products. In our study of the condensations of complexes 1–3, the data of IR and UV spectra show that the C=N bond is retained in all the products, and ^1H NMR spectra have also provided evidence of the presence of a β-hydroxyl group. All these data seem to support the structure of the condensation product to be B; products A and C are not observed as presented in Scheme 2.

In aldol condensation reactions of complex 1, the number of moles of aldehyde consumed depends on the bulkiness of the aldehyde. The crystal structure of the organotin(IV) complex shows that the α-hydrogen of the glycine fragment adopts a pseudoaxial orientation and is not shielded by any other groups [4]. As the aldol condensation of the α-carbanion with the aldehyde occurs, the steric effect of the aldehyde becomes the determining factor. With a small aldehyde, only double addition of the glycine fragment is expected. In contrast to this, the repeated addition reaction of a bulky aldehyde is more difficult. Therefore, only one molecule of an aromatic aldehyde condenses with complex 1, but two molecules of formaldehyde are consumed in the same type of condensation.

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REFERENCES

[1] A. K. Eaxens, *Appl. Organoment. Chem., 1,* 1987, 39.
[2] Jitao Wang, Fengquan Lui, Yunwen Zhang, *J. Organoment. Chem., 371,* 1989, 35.
[3] Jitao Wang, Fengquan Lui, Yunwen Zhang, *J. Organoment. Chem., 375,* 1989, 173.
[4] Jitao Wang, Yunwen Zhang, Yuming Xu, Zhiwen Wang, *Heteroatom. Chem., 3,* (5/6) 1992, 599.
[5] A. E. Martell, *Acc. Chem. Res., 22(4),* 1989, 115.
[6] Jitao Wang, Xiaoping Yang, Be Lui, Jinpei Cheng, Youji Huaxue, in press.
[7] (a) J. I. Kikuchi, T. Takashima, H. Nakao, K. I. Hie, H. Etoh, Y. Noguchi, K. Suehiro, Y. Murakami, *Chem. Lett.,* 1993, 553; (b) Y. Murakami, J. I. Kikuchi, T. Miyajima, Y. Hisaeda, *Chem. Lett.,* 1994, 55.
[8] B. N. Biddle, J. S. Gray, A. J. Crowe, *Appl. Organoment. Chem., 1,* 1987, 261.
[9] Jitao Wang, Yunwen Zhang, Yuming Xu, Zhiwen Wang, Youji Huaxue, *13,* 1993, 289.
[10] W. S. Matthews, J. E. Baras, J. E. Bartmess, F. G. Bordwell, F. J. Corno, G. E. Drucker, Z. Margolin, R. S. McCallum, G. J. McCallum, N. R. Vanier, *J. Am. Chem. Soc., 97,* 1975, 7006.
[11] Yu. N. Belokon, V. I. Bakhmutov, N. I. Chernoglazova, K. A. Kochetrov, S. V. Vitt, N. S. Garbalinskaya, V. M. Belikov, *J. Chem. Soc. Perkin Trans I.,* 1988, 305.
[12] Yu. N. Belokon, A. G. Bulychev, S. V. Vitt, Y. T. Struchkov, A. S. Batsanov, T. V. Timoreeva, V. A. Tsyryapkin, M. G. Ryzhov, I. A. Lysova, V. I. Bakhmutov, V. I. Belikov, *J. Am. Chem. Soc., 107,* 1985, 4252.