

SYNTHESIS OF ENOL CARBONATES FROM A REACTION
OF SILYL ENOLATES WITH 1H-IMIDAZOLYLURETHANE

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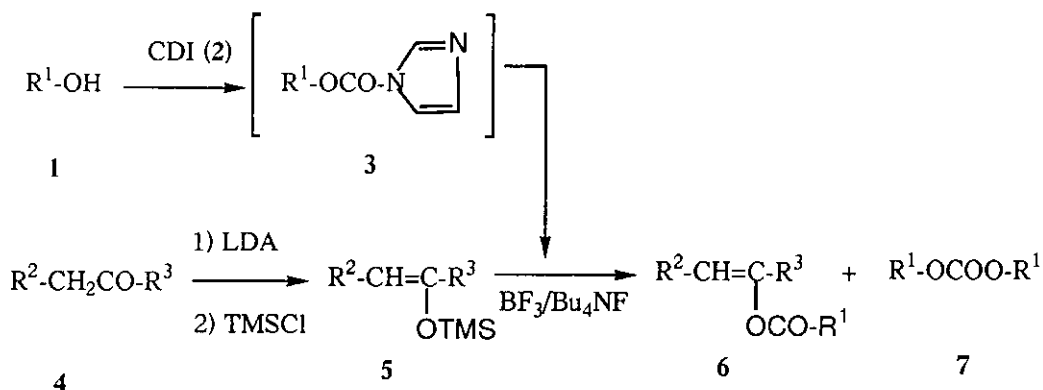
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Abstract - Enol Carbonates (6) were prepared by treatment of trimethylsilyl enolates (5) with 1-alkoxycarbonyl-1H-imidazoles (2) in the presence of boron trifluoride etherate and tetrabutylammonium fluoride.

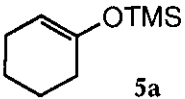
Kamijo and his co-workers reported an excellent preparation method of alkyl halides, in which alcohols were treated with *N,N'*-carbonyldiimidazole (2; CDI) and an excess of allyl halide.¹ In the course of this reaction, 1-alkoxycarbonyl-1H-imidazolium salt was presumed to be produced *in situ* as an intermediate. We have investigated the synthesis of azole derivatives,² and in this paper we report an application of the imidazolium salt to preparation of enol carbonates (6).



Scheme 1

Thus, 3-phenylpropanol (1a) was treated with CDI in dichloromethane to give 1-(3-phenylpropyl-oxycarbonyl)-1*H*-imidazole (3a). 1-Trimethylsilyloxycyclohexene (5a), boron trifluoride etherate and tetrabutylammonium fluoride were added to a solution of 3a in dichloromethane and the mixture was heated under reflux to give two unexpected products, 1-cyclohexenyl 3-phenylpropyl carbonate (6a; 17.9%) and bis(3-phenylpropyl) carbonate (7a; 8.2%).

Table 1. Enol Carbonate (6a) Formation under Various Conditions^{c)}

Entry	 5a (Equiv.)	Solvent	Temp.	Time (h)	Isolated Yield (%)	
					6a	7a
1	1.0	CH ₂ Cl ₂ ^{a)}	r.t.	2	18	8
2	1.0	CHCl ₃ ^{a)}	reflux	2	25	9
3	2.0	CHCl ₃ ^{a)}	reflux	2	33	24
4	2.0	THF ^{a)}	reflux	7	0	48
5	2.0	CHCl ₃ ^{b)}	reflux	2	61	12
6	2.0	CHCl ₃ ^{b)}	-78°C	2	56	0
7	2.0	CHCl ₃ ^{b)}	-20°C	2	84	0

- a) A solution of Bu₄NF in THF was added. b) A solution of Bu₄NF in CHCl₃ was added.
c) Use of 2 equiv. of the imidazolyl urethane (3a) against 5a gave only trace of 6a.

Result of the reaction under various condition is summarized in Table 1. The reaction of Entry 7 was carried out at -20°C in chloroform and the reaction proceeded in best yield of 6a (84.1%) without formation of 7a. Table 2 lists results of application of the reaction conditions to several alcohols and ketone silyl enolates. In literatures, enol carbonates have been prepared by treatment of ketone or metal enolate with alkyl chloroformate, however, simultaneous *O*- and *C*-alkoxycarbonylation and limitation in usable alkyl chloroformate have restricted their general use.^{3, 4} So the present reaction may be useful for preparation of not only various types of enol carbonate but also a new type of prodrugs from ketonic and alcoholic drugs.

The present reaction is presumed to proceed via an imidazolium intermediate (8).

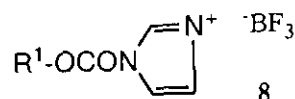


Table 2. Synthesis of Various Enol Carbonates (6) According to the Reaction Conditions of Entry 7 in Table 1

Entry	3 R ¹	5	Product (6)	Isolated Yield (%)
1	3a: Ph(CH ₂) ₃ -		6a	84
2	3b: Ph(CH ₂) ₂ -	//	6b	76
3	3c: PhCH ₂ -	//	6c	47
4	3d: PhCH(Me)-	//	6d	70
5	3e: PhCH ₂ C(Me) ₂ -	//	6e	56
6	3f:	//	6f	65
7	3a: Ph(CH ₂) ₂ -		6g	88
8	3e: PhCH ₂ C(Me) ₂ -	//	6h	48
9	3g: CH ₂ =CHCH ₂ -		6i	52

EXPERIMENTAL

General Procedure for the Preparation of the Imidazolylurethane (3); Preparation of 1-(3-Phenylpropyloxycarbonyl)-1*H*-imidazole (3a) as an Example: CDI (2; 585 mg, 3.6 mmol) was added under N₂ atmosphere to a solution of 3-phenyl-1-propanol (1a; 0.41 ml, 3.0 mmol), and the mixture was stirred for 1 h at room temperature. The reaction mixture was washed with water (5 ml × 2), dried over Na₂SO₄, and evaporated under reduced pressure. The oily residue was purified by silica gel column chromatography (solvent: AcOEt) to give a colorless

oil. Yield, 690 mg (quant.). Ir (CHCl₃): 1760 cm⁻¹ (>C=O). ¹H-Nmr (in CDCl₃, 270 MHz) δ ppm: 2.09-2.20 (m, 2H, -CH₂CH₂O-), 2.78 (t, 2H, Ar-CH₂-, J=7.4 Hz), 4.43 (t, 2H, -CH₂CH₂O-, J= 6.6 Hz), 7.06 (d, 1H, imidazole H, J=1.7 Hz), 7.18-7.38 (m, 5H, phenyl H), 7.38 (d, 1H, imidazole H, J=1.7 Hz), 8.07 (s, 1H, imidazole 2-H). Hrms (m/z): Calcd for C₁₃H₁₄N₂O₂: 230.1060. Found: 230.1068 (M⁺).

Other imidazolylurethanes were similarly prepared.

General Procedure for the Synthesis of the Enol Carbonates (6); Synthesis of 1-Cyclohexenyl 3-Phenylpropyl Carbonate (6a) as an Example : A mixture of boron trifluoride etherate (0.13 ml, 1.05 mmol), 1-trimethylsilyloxycyclohexene (5a, 340 mg, 2.0 mmol), tetrabutylammonium fluoride (523 mg, 2.0 mmol; in 1.0 ml of chloroform) and dry chloroform (1.0 ml) was added at -20°C under N₂ atmosphere to a solution of 2a (230 mg, 1.0 mmol) in dry chloroform (1.0 ml). After stirring for 3 h at the temperature, water (2.0 ml) and chloroform (3.0 ml × 3) were added, and the chloroform layer was dried over Na₂SO₄ and evaporated under reduced pressure to give an oily residue. The crude product was purified by silica gel column chromatography (solvent: CH₂Cl₂) gave a colorless oil. Yield, 220 mg (84%). Ir (CHCl₃): 1743 (>C=O), 1689 (>C=C<) cm⁻¹. ¹H-Nmr (in CDCl₃, 270 MHz) δ ppm: 1.55-1.64, 1.69-1.79 (m each, 2H each, >C=CH-CH₂CH₂CH₂-), 1.96-2.09 (m, 2H, ArCH₂CH₂-), 2.10-2.22 (m, 4H, -CH₂C=CHCH₂-), 2.73 (t, 2H, ArCH₂-, J=7.6 Hz), 4.17 (t, 2H, -CH₂CH₂O-, J=6.6 Hz), 5.47-5.50 (m, 1H, >C=CH-), 7.18-7.32 (m, 5H, phenyl H). Hrms (m/z): Calcd for C₁₆H₂₀O₃ = 260.1410. Found = 260.1437 (M⁺). When the above-mentioned reaction for the preparation of 6a was carried out under reflux, bis(3-phenylpropyl) carbonate (7a, 11.8%) and 6a (61.3%) were obtained after purification of the crude product by silica gel chromatography. 7a: Colorless oil. Ir (CHCl₃): 1739 cm⁻¹ (>C=O). ¹H-Nmr (CDCl₃, 270 MHz) δ ppm: 1.96-2.06 (m, 4H, -

$\text{CH}_2\text{CH}_2\text{O} \times 2$), 2.72 (t, 4H, $\text{ArCH}_2 \times 2$, $J=7.8$ Hz), 4.16 (t, 4H, $-\text{CH}_2\text{CH}_2\text{O} \times 2$, $J=6.6$ Hz), 7.17-7.32 (m, 10H, ArH).

6b: Colorless oil. Ir (CHCl_3): 1744 ($>\text{C}=\text{O}$), 1688 ($>\text{C}=\text{C}<$) cm^{-1} . $^1\text{H-Nmr}$ (in CDCl_3 , 270 MHz) δ ppm : 1.51-1.62, 1.69-1.77 (m each, 2H each, $>\text{C}=\text{CH}-\text{CH}_2\text{CH}_2\text{CH}_2-$), 2.07-2.17 (m, 4H, $-\text{CH}_2\text{C}=\text{CHCH}_2-$), 3.00 (t, 2H, ArCH_2- , $J=7.3$ Hz), 4.35 (t, 2H, $-\text{CH}_2\text{CH}_2\text{O}-$, $J=7.3$ Hz), 5.41-5.47 (m, 1H, $>\text{C}=\text{CH}-$), 7.22-7.34 (m, 5H, phenyl H). Hrms (m/z): Calcd for $\text{C}_{15}\text{H}_{18}\text{O}_3$: 246.1260. Found : 246.1246 (M^+).

6c: Colorless oil. Ir (CHCl_3): 1748 ($>\text{C}=\text{O}$), 1701 ($>\text{C}=\text{C}<$) cm^{-1} . $^1\text{H-Nmr}$ δ ppm (in CDCl_3 , 270 MHz): 1.55-1.63, 1.70-1.76 (m each, 2H each, $>\text{C}=\text{CH}-\text{CH}_2\text{CH}_2\text{CH}_2-$), 2.09-2.19 (m, 4H, $-\text{CH}_2\text{C}=\text{CHCH}_2-$), 5.17 (s, 2H, ArCH_2-), 5.47-5.50 (m, 1H, $>\text{C}=\text{CH}-$), 7.24-7.40 (m, 5H, phenyl H). Hrms (m/z): Calcd for $\text{C}_{14}\text{H}_{16}\text{O}_3$: 232.1100. Found : 232.1124 (M^+).

6d: Colorless oil. Ir (CHCl_3): 1741 ($>\text{C}=\text{O}$), 1689 ($>\text{C}=\text{C}<$) cm^{-1} . $^1\text{H-Nmr}$ (in CDCl_3 , 270 MHz) δ ppm : 1.55-1.62, 1.67-1.76 (m each, 2H each, $>\text{C}=\text{CH}-\text{CH}_2\text{CH}_2\text{CH}_2-$), 1.61 (d, 3H, $>\text{CH}(\text{CH}_3)$, $J=6.6$ Hz), 2.05-2.17 (m, 4H, $-\text{CH}_2\text{C}=\text{CHCH}_2-$), 5.43-5.46 (m, 1H, $>\text{C}=\text{CH}-$), 5.72 (q, 1H, $>\text{CH}(\text{CH}_3)$, $J=6.6$ Hz), 7.29-7.40 (m, 5H, phenyl H). Lrms (m/z): 105 (base, C_8H_9^+).

Hrms: M^+ was not observed.

6e: Colorless oil. Ir (CHCl_3): 1738 ($>\text{C}=\text{O}$), 1686 ($>\text{C}=\text{C}<$) cm^{-1} . $^1\text{H-Nmr}$ (in CDCl_3 , 270 MHz) δ ppm: 1.48 (s, 6H, $>\text{C}(\text{CH}_3)_2$), 1.55-1.64, 1.71-1.77 (m each, 2H each, $>\text{C}=\text{CH}-\text{CH}_2\text{CH}_2\text{CH}_2-$), 2.09-2.21 (m, 4H, $-\text{CH}_2\text{C}=\text{CHCH}_2-$), 3.12 (s, 2H, ArCH_2-), 5.45-5.48 (m, 1H, $>\text{C}=\text{CH}-$), 7.18-7.32 (m, 5H, phenyl H). Lrms (m/z): 91 (base, C_7H_7^+), 133, 215 (M^+-CO_2-

CH_3). Hrms: M^+ was not observed.

6f: Colorless oil. Ir (CHCl₃): 1744 (>C=O), 1690, 1660 (>C=C<) cm⁻¹. ¹H-Nmr (in CDCl₃, 270 MHz) δ ppm: 1.57-1.63, 1.70-1.78 (m, 2H each, >C=CH-CH₂CH₂CH₂-), 1.77 (d, 3H, -CH₃, J= 6.9 Hz), 2.08-2.21 (m, 4H, -CH₂C=CHCH₂-), 4.60-4.65 (m, 2H, -CH₂O-), 5.46-5.49 (m, 1H, >C=CH-), 5.57-5.84 (m, 2H, -CH=CHCH₃ and -OCH₂CH=CH-), 6.00-6.10 (m, 1H, -CH=CHCH₃), 6.23-6.34 (m, 1H, -OCH₂CH=CH-). Lrms (m/z): 178 (M⁺-CO₂). Hrms: M⁺ was not observed.

6g: Pale yellow oil. Ir (CHCl₃): 1750 (>C=O), 1658 (>C=C<) cm⁻¹. ¹H-Nmr (in CDCl₃, 270 MHz) δ ppm: 1.96-2.11 (m, 2H, ArCH₂CH₂-), 2.45 (dt, 2H, J=4.6, 8.1 Hz, >C=CHCH₂-), 2.74 (t, 2H, ArCH₂-, J=7.8 Hz), 2.87 (t, 1H, >C=CHCH₂CH-, J=8.1 Hz), 4.24 (t, 2H, -CH₂O-, J=6.4 Hz), 5.81 (t, 1H, >C=CH-, J=4.6 Hz), 7.17-7.33 (m, 9H, Ar-H). Hrms (m/z): Calcd for C₂₀H₂₀O₃: 308.1410. Found 308.1414 (M⁺).

6h: Colorless crystals, mp 68.2-68.9°C. Ir (CHCl₃): 1750 (>C=O), 1655 (>C=C<) cm⁻¹. ¹H-Nmr (in CDCl₃, 270 MHz) δ ppm: 1.51 (s, 6H, >C(CH₃)₂), 2.45 (dt, 2H, >C=CHCH₂-, J=4.6, 8.1 Hz), 2.88 (t, 2H, >C=CHCH₂CH-, J=8.1 Hz), 3.14 (s, 2H, ArCH₂-), 5.78 (t, 1H, >C=CH-, J=4.6 Hz), 7.15-7.33 (m, 9H, Ar-H). Hrms (m/z): Calcd for C₂₁H₂₂O₃: 322.1570. Found 322.1575 (M⁺). Anal. Calcd for C₂₁H₂₂O₃: C, 78.23; H, 6.88. Found: C, 78.10; H, 6.70.

6i: Ir (CHCl₃): 1751 (>C=O), 1657 (>C=C<) cm⁻¹. ¹H-Nmr (in CDCl₃, 270 MHz) δ ppm: 2.17-2.37 (m, 4H, -(CH₂)₂-), 4.65-4.68 (m, 6H, -CH₂O-), 5.28-6.03 (m, 6H, =CH- × 4 and -CH=CH₂). Hrms (m/z): Calcd for C₁₀H₁₂O₃: 180.0790. Found: 180.0766 (M⁺).

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Received, 20th January, 1995