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Aldol-Type Reaction by Propen-2-yl Acetate with NCS/$SnCl_2$/ROH

Yoshiro MASUYAMA,* Yumiko KOBAYASHI, Ryota YANAGI, and Yasuhiko KURUSU

Department of Chemistry, Faculty of Science and Technology, Sophia University,

7-1 Kioicho, Chiyoda-ku, Tokyo 102

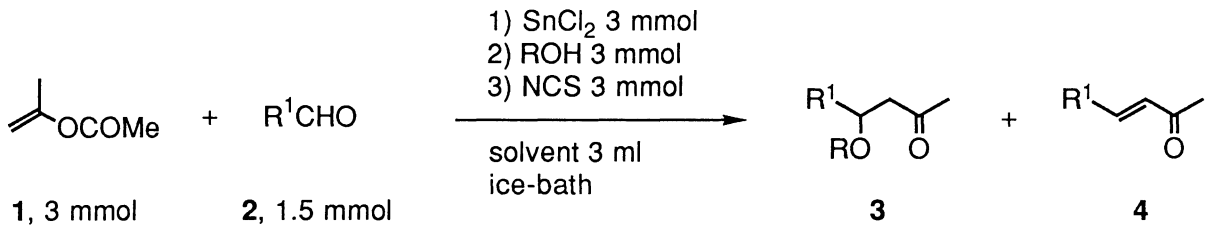
The addition of N-chlorosuccinimide (NCS) to a solution of propen-2-yl acetate, aldehydes, $SnCl_2$, and benzyl alcohol in CH_2Cl_2 or CH_3CN caused an aldol-type reaction to produce 4-substituted 4-benzyloxybutan-2-ones in high yields. Use of methanol instead of benzyl alcohol produced not only 4-methoxybutan-2-one but also 3-buten-2-one by dehydromethoxylation.

Aldol-type condensation by silyl enol ether with Lewis acid has been applied to a wide variety of organic syntheses.[1] However, enol ester, which is easily prepared and is tractable as a nucleophile, has been only employed for a few C-C bond formations, under acidic conditions[2] or neutral conditions.[3] The Lewis acid-catalyzed aldol-type reaction of a simple enol ester, propen-2-yl acetate with aldehydes, in contrast with acetals, has seldom been utilized for the formation of 4-hydroxy-2-butanones or 3-buten-2-ones.[2a] We envisioned *in situ* Lewis acid-catalyzed preparation of hemiacetal from aldehyde and alcohol, followed by aldol-type reaction of propen-2-yl acetate with the acetal. We report here *the aldol-type reaction of propen-2-yl acetate and aldehydes with N-chlorosuccinimide(NCS)/$SnCl_2$/ROH*.

The aldol-type reaction was carried out by the addition of NCS (3 mmol) to a solution of propen-2-yl acetate (**1**, 3 mmol), aldehyde (**2**, 1.5 mmol), $SnCl_2$ (3 mmol), and alcohol (3 mmol) in dichloromethane (3 ml) on an ice-bath to produce 4-alkoxybutan-2-one **3** and/or 3-buten-2-one **4**. The results are summarized in Table 1.[4] Various alcohols such as methanol, ethanol, 2-propenol, and benzyl alcohol can be employed (Entries 1-4). No reaction occurred without the alcohol. Dichloromethane is a better solvent than acetonitrile (Entries 4, 5, 10, and 11). The reaction with ethanol, 2-propenol, or benzyl alcohol afforded selectively the corresponding 4-alkoxybutan-2-one **3** in high yields (Entries 2-11). The reaction with methanol did not produce only 4-

methoxybutan-2-one **3** (R: CH_3) but also 3-buten-2-one **4**, prolonging the reaction time (Entries 1 and 12). These results show that the reaction of **1** and **2** proceeds via the formation of hemiacetal **5** (or oxycarbenium ion **6**) from aldehyde and alcohol with NCS/$SnCl_2$, followed by nucleophilic attack of **1** to **5** (or **6**), as illustrated in Scheme 1. In uses of methanol, dehydromethoxylation of **3** presumably occurred to produce **4**. If we add successively methanol, propen-2-yl acetate, and aldehydes to a solution of NCS and $SnCl_2$ in CH_3CN on an ice-bath and then stir the mixture for 30-60 min, 4-aryl-3-buten-2-ones **4** were only produced in cases of arenecarbaldehydes **2** (R^1: C_6H_5, 71%; R^1: 4-$MeOC_6H_4$, 60%; R^1: 3,4-$(CH_2O_2)C_6H_3$, 65%) and no product was obtained in cases of alkanecarbaldehydes (R^1: n-C_6H_{13}; R^1: c-C_6H_{11}).

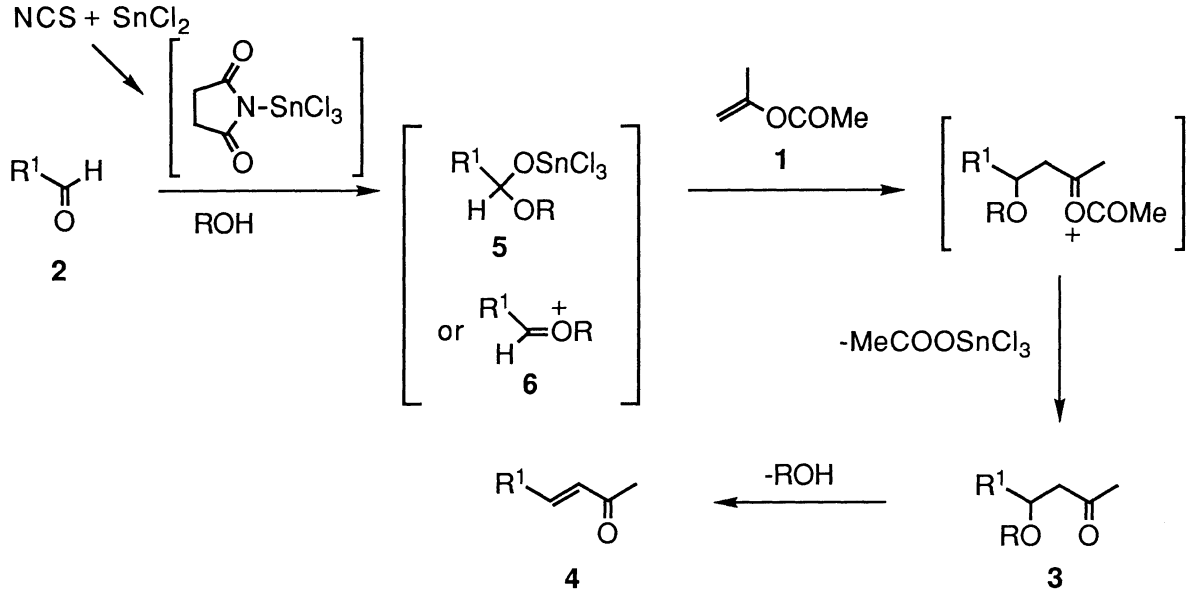
Table 1. Aldol-Type Reaction of Propen-2-yl Acetate (**1**) and Carbonyl Compound **2** with NCS/$SnCl_2$/ROH



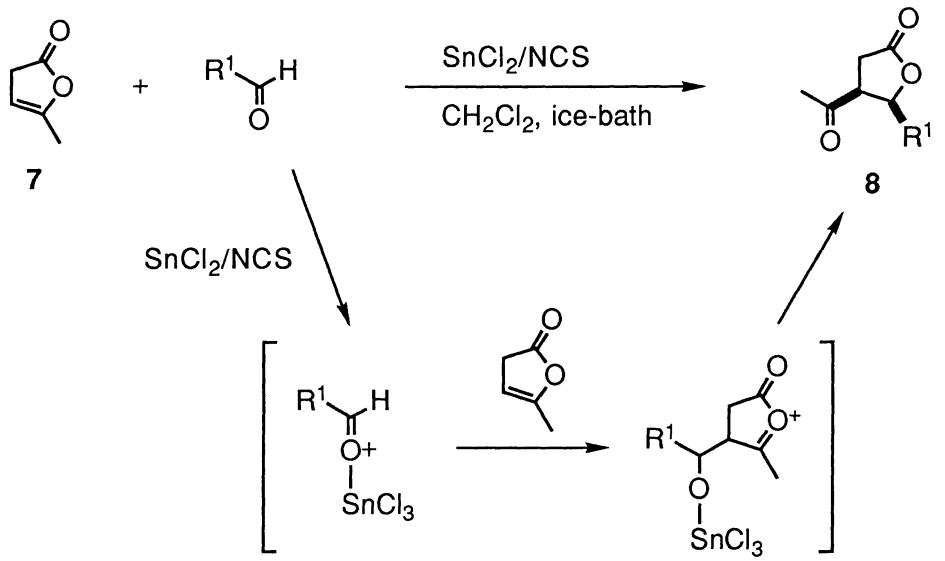
1, 3 mmol **2**, 1.5 mmol **3** **4**

Entry	Carbonyl Compound **2** R^1	Alcohol R	Solvent	Time/min[a]	Yield/%[b] **3**	**4**
1	C_6H_5	CH_3	CH_2Cl_2	10	46	50[c]
2	C_6H_5	CH_3CH_2	CH_2Cl_2	10	84	---
3	C_6H_5	CH_2=$CHCH_2$	CH_2Cl_2	10	91	---
4	C_6H_5	$C_6H_5CH_2$	CH_2Cl_2	10	87	---
5	C_6H_5	$C_6H_5CH_2$	CH_3CN	10	73	---
6	4-NCC_6H_4	$C_6H_5CH_2$	CH_2Cl_2	10	71	---
7	n-C_6H_{13}	$C_6H_5CH_2$	CH_2Cl_2	10	63	---
8	CH_2=$CH(CH_2)_8$	$C_6H_5CH_2$	CH_2Cl_2	10	62	---
9	c-C_6H_{11}	$C_6H_5CH_2$	CH_2Cl_2	20	76	---
10	$C_6H_5(CH_2)_2$	$C_6H_5CH_2$	CH_2Cl_2	10	80	---
11	$C_6H_5(CH_2)_2$	$C_6H_5CH_2$	CH_3CN	20	37	---
12	$C_6H_5(CH_2)_2$	CH_3	CH_2Cl_2	10	19	48[c]

a) The reaction was almost complete after adding NCS for 20 min. b) Isolated yields. c) >97% (*E*)-isomer.



Scheme 1.



Scheme 2.

The addition of cyclic enol ester, 5-methyl-2*(3H)*-furanone (**7**), to aldehydes with NCS/$SnCl_2$ in CH_2Cl_2 occurred in the absence of alcohol to afford the corresponding β-acetyl-γ-butyrolactones **8** stereoselectively [R^1: C_6H_5, 54% (≈100% *syn*);[5] R^1: n-C_6H_{13}, 34% (>95% *syn*); R^1: t-Bu, 44% (≈100% *syn*); R^1: CH_2=$CH(CH_2)_8$, 33% (>95% *syn*)] (Scheme 2). Even if an equimolar amount of methanol to $SnCl_2$ was added, no differences in the yield or the reaction time can be detected.

References

1) E. Colvin, "Silicon in Organic Synthesis," Butterworths, Boston (1981); W. P. Weber, "Silicon Reagents for Organic Synthesis," Springer-Verlag, New York (1983).

2) For aldol-type reaction with Lewis acid, see: a) T. Mukaiyama, T. Izawa, and K. Saigo, *Chem. Lett.*, **1974**, 323; b) T. Mukaiyama, J. Hanna, T. Inoue, and T. Sato, *Chem. Lett.*, **1974**, 381; c) T. Izawa and T. Mukaiyama, *Chem. Lett.*, **1975**, 161.

3) For palladium-catalyzed arylation, vinylation, and allylation of ketone with Bu_3SnOMe, see: M. Kosugi, I. Hagiwara, T. Sumiya, and T. Migita, *J. Chem. Soc., Chem. Commun.*, **1983**, 344; M. Kosugi, I. Hagiwara, and T. Migita, *Chem. Lett.*, **1983**, 839; J. Tsuji, I. Minami, and I. Shimizu, *Tetrahedron Lett.*, **24**, 4713 (1983).

4) A typical procedure is as follows. To a solution of propen-2-yl acetate (**1**, 0.31 g, 3 mmol), benzaldehyde (0.16 g, 1.5 mmol), $SnCl_2$ (0.57 g, 3 mmol), and benzyl alcohol (0.32 g, 3 mmol) in dichloromethane (3 ml) was added NCS (0.40 g, 3 mmol) on an ice-bath for 20 min. After being stirred for 20 min, the reaction mixture was poured into water (30 ml) and extracted with ether (100 ml). The extract was successively washed with 10% HCl, 10% Na_2SO_3, sat. $NaHCO_3$, and brine, and was dried over anhydrous $MgSO_4$. Evaporation of solvents and purification by preparative TLC (Harrison centrifugal thin-layer chromatotron; Merck Kiesel-gel 60 PF_{254} Art. 7749; hexane:ethyl acetate=20:1) afforded 0.33 g (87%) of 4-benzyloxy-4-phenylbutan-2-one as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 2.02 (s, 3H), 2.52 (dd, *J*=15.8, 4.0 Hz, 1H), 2.96 (dd, *J*=15.8, 9.4 Hz, 1H), 4.23 (d, *J*=11.4 Hz, 1H), 4.35 (d, *J*=11.4 Hz, 1H), 4.84 (dd, *J*=9.4, 4.0 Hz, 1H), 7.13-7.40 (m, 10H).

5) **8** (R^1: Ph): IR (KBr) 3066, 3035, 3006, 2929, 1773, 1717, 1497, 1458, 1419, 1363, 1300, 1270, 1174, 1016, 956, 765, 701; ^{1}H NMR ($CDCl_3$) δ 2.16 (s, 3H), 2.86 (dd, *J*=19.7, 10.4 Hz, 1H), 2.96 (dd, *J*=19.7, 10.4 Hz, 1H), 3.51 (dt, *J*=10.4, 8.7 Hz, 1H), 5.57 (d, *J*=8.7 Hz, 1H), 7.30-7.43 (m, 5H); MS (relative intensity) *m/z* 204 (M^+, 50), 176 (22), 162 (92), 161 (100), 147 (66), 133 (26), 115 (21), 105 (59), 98 (43), 77 (28), 71 (26), 70 (20), 57 (36), 55 (47); HRMS Found: 204.0787, Calcd for $C_{12}H_{12}O_3$: 204.0786.

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