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Allyl Isopropenyl Dicarbonate; A Convenient Reagent for the Preparation of Allyl Esters of Carboxylic Acids

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Abstract: Allyl isopropenyl dicarbonate(**1**) reacts with carboxylic acids in the presence of 4-dimethylaminopyridine(DMAP) catalyst to give allyl esters in high yields under mild conditions such as in a near-neutral medium at room temperature.

Esterification of carboxylic acids is an important unit reaction in organic synthesis, and many esterification methods and reagents have been published. We have previously described the preparations of *N*-succinimide ester for *N*-protected amino acids [1] and alkyl (Me, Et, *tert*-Bu, Allyl and Benzyl) ester of carboxylic acids [2] by use of carbonates having *N*-succinimide ester group and commercially available dialkyl dicarbonates, respectively. In these esterifications, DMAP was a remarkably effective catalyst. Allyl esters which could be deprotected by palladium catalysts under neutral conditions are especially useful as a protecting group for carboxylic acids; therefore, the allyl ester group has been widely used with unstable compounds under acid or base conditions, for example, peptides, *O*-glycopeptides, [3] penicillin derivative synthesis, [4] etc.

As part of our continuing research program on the chemistry of carbonates, we now wish to report the preparation of allyl esters of carboxylic acids using allyl isopropenyl dicarbonate **1** in the presence of DMPA catalyst. The reaction of reagent **1** with carboxylic acids **2** in the presence of a catalytic amount of DMAP in acetonitrile at room temperature resulted in liberation of carbon dioxide to give esters **3** in good yields.(Scheme) In this reaction, the most striking characteristic is the byproducts, namely, acetone and carbon dioxide; that is to say, the reaction may proceed in an almost neutral medium. On the other hand, in THF solution, although the reaction of **1** with *N*-carbobenzyloxy proline (Z-Pro) proceeded rapidly, a small amount of acid anhydride of Z-Pro was obtained together with allyl ester **3**. Allyl isopropenyl dicarbonate **1**[5] was prepared from isopropenyl chloroformate in the presence of 15-crown-5 catalyst and sodium allyl carbonate which could be prepared *in situ* from sodium allyl alkoxide (from allyl alcohol and sodium hydride) with excess carbon dioxide in THF at room temperature (yield 49%). Reagent **1** is a stable liquid under refrigeration (< ca. 5°C) and easy to handle. A typical experimental procedure is as follows (run 8): A solution of reagent **1**(81mg, 0.435 mmol (1.7 equiv. based on **2**)) in acetonitrile (0.5 ml) was added dropwise with stirring to a solution of cinnamic acid (37.1mg, 0.25 mmol.) in acetonitrile (1.5 ml) in the presence of DMAP (3mg, 0.025 mmol (10 mol%)) over 20 min. at room temperature. After a few minutes, the carboxylic acid in the reaction mixture was checked by TLC analysis. (If necessary, a few equivalents of reagent **1** are added to the reaction mixture until carboxylic acid disappears on TLC.) The reaction mixture was concentrated and the residue was purified by preparative TLC (SiO_2) to give allyl ester **3**. As shown in Table 1, the yields for several kinds of carboxylic acids are high. Even sterically hindered carboxylic acid such as camphanic acid (run 1) was reacted in good yield. $[\alpha]_D$ values of *N*-protected amino acids (runs 3 and 9) were in agreement with those reported. Although right now we have no accurate explanation for the reaction mechanism, carboxylate anion may attack the carbonyl group of the isopropenyloxy side which shows smaller partial atomic charge[6] than that of the allylic side of **1**; then eliminated allyl alcohol reacts with mixed anhydride **A** to give ester **3** with the release of acetone and CO_2.

In conclusion, preparation of allyl esters of carboxylic acids using **1** in the presence of DMAP catalyst proceeds in an almost neutral medium; therefore, this esterification method can be applied to acid and base-labile systems.

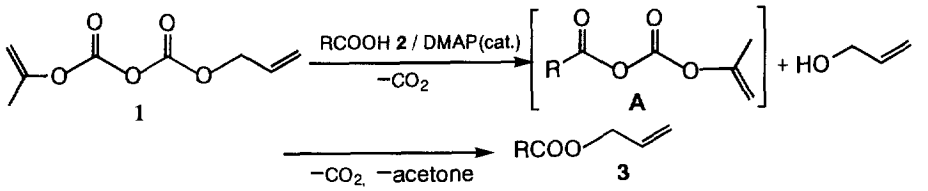
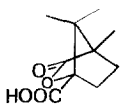
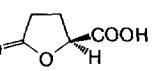
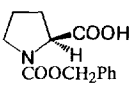
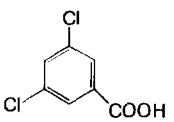
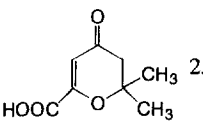
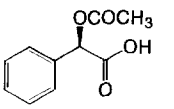
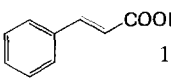


Table 1. Esterification of carboxylic acids using **1** in the presence of DMAP

Entry	RCOOH 2 (1 equiv.)	1 (equiv.)	Time (h)	3[a] Yield (%)
1		2.0	1	81[b]
2		1.9	3.5	91[c]
3	 (Z-Pro)	1.6	1	98[d]
4		2.0	2	84
5	$C_{17}H_{31}COOH$ (Linoleic Acid)	1.6	1	85
6		2.1	10	90
7		1.7	1	85[e]
8		1.7	1	100
9	*N*-(*t*-Butoxycarbonyl)-phenylalanine (Boc-Phe)	1.8	1	81[f]

a) All products were characterized by their IR, ^{1}H-NMR and mass spectra. b) $[\alpha]_D^{29}$= +14.6(*c* =1.14, $CHCl_3$), c) $[\alpha]_D^{30}$= +8.3 (*c* =0.53, $CHCl_3$), d) $[\alpha]_D^{26}$= -54.9 (*c* =1.2, MeOH), $[\alpha]_D^{21}$= -54.3 (*c* =1.2, MeOH)[Ref 2], e) $[\alpha]_D^{28}$= +97.7 (*c* =1.12, $CHCl_3$), f) $[\alpha]_D^{29}$= -10.7 (*c* =1.01, MeOH), $[\alpha]_D^{29}$= -10.2 (*c* =1.1, MeOH)[Ref 2],

References and notes

1) K. Takeda, A. Ayabe, M. Suzuki, Y. Konda, Y. Harigaya, *Synthesis*, **1991**, 689.
2) K. Takeda, A. Akiyama, H. Nakamura, S. Takizawa, Y. Mizuno, H. Takayanagi, Y. Harigaya, *Synthesis*, in press
3) H. Kunz, H.Waldman, *Angew. Chem. Int. Ed. Engl.*, *23*, 71(1984).
4) P.D. Jeffrey, S.W. McCombie, *J. Org. Chem.*, *47*, 587(1982).
5) This reaction was carried out for 48 h. IR νcm^{-1}(film): 2980,1840,1800,1780,1690. MS: m/z 142(M^+-CO_2).^{1}H-NMR (300 MHz,$CDCl_3$) δ: 2.02(3H, d, *J* CH_3,1-Ha=1.0 Hz, CH_3), 4.76(2H,dt, *J* 8-H_2,10-Ha=8-H_2,10-Hb=1.0 Hz, OCH_2), 4.80(1H, dt, J_1-Ha,CH_3=1.0 Hz, *J* 1-Ha,1-Hb=3.0 Hz, 1-Ha), 4.93(1H, d, *J* 1-Hb, 1-Ha=3.0 Hz, 1-Hb), 5.35(1H, ddd, *J* 10-Hb,10-Ha=1.0, J_{10}-Ha, 8-Ha or 8-Hb=3.0, J_{10}-Ha, 9-H=10.0Hz, 10-Ha), 5.43(1H, ddd, J_{10}-Ha,10-Hb=1.0Hz,J_{10}-Hb, 8-Ha or 8-Hb=3.0, *J* 9-H,10-Hb=17.0 Hz), Hb,8-Ha or 8-Hb=3.0, *J* 9-H,10-Hb=17.0 Hz), 5.95(1H, ddt, *J* 8-H_2,9-H=6.0, *J* 10-Ha,9-H=10.0, *J* 10-Hb,9-H=17.0 Hz, 9-H): ^{13}C-NMR(100 MHz,$CDCl_3$), δ 18.59, 70.20, 102.72, 12.344, 130.02, 146.02, 147.98, 152.62: Anal. Calcd for $C_8H_{10}O_5$: C,51.61; H,5.41. Found: C,51.24; H,5.62.
6) The partial atomic charge of compound **1** was calculated by *Nemesis* V2.11, R. J. Abraham, L. Griffiths, P. Loftus, *J. Comp.Chem.*,*3*, 407(1982), R. Abraham, G.H. Grant, I. S. Haworth, P. E. Smith, *J. Comput.-Aided Mol. Design*, *5*, 21(1991) and references cited therein.

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