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A FACILE SYNTHESIS OF α,β-DIHYDROXYKETONES VIA TIN(IV) ENEDIOLATES BY UTILIZING THE REDUCING POWER OF BIS(2-PYRIDINETHIOLATO)TIN(II)

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Bis(2-pyridinethiolato)tin(II), a stable stannylene, effects oxidative addition to α-dicarbonyl compounds to generate tin(IV) enediolates, which in turn react with aldehydes to give α,β-dihydroxyketones in good yields with moderate diastereoselectivities.

In the course of our investigation on exploration of new synthetic reactions by using divalent tin,1) it becomes apparent that tin(II) compounds have a number of interesting characteristics. One of the outstanding features of the divalent tin chemistry is the ease of its oxidation to tetravalent tin. This property has been successfully applied to carbon-carbon bond forming reactions in our laboratory, for example, stannous halides add to the organic compounds to give the organotin(IV) compounds, which in turn react with aldehydes or ketones to form new carbon-carbon bonds.2)

On the other hand, it has been known in the literature that organostannylenes (R_2Sn:) are very attractive compounds with strong reducing ability compared with the other tin(II) compounds. For example, dialkylstannylenes react with α-diketones to yield the corresponding 1,3,2-dioxastannolenes, tin(IV) enediolates,3) however, these organotin compounds thus formed have not yet been used in carbon-carbon bond forming reactions. Moreover, few examples have been reported concerning the application of dialkylstannylene to organic synthesis in spite of its potential reducing ability.4) This is probably due to its difficulties in generation5) and handling because the monomeric stannylenes exist only as short-lived intermediates which readily self-react to give oligomers ($(R_2Sn)_n$).

These facts prompted us to develop a new and readily available tin(II) compound which has the reducing power comparable to that of dialkylstannylene in order to explore new possibility in organic synthesis. After examination of various tin(II) compounds, we have found that bis(2-pyridinethiolato)tin(II) (1) is easily prepared from 1,1'-dimethylstannocene6) and 2-mercaptopyridine or from stannous chloride and lithium 2-pyridylmercaptide, and acts as an effective reducing agent. We also report here that tin(IV) enediolate (2),7) the oxidative addition product generated from bis(2-pyridinethiolato)tin(II) and α-dicarbonyl compound, reacts smoothly with aldehyde to give the corresponding α,β-dihydroxyketone in good yield with moderate diastereoselectivity.

In the first place, bis(2-pyridinethiolato)tin(II) (1) was generated *in situ* from 1,1'-dimethylstannocene and 2-mercaptopyridine, and then 3-phenylpropanal and 2,3-butanedione were added successively at 0 °C. After stirring overnight, usual work-up afforded the desired α,β-dihydroxyketone (3) in 82% yield.

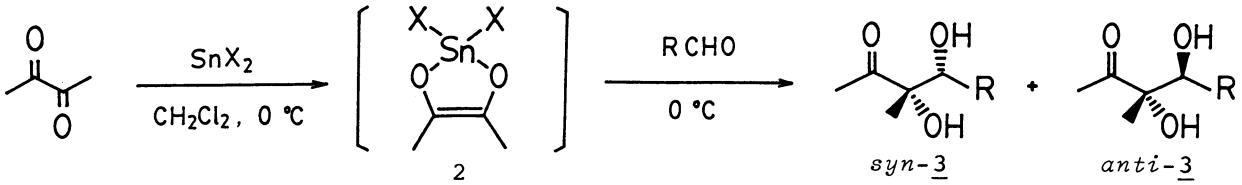
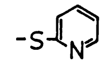
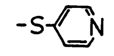
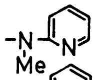
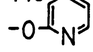
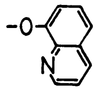


Table 1. The Effect of Tin(II) Compounds[a]

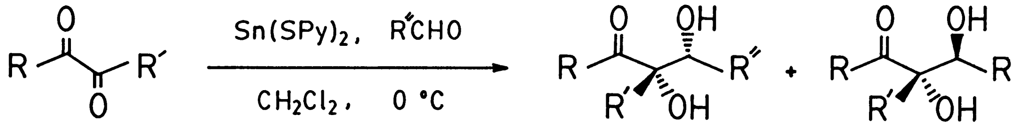
Entry	$X(SnX_2)$	Method[b]	Yield of 3/%[c]	*syn*:*anti*[d]
1	 (1)	A	82	77:23
2		B	87	50:50[8]
3		A	19	63:37
4		B	0	——
5		A	18	66:34
6		A	57	67:33
7	$-OCH_2CH_2N(CH_3)_2$[3d]	A	trace	——
8[e]	-Cl	——	0	——

a) Reaction was carried out in CH_2Cl_2 at 0 °C for 15-20 h. Molar ratio of SnX_2:2,3-butanedione:3-phenylpropanal = 1 : 1 : 0.67. b) A: SnX_2 prepared from 1,1'-dimethylstannocene and HX (1:2 molar ratio) in CH_2Cl_2. B: SnX_2 prepared from stannous chloride and LiX (1:2 molar ratio) in THF. c) Isolated yield. d) The ratio was determined by ^1H NMR measurement. See Ref.9. e) Reaction was carried out in THF.

Screening of the same reaction in the presence of various tin(II) compounds, as summarized in Table 1, reveals that i) the reducing power of tin(II) compounds (SnX_2) varied dramatically depending on substituents (X); ii) bis(2-pyridinethiolato)tin(II) (1) gave the best result both in yield and in diastereoselectivity (Entry 1); iii) concerning the hetero atom bonded to tin atom, sulfur atom was more effective than oxygen and nitrogen atoms (Entries 1, 4, and 5); iv) the intramolecular coordination of nitrogen atom on pyridine ring to tin atom played an important role in this reaction (Entries 1 and 3; 5, 6, and 7); v) the oxidative addition reaction of stannous chloride hardly proceeded for α-diketone (Entry 8).[10a]

These facts suggest that both the coordination of nitrogen atom and the electron donation of sulfur atom in bis(2-pyridinethiolato)tin(II) (1) should increase the electron density on the center tin atom to result in the enhancement of its reducing power.

Next, the reactions of various α-dicarbonyl compounds with aldehydes were examined and results are summarized in Table 2.



syn-4 *anti*-4

Table 2. Synthesis of α,β-Dihydroxyketones a)

Entry	R	R'	R"	Time/h	Yield of 4/%b)	*syn*:*anti*
1	CH_3	CH_3	$Ph(CH_2)_2$	17	82	77:23c,9,11)
2	CH_3	CH_3	n-C_5H_{11}	22	97	81:19d,11)
3	CH_3	CH_3	$PhCH_2O(CH_2)_2$	16	80	71:29c,11)
4	CH_3	CH_3	$CH_3CH_2CO_2(CH_2)_9$	23	89	——e)
5	CH_3	CH_3	$CH_3CO(CH_2)_8$	23	87	——e)
6	CH_3	CH_3	2-Furyl	34	57	70:30c,11)
7	CH_3CH_2	CH_3CH_2	n-C_5H_{11}	27	95	64:36d,11)
8	Ph	H	$Ph(CH_2)_2$	16	51	78:22d,12)

a) Molar ratio of $Sn(SPy)_2$:α-dicarbonyl compound:aldehyde = 1 : 1 : 0.67-0.5. b) Isolated yield. Satisfactory ^1H NMR and IR spectra were obtained for each compound. c) Determined by ^1H NMR measurement. d) Determined by separating each isomer. e) Not determined.

As shown in Table 2, a variety of α,β-dihydroxyketones including functionalized ones (Entries 3, 4, 5, and 6) were synthesized under mild conditions in good yields. Furthermore, moderate diastereoselectivity was observed to give *syn* isomer predominantly in the present reaction of tin(IV) enediolate, in contrast to tin(II) enediolate, where *anti* isomer is a major product.10)

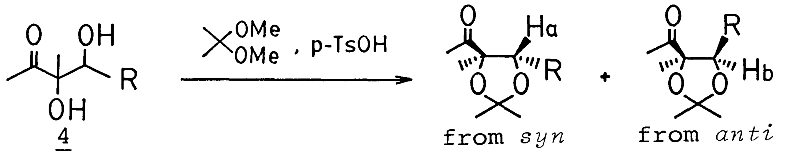
The following example is representative; to a dichloromethane solution (1 ml) of 1,1'-dimethylstannocene (161 mg, 0.58 mmol) was added 2-mercaptopyridine (129 mg, 1.16 mmol) in solid form at room temperature under an argon atmosphere. After stirring for 30 min at that temperature, dichloromethane solutions (1 ml) of 3-phenylpropanal (52 mg, 0.39 mmol) and 2,3-butanedione (50 mg, 0.58 mmol) were added successively at 0 °C. The reaction mixture was further stirred for 17 h at the same temperature, then quenched with pH 7 phosphate buffer. The organic materials were extracted with dichloromethane three times, and combined extracts were dried over $MgSO_4$. After evaporation of the solvent, 3,4-dihydroxy-3-methyl-

6-phenyl-2-hexanone (71 mg, 82%) was isolated by thin layer chromatography on silica gel (hexane : AcOEt = 2 : 1).

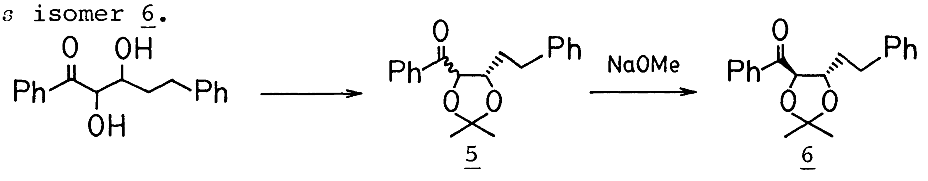
It should be noted that bis(2-pyridinethiolato)tin(II) (1) is a new and stable stannylene which acts as an effective reducing agent for α-dicarbonyl compounds. Further synthetic approaches using the reducing ability of bis(2-pyridinethiolato)tin(II) are now in progress.

References

1) For example; T. Mukaiyama, T. Harada, and S. Shoda, Chem. Lett., 1980, 1507; T. Harada and T. Mukaiyama, ibid., 1982, 467; T. Mukaiyama, N. Iwasawa, R. W. Stevens, and T. Haga, Tetrahedron, 40, 1381 (1984); T. Mukaiyama, J. Ichikawa, M. Toba, and M. Asami, Chem. Lett., 1983, 879; T. Oriyama and T. Mukaiyama, ibid., 1984, 2071.
2) T. Mukaiyama, M. Yamaguchi, and J. Kato, Chem. Lett., 1981, 1505, and references cited therein.
3) a) K. -H. Scherping and W. P. Neumann, Organometallics, 1, 1017 (1982); b) W. P. Neumann and A. Schwarz, Angew. Chem., Int. Ed. Engl., 14, 812 (1975). See also; c) A. G. Davies and J. A. -A. Hawari, J. Chem. Soc., Perkin Trans. 1, 1983, 875; d) I. Wakeshima and I. Kijima, Bull. Chem. Soc. Jpn., 54, 2345 (1981).
4) C. Grugel, W. P. Neumann, J. Sauer, and P. Seifert, Tetrahedron Lett., 1978, 2847.
5) Dialkylstannylenes are usually generated by thermolysis or photolysis of distannanes or polystannanes. See Ref. 3a and 4; L. -W. Gross, R. Moser, W. P. Neumann, and K. -H. Scherping, Tetrahedron Lett., 23, 635 (1982).
6) T. Mukaiyama, J. Ichikawa, and M. Asami, Chem. Lett., 1983, 293, and references cited therein.
7) Aldol reaction of tin(IV) enolate: H. Urabe and I. Kuwajima, Tetrahedron Lett., 24, 5001 (1983), and references cited therein.
8) This significant decrease in diastereoselectivity may be attributed to lithium chloride formed as a by-product. In fact, when the reaction (Method A) was carried out in the presence of lithium chloride, the salt effect like this was observed (yield = 87%; *syn*:*anti* = 47 : 53).
9) The stereochemistry was assigned by comparison of ^{1}H NMR spectrum and TLC analysis with those of authentic sample, which was prepared by stereospecific hydroxylation of (*E*)-3-methyl-6-phenyl-3-hexen-2-one13) using OsO$_4$.
10) a) Activated metallic tin prepared from stannous chloride and metallic potassium reacts readily with *α*-diketone to form tin(II) enediolate. T. Mukaiyama, J. Kato, and M. Yamaguchi, Chem. Lett., 1982, 1291, in which, however, the stereochemistry of two isomers should be reversed. See also; b) F. Ramirez, A. V. Patwardhan, N. Ramanathan, N. B. Desai, C. V. Greco, and S. R. Heller, J. Am. Chem. Soc., 87, 543 (1965).
11) The stereochemistry was assigned by LIS method14) as follows: H$_a$ was shifted downfield upon addition of Eu(fod)$_3$ in CCl$_4$ more strongly than H$_b$.



12) The stereochemistry was assigned by NaOMe catalyzed isomerization of 5 to *trans* isomer 6.



13) A. Sato, A. Ogiso, H. Noguchi, S. Mitsui, I. Kaneko, and Y. Shimada, Chem. Pharm. Bull., 28, 1509 (1980).
14) O. Hofer, "The Lanthanide Induced Shift Technique: Applications in Conformational Analysis," in "Topics in Stereochemistry," ed by N. L. Allinger and E. L. Eliel, John Wiley & Sons, Inc., New York (1976), Vol.9, pp.111-197.

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