

Aldol-Type Reaction by Propen-2-yl Acetate with NCS/SnCl₂/ROH

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The addition of N-chlorosuccinimide (NCS) to a solution of propen-2-yl acetate, aldehydes, SnCl₂, and benzyl alcohol in CH₂Cl₂ or CH₃CN 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 conditions²⁾ 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)/SnCl₂/ROH*.

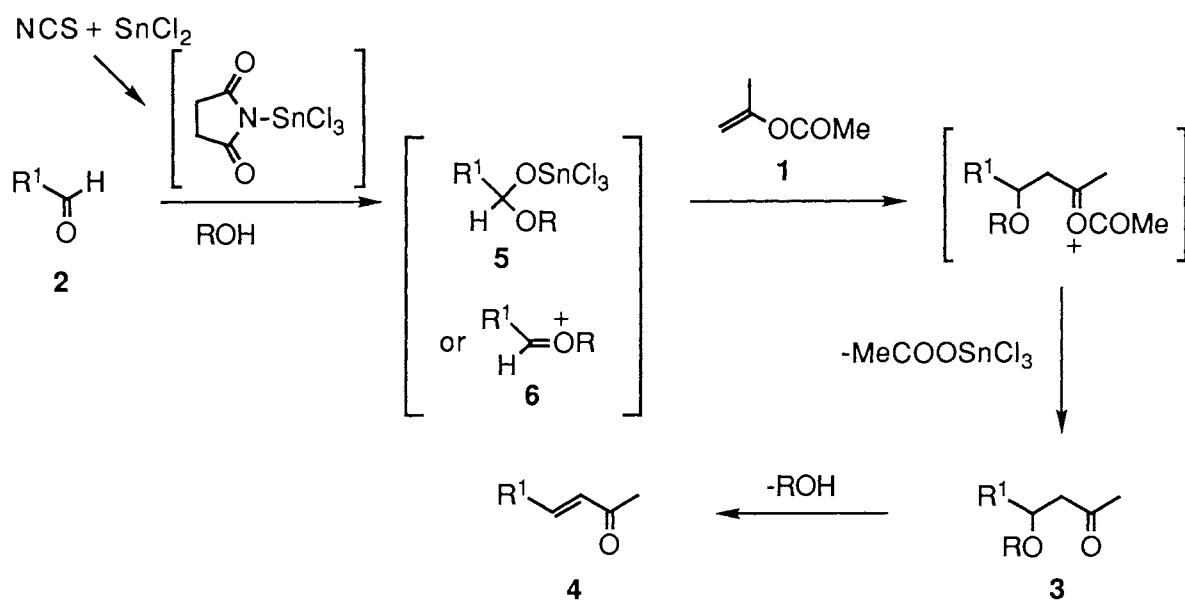
The aldol-type reaction was carried out by the addition of NCS (3 mmol) to a solution of propen-2-yl acetate (**1**, 3 mmol), aldehyde (**2**, 1.5 mmol), SnCl₂ (3 mmol), and alcohol (3 mmol) in dichloromethane (3 ml) on an ice-bath to produce 4-alkoxybutan-2-one **3** and/or 3-buten-2-one **4**. The 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: CH₃) 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/SnCl₂, followed by nucleophilic attack of **1** to **5** (or **6**), as illustrated in Scheme 1. In cases 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 SnCl₂ in CH₃CN 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** (R¹: C₆H₅, 71%; R¹: 4-MeOC₆H₄, 60%; R¹: 3,4-(CH₂O₂)C₆H₃, 65%) and no product was obtained in cases of alkanecarbaldehydes (R¹: n-C₆H₁₃; R¹: c-C₆H₁₁).

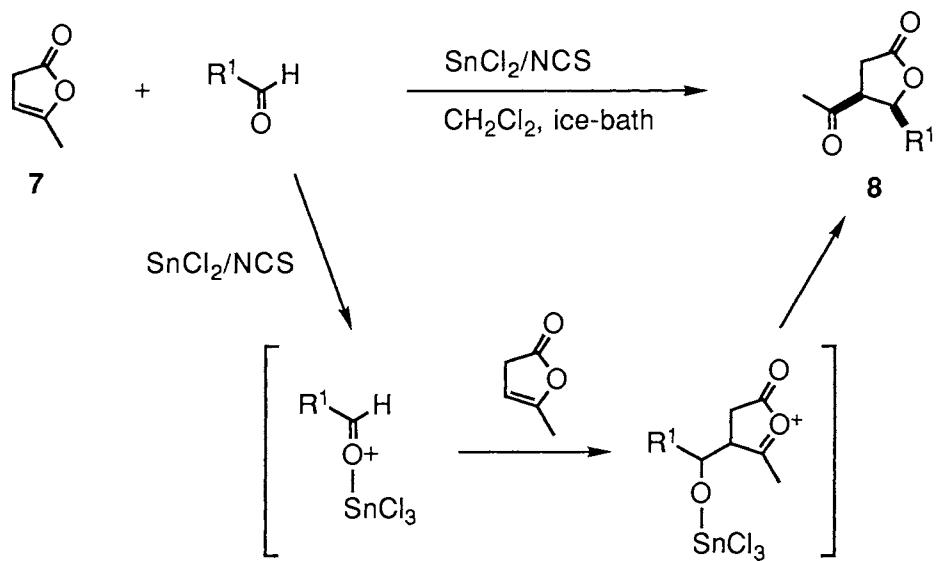
Table 1. Aldol-Type Reaction of Propen-2-yl Acetate (**1**) and Carbonyl Compound **2** with NCS/SnCl₂/ROH

Entry	Carbonyl Compound 2	Alcohol	Solvent	Time/min ^{a)}	Yield/% ^{b)}	
					R ¹	3
1	C ₆ H ₅	CH ₃	CH ₂ Cl ₂	10	46	50 ^{c)}
2	C ₆ H ₅	CH ₃ CH ₂	CH ₂ Cl ₂	10	84	---
3	C ₆ H ₅	CH ₂ =CHCH ₂	CH ₂ Cl ₂	10	91	---
4	C ₆ H ₅	C ₆ H ₅ CH ₂	CH ₂ Cl ₂	10	87	---
5	C ₆ H ₅	C ₆ H ₅ CH ₂	CH ₃ CN	10	73	---
6	4-NCC ₆ H ₄	C ₆ H ₅ CH ₂	CH ₂ Cl ₂	10	71	---
7	n-C ₆ H ₁₃	C ₆ H ₅ CH ₂	CH ₂ Cl ₂	10	63	---
8	CH ₂ =CH(CH ₂) ₈	C ₆ H ₅ CH ₂	CH ₂ Cl ₂	10	62	---
9	c-C ₆ H ₁₁	C ₆ H ₅ CH ₂	CH ₂ Cl ₂	20	76	---
10	C ₆ H ₅ (CH ₂) ₂	C ₆ H ₅ CH ₂	CH ₂ Cl ₂	10	80	---
11	C ₆ H ₅ (CH ₂) ₂	C ₆ H ₅ CH ₂	CH ₃ CN	20	37	---
12	C ₆ H ₅ (CH ₂) ₂	CH ₃	CH ₂ Cl 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/SnCl₂ in CH₂Cl₂ occurred in the absence of alcohol to afford the corresponding β-acetyl-γ-butyrolactones 8 stereoselectively [R¹: C₆H₅, 54% (\approx 100% *syn*);⁵⁾ R¹: n-C₆H₁₃, 34% ($>$ 95% *syn*); R¹: t-Bu, 44% (\approx 100% *syn*); R¹: CH₂=CH(CH₂)₈, 33% ($>$ 95% *syn*)] (Scheme 2). Even if an equimolar amount of methanol to SnCl₂ 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 PF₂₅₄ Art. 7749; hexane:ethyl acetate=20:1) afforded 0.33 g (87%) of 4-benzyloxy-4-phenylbutan-2-one as a colorless oil: ^1H 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; ^1H 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 $\text{C}_{12}\text{H}_{12}\text{O}_3$: 204.0786.

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