CHEMISTRY LETTERS, pp. 1825-1828, 1983.

TIN(II) ENEDIOLATE FROM METHYLGLYOXAL

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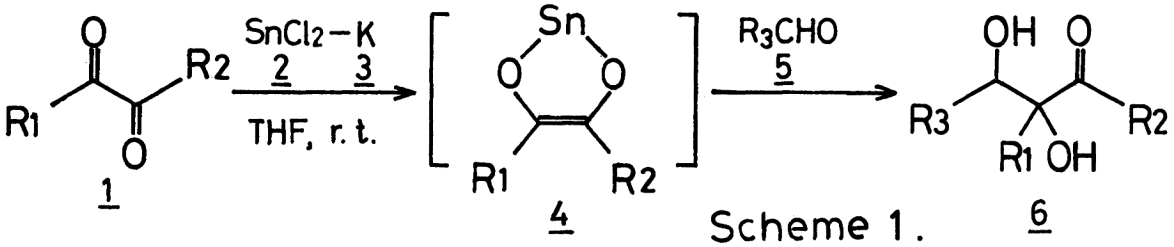
Methylglyoxal is successfully converted to the tin(II) enediolate on treatment with activated metallic tin. The tin(II) enediolate reacts with several aldehydes to give α,β-dihydroxyketones in good yields.

In the previous paper,[1] a new method for the synthesis of α,β-dihydroxyketones (6) was reported based on the aldol-type addition reaction of 1,2-diketones (1) to aldehydes (5) in the presence of the activated metallic tin prepared *in situ* from stannous chloride (2) and metallic potassium (3). And it was explained there that the reaction proceeded *via* enediolate (4) formed by the oxidative addition of 1,2-diketones to metallic tin (Scheme 1).



Scheme 1.

Further, there were also reported the successful examples using phenylglyoxal, an α-ketoaldehyde, instead of 1,2-diketones in the cross aldol reaction.

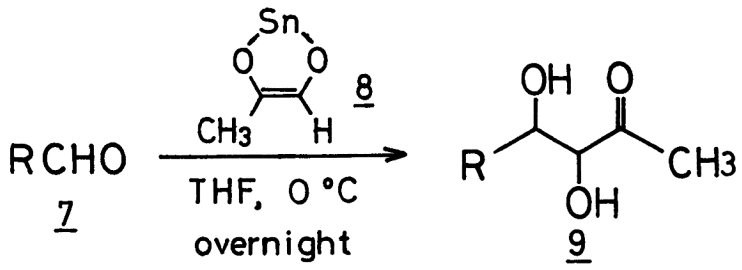
In this communication, we wish to report some results of the cross aldol reaction of the enediolate (8) derived from methylglyoxal and several aldehydes with the expectation that the unbranched dihydroxyketone (11), a very useful precursor of L-sugars, would be produced by the coupling of methylglyoxal with 4-O-benzyl-2,3-O-isopropylidene-L-threose (10).

Methylglyoxal[2,3] is a volatile liquid and polymerizes so rapidly that it is impossible to preserve it as a pure monomer, and it should be prepared every time it is needed. For this reason, methylglyoxal is troublesome to use as a reagent in organic synthesis. Recently, it was reported that methylglyoxal monomer could be formed in a medium yield when its polymer was heated under a reduced pressure on phosphorus pentoxide.[3]

Reaction conditions were examined by taking the reaction of methylglyoxal and 3-phenylpropanal (7a) as a model. And it was found that the cross aldol adduct (9a) was obtained in a yield of 70% when 6 – 7 times molar excess of methylglyoxal was treated with 3-phenylpropanal at 0 °C.

Then, under a similar condition, the reactions of some other aldehydes (7b-d) with methylglyoxal were tried and the results are summarized in Table 1.

Table 1. Cross aldol reactions of methylglyoxal with aldehydes (7).[a)]



	RCHO (7)	Yield of 9/%	Diastereomer ratio[b)]
a	$PhCH_2CH_2CHO$	70	3 : 4 [c)]
b	$PhCH_2O(CH_2)_3CHO$	80	1 : 5 [c)]
c	$n\text{-}C_7H_{15}CHO$	55	1 : 2 [c)]
d	$p\text{-}ClC_6H_4CHO$	54	1 : 3 [d)]

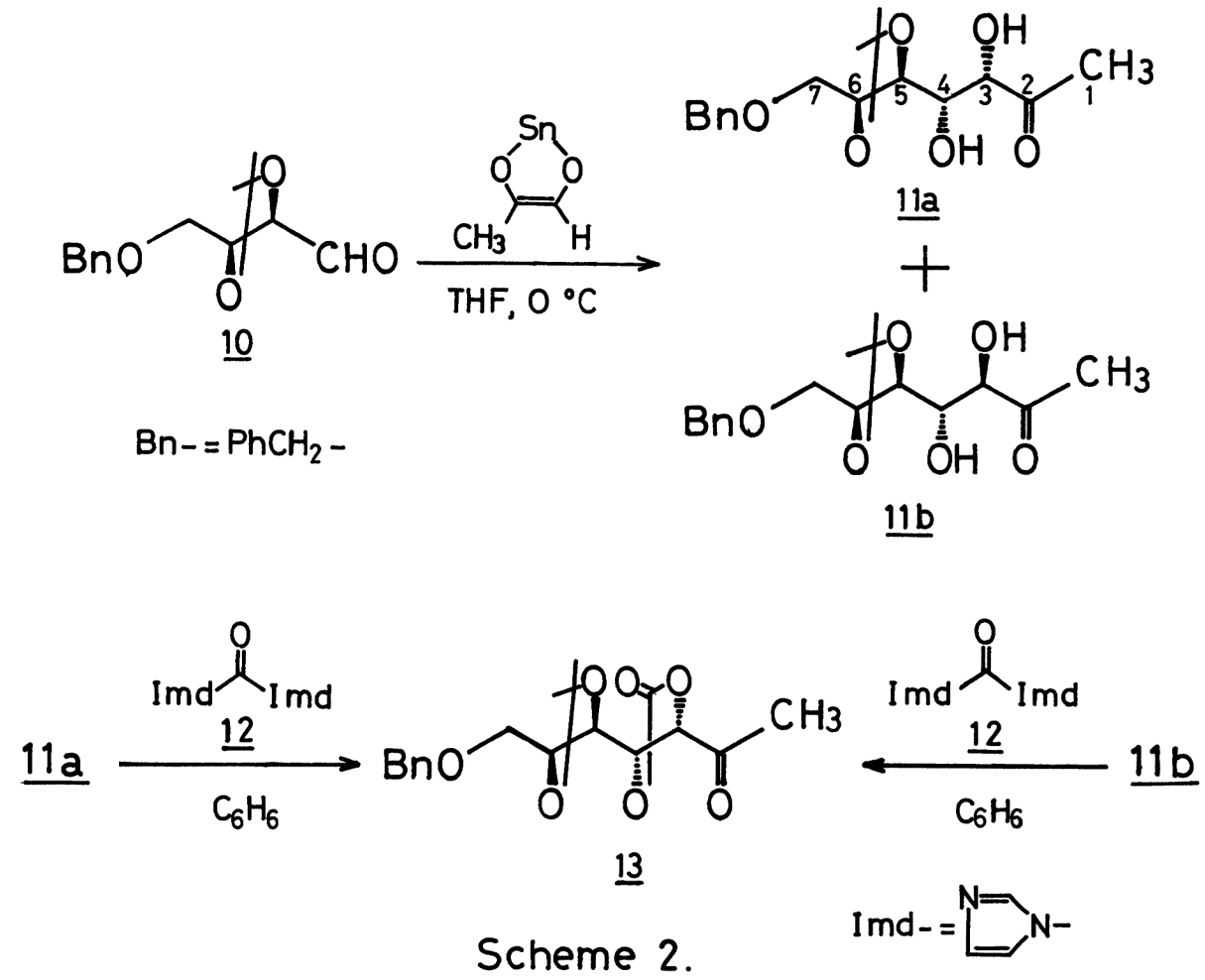
a) All the products gave satisfactory ^{1}H-NMR and IR spectra.
b) The structures of the diastereomers have not yet been assigned except 9a . In the case of 9a , the major and minor products were assigned to *syn*- and *anti*-form respectively by means of the ^{1}H-NMR spectra of the acetonide-derivatives of 9a .
c) Each isomer was isolated.
d) Determined by ^{1}H-NMR.

A typical reaction procedure is as follows: undre an argon atmosphere a tetrahydrofuran (THF) suspension of stannous chloride (1.52 g, 8 mmol) and metallic potassium (313 mg, 8 mmol) was stirred at room temperature for 1 h and was refluxed carefully for another 30 min. After the suspension had been cooled to 0 °C in an ice-bath, a THF solution (2 ml) of 3-phenylpropanal (7a, 67.1 mg, 0.5 mmol) was added and a THF solution (8 ml) of fresh methylglyoxal (0.24 g, 3.3 mmol) was added dropwise. The reaction mixture was stirred at 0 °C overnight and poured into a phosphate buffer solution (pH 7, 20 ml). After the filtration of insoluble materials, organic materials of the filtrate were extracted with ethyl acetate (AcOEt) and the extracts were dried over anhydrous $MgSO_4$. After the evaporation of the solvent, the residue was purified by thin layer chromatography on silica-gel (AcOEt : petroleum ether = 1 : 1.5). Thus (3R, 4S)- and (3S, 4R)-3,4-dihydroxy-6-phenyl-2-hexanones (9a, 29.6 mg, 28%) were obtained. NMR ($CDCl_3$) δ 1.67-2.50 (3H, m), 2.21 (3H, s), 2.57-3.00 (2H, m), 3.17-4.30 (3H, m), 7.23 (5H, s). IR (NaCl) 3430, 1710 cm^{-1}. At the same time, (3R, 4R)- and (3S, 4S)-3,4-dihydroxy-6-phenyl-2-hexanones (9a, 43.5 mg, 42%) were obtained. NMR ($CDCl_3$) δ

1.45-1.92 (2H, m), 2.12 (3H, s), 2.18-2.41 (1H, m), 2.55-2.93 (2H, m), 3.55 (1H, d, J = 5 Hz), 3.68-4.02 (1H, m), 4.24 (1H, dd, J_1 = 3 Hz, J_2 = 3 Hz), 7.22 (5H, s). IR (NaCl) 3430, 1710 cm^{-1}.

Recently, a new four-carbon synthetic unit, that is 4-O-benzyl-2,3-isopropylidene-L-threose (10),[5] was prepared in our laboratory. When the aldehyde (10) was treated with methylglyoxal in a similar procedure, the corresponding α,β-dihydroxyketone (11) was formed in a yield of 64% (11a : 11b = 1 : 1, Scheme 2). Further, it was found that when methylglyoxal was charged slowly in 3 h by means of a microfeeder, the yield of α,β-dihydroxyketones (11) increased up to 80% (11a : 11b = 2 : 1).[6]

Finally, we attempted to protect the hydroxy functions at the C-3, C-4 positions of the diol (11), and found that the cyclic carbonate derivative (13) was obtained from 11a in a yield of 79% in the presence of N, N'-carbonyldiimidazole (12).[7] Further, to our surprise, from the diol (11b) was also obtained the carbonate (13) in a yield of 56%, probably as a result of the isomerization by imidazole formed in the reaction solution.



Scheme 2.

Thus, we could successfully synthesize the pentahydroxyketone derivative (13), and it should be noted that this substance will be a new precursor for the

synthesis of L-sugars.

References

1) T. Mukaiyama, J. Kato, and M. Yamaguchi, Chem. Lett., 1982, 1291.
2) L. de V. Moulds and H. L. Riley, J. Chem. Soc., 1938, 621.
3) H. Yonehara and S. Fujii, Nippon Kagaku Kaishi, 1975, 107.
4) Methylglyoxal polymer was obtained as follows: Commercial 40% aqueous solution of methylglyoxal was distilled under a reduced pressure to remove most of water. Then, the residue was dissolved in ether and dried over Na_2SO_4. After the evaporation of the ether, the residual viscous oil was well dried under a reduced pressure.
5) T. Mukaiyama, K. Suzuki, and T. Yamada, Chem. Lett., 1982, 929.
6) 11a: NMR ($CDCl_3$) δ 1.42 (6H, s), 2.24 (3H, s), 3.07-4.48 (8H, m), 4.54 (2H, s), 7.30 (5H, s). IR (NaCl) 3450, 1710 cm^{-1}.
11b: NMR ($CDCl_3$) δ 1.27 (6H, s), 2.25 (3H, s), 3.00-4.40 (8H, m), 4.57 (2H, s), 7.28 (5H, s). IR (NaCl) 3450, 1710 cm^{-1}.
7) J. P. Kutney and A. H. Ratcliffe, Synth. Commun., 5, 47 (1975).
8) 13: NMR ($CDCl_3$) δ 1.40 (6H, s), 2.30 (3H, s), 3.44-3.78 (2H, m), 3.88-4.29 (2H, m), 4.52 (2H, s), 4.65-4.88 (2H, m), 7.30 (5H, s). IR (NaCl) 1820, 1722 cm^{-1}.

(Received September 13, 1983)