(d, 1 H, H-7, $J_{7,9}$ = 1.6 Hz), 8.36 (d, 1 H, H-10, $J_{9,10}$ = 9.1 Hz), 8.82 (s, 1 H, H-6), 10.2-10.8 (br, 1 H, NH); MS, *m/z* (relative intensity) 234 (27.4, $M^+ + 2$), 232 (83.3, $M^+$), 205 (37.8), 203 (100). Anal. Calcd for $C_{12}H_9ClN_2O$: C, 61.89; H, 3.90; N, 12.04. Found: C, 62.00; H, 3.97; N, 12.00.

**1-[(3-Chloro-2-cyanophenyl)methyl]-1,5-dihydro-2*H*-pyrrol-2-one (7a).** In a similar manner as described for the synthesis of **6a**, oxime **3c** (1.67 g, 6.67 mmol) was added to hot polyphosphoric acid (31 g) to afford a product mixture (TLC, silica gel, ethyl acetate; $R_f$ **7a**, 0.28). Separation of the mixture by preparative HPLC (ethyl acetate) gave **7a** (0.68 g, 44%) as the major product (slightly yellow crystals). Recrystallization from absolute ethanol provided the analytical sample: mp 106.5-108.5 °C; IR ($CHCl_3$) 2240 (C≡N), 1680 (C=O) $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 4.07 (m, 2 H, H-5), 4.86 (s, 2 H, $NCH_2$), 6.22-6.26 (dt, 1 H, H-3, $J_{3,4}$ = 6 Hz, $J_{3,5}$ = 1.9 Hz), 7.15-7.20 (dt, 1 H, H-4, $J_{3,4}$ = 6 Hz, $J_{4,5}$ = 1.8 Hz), 7.31-7.57 (m, 3 H, Ar H); MS, *m/z* (relative intensity) 234 (10.3, $M^+ + 2$), 232 (36.4, $M^+$), 206 (29.7), 205 (39.9), 204 (97.6), 203 (100), 191 (18.4), 168 (19.1), 167 (24.6), 165 (76.2), 152 (29.8), 150 (96.3). Anal. Calcd for $C_{12}H_9ClN_2O$: C, 61.95; H, 3.90; N, 12.04. Found: C, 61.76; H, 4.06; N, 12.04.

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**Registry No.** (±)-**1a**, 78964-11-1; (±)-**1a** (methyl ester), 103301-78-6; (±)-**1b**, 103201-07-6; (±)-**1b** (methyl ester), 103201-06-5; (±)-**2a**, 103201-08-7; (±)-**2b**, 103201-09-8; (±)-**2c**, 103201-10-1; (±)-(*Z*)-**3a**, 103201-11-2; (±)-(*Z*)-**3b**, 103201-12-3; (±)-(*Z*)-**3c**, 103201-13-4; **6a**, 103201-14-5; **6b**, 103201-15-6; **7a**, 103201-16-7; (DL)-$HO_2C(CH_2)_2CH(NH_2)CO_2H \cdot H_2O$, 617-65-2; $3\text{-}ClC_6H_4CH_2Br$, 766-80-3; $H_2NOH \cdot HCl$, 5470-11-1; (±)-5-oxoproline, 149-87-1.

## Oxidation of Enolates by Dibenzyl Peroxydicarbonate to Carbonates of α-Hydroxy Carbonyl Compounds

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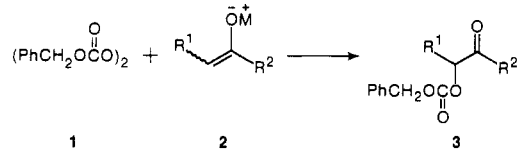
The importance of α-hydroxy carbonyl compounds has encouraged development of a variety of methods for their production,[1] including introduction of oxygen functionality adjacent to the carbonyl either directly[2,3] or via an intermediate derivative of an enol.[4,5] Studies on asymmetric oxidation of enolates bearing chiral ester[3a,b,e] or amide groups[3c,d] have achieved good to excellent diastereoselectivity by using MoOPH[2c] or 2-(phenylsulfonyl)-3-phenyloxaziridine[2e] as an oxidant. In related work, asymmetric lead tetraacetate oxidation of silyl ketene acetals derived from chiral esters gave α-acetoxy esters with 88-96% diastereoselection.[5a] Our interest in oxygen-18 labeling studies[6] led us to search for reagents that would accomplish such selective oxidations of chiral enolates and could also be readily prepared from isotopically enriched oxygen gas or hydrogen peroxide.[7] Preparation of the labeled oxaziridine reagent[8] would require several steps while the more accessible MoOPH[2c] often gives lower yields.[3c] Direct oxygenation using $O_2$ gas is less likely to allow stereochemical control[3a] and is often problematic if the product still bears a hydrogen at the α-carbon.[2b] This study describes the use of dibenzyl peroxydicarbonate (1) for oxidation of both chiral and achiral enolates **2** to form carbonates of α-hydroxy carbonyl compounds **3** (Scheme I).

**Scheme I**




Dibenzyl peroxydicarbonate (1) is easily prepared in one step from aqueous hydrogen peroxide and benzyl chloroformate under basic conditions.[9] It is an unexpectedly stable nonhygroscopic material that can be stored indefinitely without decomposition under normal conditions.[10] Although attack of carbon nucleophiles on the peroxy oxygen of benzoyl peroxide is well precedented,[2a,11] this type of reaction with dialkyl peroxydicarbonates has been examined primarily with enamine derivatives of β-di-

(1) For some recent stereocontrolled examples not involving introduction of α-oxygen functionality, see: (a) Lee, S. D.; Chan, T. H.; Kwon, K. S. *Tetrahedron Lett.* **1984**, *32*, 3399-3402. (b) Brown, H. C.; Pai, G. G.; Jadhav, P. K. *J. Am. Chem. Soc.* **1984**, *106*, 1531-1533. (c) Helmchen, G.;Wierzchowski, R. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 60-61. (d) Enomoto, M.; Ito, Y.; Katsuki, T.; Yamaguchi, M. *Tetrahedron Lett.* **1985**, *26*, 1343-1344. (e) Boireau, G.; Korenova, A.; Deberly, A.; Abenhaim, D. *Ibid.* **1985**, *26*, 4181-4182. (f) Wong, C. H.; Matos, J. R. *J. Org. Chem.* **1985**, *50*, 1992-1994.

(2) For leading references to some methods, see: (a) Lawesson, S. O.; Frisell, C.; Denney, D. Z.; Denney, D. B. *Tetrahedron Lett.* **1963**, *19*, 1229-1236. (b) Adam, W.; Cueto, O. *J. Org. Chem.* **1977**, *42*, 38-40. (c) Vedejs, E.; Engler, D. A.; Telschow, J. E. *Ibid.* **1978**, *43*, 188-196. (d) Bouillion, G.; Schank, K. *Chem. Ber.* **1980**, *113*, 2630-2635. (e) Davis, F. A.; Vishwakarma, L. C.; Billmers, J. M.; Finn, J. *J. Org. Chem.* **1984**, *49*, 3241-3243. (f) Moriarty, R. M.; Hou, K. C. *Tetrahedron Lett.* **1984**, *25*, 691-694. (g) Dunlap, N. K.; Sabol, M. R.; Watt, D. S. *Ibid.* **1984**, *25*, 5839-5842. (h) Williams, R. M.; Dung, J. S. *Ibid.* **1985**, *26*, 37-38. (i) Morizawa, Y.; Yasuda, A.; Uchida, K. *Ibid.* **1986**, *27*, 1833-1836.

(3) Asymmetric syntheses using direct oxidation: (a) Takano, S.; Morimoto, M.; Ogasawara, K. *J. Chem. Soc., Chem. Commun.* **1984**, 82-83. (b) Gamboni, R.; Mohr, P.; Waespe-Sardevic, N.; Tamm, C. *Tetrahedron Lett.* **1985**, *26*, 203-206. (c) Evans, D. A.; Morrissey, M. M.; Dorow, R. L. *J. Am. Chem. Soc.* **1985**, *107*, 4346-4348. (d) Davis, F. A.; Vishwakarma, L. C. *Tetrahedron Lett.* **1985**, *26*, 3539-3542. (e) Gamboni, R.; Tamm, C. *Helv. Chim. Acta* **1986**, *69*, 615-620.

(4) Some general methods: (a) Nambara, H.; Fishman, T. *J. Org. Chem.* **1962**, *27*, 2131-2135. (b) Maume, G. M.; Horning, E. C. *Tetrahedron Lett.* **1969**, 343-346. (c) Lee, T. V.; Toczek, J. *Tetrahedron Lett.* **1982**, *23*, 2917-2920. (d) Rubottom, G. M.; Gruber, J. M.; Marrero, R.; Juve, H. D., Jr.; Kim, C. W. *J. Org. Chem.* **1983**, *48*, 4940-4944. (e) Iwata, C.; Takemoto, Y.; Nakamura, A.; Imanishi, T. *Tetrahedron Lett.* **1985**, *26*, 3227-3230. (f) Andriamialisoa, R. Z.; Langlois, N.; Langlois, Y. *Ibid.* **1985**, *26*, 3563-3566. (g) Hoffman, R. V.; Carr, C. S.; Jankowski, B. C. *J. Org. Chem.* **1985**, *50*, 5148-5151. (h) McCormick, J. P.; Tomasik, W.; Johnson, M. W. *Tetrahedron Lett.* **1981**, *22*, 607-610.

(5) Asymmetric syntheses using enol derivative oxidation: (a) Oppolzer, W.; Dudfield, P. *Helv. Chim. Acta* **1985**, *68*, 216-219. (b) Iwata, C.; Takemoto, Y.; Kubota, H.; Kuroda, T. *Tetrahedron Lett.* **1985**, *26*, 3231-3234.

(6) Moore, R. N.; Bigam, G.; Chan, J. K.; Hogg, A. M.; Nakashima, T. T.; Vederas, J. C. *J. Am. Chem. Soc.* **1985**, *107*, 3694-3701 and references therein.

(7) Hydrogen peroxide labeled with oxygen-18 can be prepared in one step (>90% yield) from $^{18}O_2$: Sawaki, Y.; Foote, C. S. *J. Am. Chem. Soc.* **1979**, *101*, 6292-6296.

(8) Davis, F. A.; Stringer, O. D. *J. Org. Chem.* **1982**, *47*, 1774-1775.

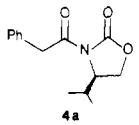
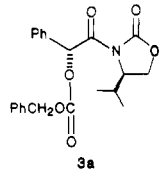
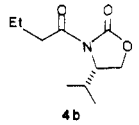
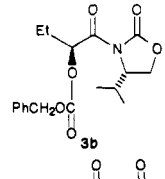
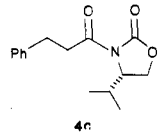
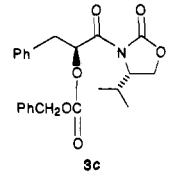
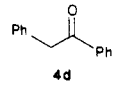
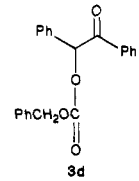
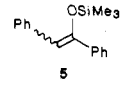
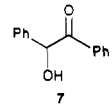
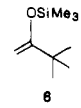
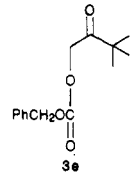
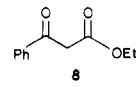
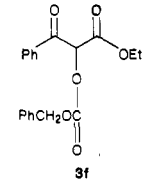
(9) Strain, F.; Bissinger, W. E.; Dial, W. R.; Rudoff, H.; DeWitt, B. J.; Stevens, H. C.; Langston, J. H. *J. Am. Chem. Soc.* **1950**, *72*, 1254-1263.

(10) Although many dialkyl peroxydicarbonates explode readily,[9] small quantities of solid dibenzyl peroxydicarbonate (1) from various preparations could not be detonated by heating, grinding, or striking with a hammer. Nevertheless, all preparations of 1 were done on modest scale (≤0.1 mol) behind a safety shield, and the usual precautions for dealing with peroxides were observed (avoidance of metals, heat, intense light, etc.).

(11) Rawlinson, D. J.; Sosnovsky, G. *Synthesis* **1972**, 1-28. See also: Rawlinson, D. J.; Sosnovsky, G. *Ibid.* **1973**, 567-603.

0022-3263/86/1951-3700$01.50/0 

**Table I. Oxidation of Enolates by 1 at −78 °C**

| starting material | base/reagent | product | % yield[a] | isomer ratio |
|---|---|---|---|---|
|  4a | $LiN(Me_3Si)_2$ |  3a | 82 | >99:1[b] |
|  4b | $LiN(Me_3Si)_2$ |  3b | 87 | >98:2[c] |
|  4c | $LiN(Me_3Si)_2$ |  3c | 81 | 94:6[c] |
|  4d | $LiN(Me_3Si)_2$ |  3d | 8 | |
| 4d | *t*-BuLi | 3d | 36 | |
| 4d | $KN(Me_3Si)_2$ | 3d | 71 | |
|  5 | *n*-BuLi | 3d | 66 | |
| 5 | $TiCl_4$ |  7 | 33 | |
| 5 | $SnCl_4$ | 7 | 19 | |
|  6 | *n*-BuLi |  3e | 62 | |
|  8 | $LiN(Me_3Si)_2$ |  3f | 45[d] | |

[a] Yield of isolated compound. Structure of the major diastereomer is shown. [b] Diastereomeric ratio determined by HPLC (see Experimental Section). [c] Diastereomeric ratio determined by NMR. [d] Yield is 58% based on recovered starting material.

carbonyl compounds.[2d,12,13] Schank and co-workers have shown in those studies that if the initial product still bears an α-hydrogen a second oxidation can occur very rapidly.[12a] This was not expected to be a problem with the far less acidic monocarbonyl compounds **3**. The benzyloxycarbonyl group of **3** can be readily removed by hydrogenolysis to afford the α-hydroxy carbonyl compound.[14]

Chiral enolates derived from readily available oxazolidinone carboximides **4a–c** (Table I) were chosen for oxidation by **1** because elegant studies by Evans and coworkers had previously demonstrated that such systems afford a high degree of diastereoselectivity and excellent yields in reactions with electrophiles (including oxygen donors).[3c] Reaction of these enolates with dibenzyl peroxydicarbonate (**1**) in THF at −78 °C rapidly produced the carbonates **3a–c**. The isolated yields and diastereomeric ratios (Table I) are within a few percent of those obtained by Evans and co-workers for direct hydroxylation using 2-(phenylsulfonyl)-3-phenyloxaziridine.[3c] Since the present

(12) (a) Schank, K.; Adler, M. *Chem. Ber.* **1981**, *114*, 2019–2028 and references therein. (b) Schank, K.; Blattner, R.; Schmidt, V.; Hasenfratz, H. *Ibid.* **1981**, *114*, 1938–1950.

(13) A tin nucleophile, tris(trimethylsilylmethyl)stannyllithium, has been reported to attack dicyclohexyl peroxydicarbonate on oxygen: Kalinina, G. S.; Basalgina, T. A.; Vyazankin, N. S.; Razuvaev, G. A.; Yablokov, V. A.; Yablokova, N. V. *J. Organomet. Chem.* **1975**, *96*, 212–223.

(14) Greene, T. W. *Protective Groups in Organic Synthesis*; Wiley: New York, 1981; p 61.

procedure generates the latent α-hydroxy group protected as a carbonate, no special precautions are necessary during quenching of the reaction mixture to avoid intramolecular acyl transfer.[15]

The isomeric ratios were determined by high-field $^1H$ NMR of the carbonates **3a–c** and by high-pressure liquid chromatography (HPLC) of **3a**. Compound **3a** and its diastereomer with the opposite configuration (*S*) at the α position were also synthesized independently from racemic mandelic acid and separated by HPLC. Cleavage of **3a** (prepared by oxidation of **4a** by **1**) with potassium hydroxide to (*R*)-(−)-mandelic acid confirmed its stereochemistry. Although 8% epimerization occurred during this cleavage, isomerically pure methyl mandelate should be available by hydrogenolysis of the benzyl carbonate functionality[14] followed by methanolysis of the chiral auxiliary.[3c]

The oxidation of simple achiral ketones and esters by **1** proved to be much more difficult. In many cases the presence of amines derived from the base used to generate the enolate (e.g., lithium diisopropylamide, $LiN(Me_3Si)_2$, etc.) leads to complex mixtures and low yields. This appears to be due at least partly to their rapid reaction with the oxidizing agent **1**. Under such conditions, more reactive potassium enolates formed with $KN(Me_3Si)_2$ (KHMDS)[16] generally give better yields than the lithium analogues (e.g., deoxybenzoin (**4d**) → **3d**), in agreement with observations reported for the oxaziridine method.[2e] The higher yields of oxazolidinone derivatives **3a–c** may also be partly due to steric inhibition of their reaction with the amine byproducts. To avoid complications caused by amines, deoxybenzoin (**4d**) and 3,3-dimethyl-2-butanone were converted to their silyl enol ethers **5** and **6**,[17] respectively, which were then cleaved to their enolates with butyllithium.[18] Reaction with dibenzyl peroxydicarbonate (**1**) gave reasonable yields of **3d** and **3e**. Attempts to perform the oxidation by generation of the stannic or titanium enolates[19,20] from **5** resulted in complex mixtures from which low yields of benzoin (**7**) could be obtained.

Monooxidation at an active *methylene* group of a β-dicarbonyl compound is often difficult by other methods. For example MoOPH complexes with ethyl benzoylacetate (**8**) and fails to react,[2c] whereas previous attempts to oxidize 1,3-cyclohexandiones with **1** gave primarily bisacyloxylation and subsequent transformation products.[12b] Although benzoyl peroxide can give good yields of benzoyloxylation, the benzoyl group is difficult to remove without fission of a bond to the α-carbon (i.e., deacylation, decarboxylation).[2a,11] With the present method, ethyl benzoylacetate (**8**) can be converted in reasonable yield to **3f**, which should be more easily deprotected to the parent hydroxy compound.[14]

In summary, dibenzyl peroxydicarbonate (**1**) is a stable easily prepared reagent that reacts with a variety of enolates **2** to form carbonate derivatives **3** of α-hydroxy carbonyl compounds in modest to good yields. This approach is especially useful for asymmetric oxidation of enolates of oxazolidinone carboximides **4a–c**. Simpler ketones and esters are often best oxidized with **1** by using amine-free lithium enolates generated from the corresponding silyl enol ethers with butylithium. Although with simpler achiral carbonyl compounds the oxaziridine oxidation generally gives higher yields,[2e] the present method should allow more ready access to $^{18}O$-labeled compounds.

## Experimental Section

The general procedures and instrumentation that were employed have been described previously.[21] In the present work, Bruker WM360 and AM300 NMR spectrometers were also used. High-pressure liquid chromatography (HPLC) was done with a Hewlett-Packard 1082B instrument equipped with a variable wavelength UV detector set to 254 nm.

**Dibenzyl Peroxydicarbonate (1).** A modification of the literature procedure[9] was used with precautions appropriate to dealing with organic peroxides.[10] Cold (0 °C) solutions of hydrogen peroxide (2.7 mL, 30% in $H_2O$, 24 mmol) and 2.35 N NaOH (20 mL) were mixed and added with rapid stirring over 15 min to benzyl chloroformate (8.02 g, 47 mmol) at 0 °C. Hexane (30 mL) was added, and the mixture was stirred 15 min and filtered. The precipitate was washed with hexane (3 × 15 mL), dissolved in $CHCl_3$, and dried ($MgSO_4$). Slow addition of hexane gave a crystalline precipitate, which was filtered, washed with hexane (2 × 15 mL), and dried in vacuo (20 °C) to give 2.8 g (53% yield) of dibenzyl peroxydicarbonate (**1**): mp 101 °C dec (lit.[9] mp 101–102 °C); IR ($CH_2Cl_2$ cast) 1798, 1456, 1376, 1228, 1206 $cm^{-1}$; $^1H$ NMR (80 MHz, $CDCl_3$) δ 7.40 (br s, 10 H), 5.32 (s, 4 H). Anal. Calcd for $C_{16}H_{14}O_6$: C, 63.57; H, 4.66. Found: C, 63.52; H, 4.64.

**(*R*)-3-(Phenylacetyl)-4-isopropyloxazolidin-2-one (4a).** This compound was prepared according to the procedure of Evans and co-workers[22] from phenylacetyl chloride and (*R*)-4-isopropyloxazolidin-2-one: $[\alpha]_D$ −82.9° (*c* 2.6, $CHCl_3$); IR ($CHCl_3$ cast) 2960, 1776, 1700, 1395, 1355 $cm^{-1}$; $^1H$ NMR (80 MHz, $CDCl_3$) δ 7.31 (br s, 5 H), 4.6–4.1 (m, 5 H), 2.6–2.2 (m, 1 H), 0.90 (d, 3 H, *J* = 7 Hz), 0.82 (d, 3 H, *J* = 7 Hz); exact mass 247.1206 (247.1208 calcd for $C_{14}H_{17}NO_3$). Anal. Calcd for $C_{14}H_{17}NO_3$: C, 67.99; H, 6.92; N, 5.66. Found: C, 68.10; H, 6.81; N, 5.39.

**Oxidation of 4a to (4*R*,2′*R*)-3-[2-(((Benzyloxy)carbonyl)oxy)-2-phenyl-1-oxoethyl]-4-isopropyloxazolidin-2-one (3a).** A 0.44 M solution of $LiN(Me_3Si)_2$ (4.0 mL, 1.7 mmol) was added to a solution of oxazolidinone carboximide **4a** (401 mg, 1.62 mmol) in THF (2 mL) at −78 °C. The solution was stirred for 0.5 h, and a solution of dibenzyl peroxydicarbonate (**1**) (480 mg, 1.59 mmol) in THF (4 mL) was added. Stirring at −78 °C was continued for 0.5 h, and acetic acid (96 mg, 1.6 mmol) was added. The solution was warmed to 0 °C, water (20 mL) was added, and the resulting mixture was extracted with ether (3 × 20 mL) and $CH_2Cl_2$ (2 × 10 mL). The combined organic layers were dried ($Na_2SO_4$), concentrated in vacuo, and purified by flash chromatography[23] (30% EtOAc/hexane). Recrystallization (EtOAc/hexane) gave 526 mg (82%) of **3a**: mp 160–161 °C; $[\alpha]_D$ −121.7° (*c* 3.01, $CHCl_3$); IR ($CH_2Cl_2$ cast) 3060, 1782, 1746, 1709, 1387, 1244 $cm^{-1}$; $^1H$ NMR (80 MHz, $CDCl_3$) δ 7.7–7.3 (m, 10 H), 7.37 (s, 1 H), 5.16 (s, 2 H), 4.4–4.0 (m, 3 H), 2.6–2.2 (m, 1 H), 0.95 (d, 3 H, *J* = 6 Hz), 0.85 (d, 3 H, *J* = 6 Hz); exact mass 397.1525 (397.1526 calcd for $C_{22}H_{23}NO_6$). Anal. Calcd for $C_{22}H_{23}NO_6$: C, 66.48; H, 5.83; N, 3.41. Found: C, 66.50; H, 5.83; N, 3.56.

**Independent Preparation and Separation of 3a and Its 2′*S* Diastereomer.** Butyllithium (0.91 M in hexane, 24.1 mL, 20. mmol) was added to a solution of (±)-mandelic acid (1.52 g, 10. mmol) in THF (25 mL) at −78 °C. A solution of benzyl chloroformate (2.85 mL, 20. mmol) in THF (5 mL) was added, and the mixture was warmed to 20 °C for 30 min. Water (25 mL) was added, the mixture was extracted with ether (3 × 25 mL) to remove impurities, and the aqueous phase was acidified to pH 2 with HCl before extraction of the product with ether (3 × 25 mL). These ether extracts were dried ($Na_2SO_4$) and concentrated in vacuo to give 2.51 g (87% yield) of 2-[((benzyloxy)carbonyl)-

(15) See footnote 12 in ref 3c.
(16) Brown, C. A. *J. Org. Chem.* **1974**, *39*, 3913–3918.
(17) (a) Miyano, S.; Hokari, H.; Hashimoto, H. *Bull. Chem. Soc. Jpn.* **1982**, *55*, 534–539. (b) House, H. O.; Czuba, L. J.; Gall, M.; Olmstead, H. D. *J. Org. Chem.* **1969**, *34*, 2324–2336.
(18) Kuwajima, I.; Nakamura, E. *Acc. Chem. Res.* **1985**, *18*, 181–187.
(19) Nakamura, E.; Kuwajima, I. *Chem. Lett.* **1983**, 59–62.
(20) Reetz, M. T.; Mainer, W. F. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 48–49.
(21) Arnold, L. D.; Kalantar, T. H.; Vederas, J. C. *J. Am. Chem. Soc.* **1985**, *107*, 7105–7109.
(22) (a) Evans, D. A.; Bartroli, J.; Shih, T. L. *J. Am. Chem. Soc.* **1981**, *103*, 2127–2129. (b) Evans, D. A.; Mathre, D. J.; Scott, W. L. *J. Org. Chem.* **1985**, *50*, 1830–1835.
(23) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923–2925.

oxy]-2-phenylacetic acid: mp 117–119 °C (lit.[24] mp 123–125 °C); IR ($CHCl_3$ cast) 3450, 3000, 1727, 1247 $cm^{-1}$; $^1H$ NMR (80 MHz, $CDCl_3$) $\delta$ 9.97 (br s, 1 H), 7.32 (br s, 10 H), 5.87 (s, 1 H); 5.17 (s, 2 H); MS (CI, $NH_3$), $m/e$ 304 ($M^+ \cdot NH_4$). Anal. Calcd for $C_{16}H_{14}O_5$: C, 67.12; H, 4.92. Found: C, 67.24; H, 5.04.

A solution of 2-[((benzyloxy)carbonyl)oxy]-2-phenylacetic acid (344 mg, 1.20 mmol) in benzene (5 mL) at 5 °C was treated with oxalyl chloride (0.20 mL, 2.4 mmol) and stirred for 12 h. The volatile components were removed in vacuo (5 mmHg), and the residue was dissolved in dry THF (2 mL). This solution was added dropwise to a cooled (0 °C) solution of the anion generated from (*R*)-4-isopropyloxazolidin-2-one (129 mg, 1.0 mmol) and butyllithium (0.91 M in hexane, 1.20 mL, 1.09 mmol) in THF (5 mL).[22,25] The mixture was stirred for 30 min, 5% sodium bicarbonate solution (4 mL) was added, and the product was extracted with ether (3 × 25 mL). The organic phase was dried ($Na_2SO_4$), concentrated in vacuo, and purified by flash chromatography[23] (30% EtOAc/hexane) to give 154 mg (38%) of a mixture of **3a** and its 2′*S* diastereomer. Although the two compounds showed similar spectral and thin-layer chromatographic behavior, the 2′*S* isomer could be clearly seen in $^1H$ NMR by its 2′ hydrogen resonance at $\delta$ 7.08 (s, 1 H) and by its isopropyl methyl resonances at $\delta$ 0.76 (d, 3 H, $J$ = 6 Hz) and 0.43 (d, 3 H, $J$ = 6 Hz).

Separation of the two isomers was achieved by HPLC on a silica gel column (Whatman Partisil 10 M9/25) using a 35–40% gradient of EtOAc/hexane at 20 °C with a flow of 2 mL/min. The retention times of **3a** and its 2′*S* isomer were 9.30 and 10.33 min, respectively. Injections of **3a** obtained by oxidation of **4a** with **1** gave the peak at 9.3 min but showed no detectable peak at 10.3 min.

**Hydrolysis of 3a to (*R*)-(−)-Mandelic Acid.** Solid potassium hydroxide (170 mg, 3.04 mmol) was added to a solution of **3a** (obtained from oxidation of **4a**) (238 mg, 0.609 mmol) in water/THF (1:3, 4 mL). The mixture was stirred at 20 °C for 4 h, extracted with ether (3 × 15 mL), acidified to pH 2, and extracted with ether (3 × 15 mL). The organic phases from the second extraction were dried ($MgSO_4$) and concentrated in vacuo. The resulting crude mandelic acid was converted to its potassium salt by using aqueous $KHCO_3$, and this was purified by ion-exchange chromatography on Biorad AG1 (acetate form) with water and aqueous 2.5 N $CF_3COOH$ as eluent. Concentration in vacuo gave (*R*)-(−)-mandelic acid: mp 129–130 °C (lit.[26] mp 131–133 °C); $[\alpha]_D$ −128.5° (*c* 2.5, $H_2O$) [lit.[26] $[\alpha]_D$ −153.0° (*c* 2.5, $H_2O$).

**(4*S*,2′*S*)-3-[2-(((Benzyloxy)carbonyl)oxy)-1-oxobutyl]-4-isopropyloxazolidin-2-one (3b).** The procedure used to transform **4a** to **3a** was employed to convert the known oxazolidinone **4b**[25] (1.0 mmol) to **3b** in 87% isolated yield: mp 96–97 °C; $[\alpha]_D$ +13.8° (*c* 2.6, $CHCl_3$); IR ($CHCl_3$ cast) 2880, 1781, 1748, 1713, 1389, 1280, 1247, 1205 $cm^{-1}$; $^1H$ NMR (360 MHz, $CDCl_3$) $\delta$ 7.4–7.3 (m, 5 H), 5.85 (dd, 1 H, $J$ = 3.2, 8.4 Hz), 5.18 (br s, 2 H), 4.5–4.2 (m, 3 H), 2.5–2.3 (m, 1 H), 2.0–1.7 (m, 2 H), 1.04 (t, 3 H, $J$ = 7 Hz), 1.0–0.80 (m, 6 H); exact mass 349.1525 (349.1525 calcd for $C_{18}H_{23}NO_6$). Anal. Calcd for $C_{18}H_{23}NO_6$: C, 61.88; H, 6.63; N, 4.00. Found: C, 61.49; H, 6.61; N, 4.16.

**(4*S*,2′*S*)-3-[2-(((Benzyloxy)carbonyl)oxy)-3-phenyl-1-oxopropyl]-4-isopropyloxazolidin-2-one (3c).** The procedure used to transform **4a** to **3a** was employed to convert the known oxazolidinone **4c**[22b] (1.0 mmol) to **3c** in 81% isolated yield. In this reaction 6% of the other diastereomer with 2′*R* configuration could be detected by NMR: mp 89–90 °C; $[\alpha]_D$ +43.6° (*c* 2.5, $CHCl_3$); IR ($CHCl_3$ cast) 2960, 1779, 1747, 1712, 1388, 1245, 1205 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.4–7.2 (m, 10 H), 6.16 (dd, 1 H, $J$ = 3.5, 10. Hz), 5.10 (m, 2 H), 4.36 (m, 1 H), 4.3–4.2 (m, 2 H), 3.18 (dd, 1 H, $J$ = 3.5, 14 Hz), 3.02 (dd, 1 H, $J$ = 10, 14 Hz), 2.42 (m, 1 H), 0.89 (d, 3 H, $J$ = 5 Hz), 0.82 (m, 3 H); MS (CI, $NH_3$), $m/e$ (relative intensity) 429 (100, $M^+ \cdot NH_4$). Anal. Calcd for $C_{23}H_{25}NO_6$: C, 67.14; H, 6.12; N, 3.40. Found: C, 67.19; H, 6.29; N, 3.55.

The minor isomer (6%) showed similar spectral and thin-layer chromatographic behavior, but it could be easily seen in $^1H$ NMR by its 2′ hydrogen resonance at $\delta$ 6.10 (dd, 1 H, $J$ = 3.5, 10.0 Hz) and by its isopropyl methyl resonances at $\delta$ 0.87 (d, 3 H, $J$ = 5 Hz) and 0.78 (m, 3 H).

**2-[((Benzyloxy)carbonyl)oxy]-1,2-diphenylethanone (3d).** The oxidation of deoxybenzoin (**4d**) (1.0 mmol) to **3d** was best done by using the procedure outlined for conversion of **4a** to **3a** except with substitution of $KN(Me_3Si)_2$ for $LiN(Me_3Si)_2$. Flash chromatography[23] (1% $CHCl_3$, 18% EtOAc, hexane) of the crude product gave a 71% yield of pure **3d**: mp 108 °C; IR ($CHCl_3$ cast) 1745, 1696, 1276, 1244, 948 $cm^{-1}$; $^1H$ NMR (80 MHz, $CDCl_3$) $\delta$ 8.2–7.9 (m, 2 H), 7.7–7.2 (m, 13 H), 6.82 (s, 1 H), 5.26 (s, 2 H); MS (CI, $NH_3$), $m/e$ 364 ($M^+ \cdot NH_4$). Anal. Calcd for $C_{22}H_{18}O_4$: C, 76.28; H, 5.23. Found: C, 76.06; H, 5.28.

**Formation of 3d from Deoxybenzoin Trimethylsilyl Enol Ether 5.** The silyl enol ether **5**[17] (268 mg, 1.00 mmol) in THF (5 mL) was treated at 0 °C with butyllithium (0.63 mL, 1.58 M in hexane, 1.00 mmol) and stirred for 1.5 h. The solution was cooled to −78 °C, and a solution of dibenzyl peroxydicarbonate (**1**) (304 mg, 1.00 mmol) in THF (3 mL) was added. The mixture was stirred 15 min at −78 °C and warmed to −40 °C for 1 h before being poured into concentrated $NH_4Cl$ solution. This was extracted with ether (3 × 20 mL), and the extracts were dried and concentrated in vacuo. Flash chromatography[23] (1% $CHCl_3$, 18% EtOAc, hexane) of the residue gave 228 mg (66% yield) of **3d**, whose chromatographic and spectral properties were identical with those described above.

**Benzoin (7) from 5.** Titanium tetrachloride (0.14 mL, 1.0 mmol) was added to a solution of the silyl enol ether **5**[17] (268 mg, 1.00 mmol) in dry $CH_2Cl_2$ (2 mL) at −78 °C. The mixture was stirred 15 min, a solution of dibenzyl peroxydicarbonate (**1**) (303 mg, 1.00 mmol) in THF (3 mL) was added, and the reaction mixture was warmed to 20 °C for 0.5 h before being poured into ice–water (15 mL). The aqueous phase was extracted with $CHCl_3$ (3 × 15 mL), and the combined organic extracts were dried and concentrated in vacuo. Flash chromatography[23] (20% EtOAc, hexane) gave 70.0 mg (33% yield) of benzoin (**7**) identical in all respects with authentic material. The stannic chloride reaction was done similarly except that the temperature was kept at 5 °C throughout.

**1-[((Benzyloxy)carbonyl)oxy]-3,3-dimethyl-2-butanone (3e).** The silyl enol ether **6**[17] (172 mg, 1.00 mmol) was oxidized with dibenzyl peroxydicarbonate (**1**) by using the procedure described for conversion of **5** to **3d**. Chromatography of the crude product as before gave 155 mg (62% yield) of **3c**: mp 58 °C; IR ($CHCl_3$ cast) 2990, 1762, 1731, 1285, 1273 $cm^{-1}$; $^1H$ NMR (80 MHz, $CDCl_3$) $\delta$ 7.30 (br s, 5 H), 5.20 (s, 2 H), 4.92 (s, 2 H), 1.15 (s, 9 H); exact mass 250.1214 (250.1205 calcd for $C_{14}H_{18}O_4$). Anal. Calcd for $C_{14}H_{18}O_4$: C, 67.18; H, 7.24. Found: C, 67.17; H, 7.29.

**Ethyl 2-Benzoyl-2-[((benzyloxy)carbonyl)oxy]acetate (3f).** Ethyl benzoylacetate (**8**) (190 mg, 1.0 mmol) was oxidized with **1** (312 mg, 1.0 mmol) by using the procedure described for the conversion of **4a** to **3a** except that the mixture was not quenched with acetic acid at −78 °C but instead was warmed over 1 h to 0 °C. Concentrated $NH_4Cl$ (20 mL) was added, and the mixture was extracted with ether (3 × 15 mL). The dried ether extracts were concentrated in vacuo and purified by flash chromatography[23] (14% EtOAc, hexane) to give 26 mg (13%) of recovered ethyl benzoylacetate and 154 mg (45% yield) of **3f** as an oil: IR ($CHCl_3$ cast) 1751, 1695, 1278, 1234 $cm^{-1}$; $^1H$ NMR (80 MHz, $CDCl_3$) $\delta$ 8.2–8.0 (m, 2 H), 7.8–7.2 (m, 8 H), 6.20 (s, 1 H), 5.25 (s, 2 H), 4.27 (q, 2 H, $J$ = 7.3 Hz), 1.20 (t, 3 H, $J$ = 7.3 Hz); exact mass 342.1101 (342.1104 calcd for $C_{19}H_{18}O_6$). Anal. Calcd for $C_{19}H_{18}O_6$: C, 66.66; H, 5.29. Found: C, 66.56; H, 5.40.

**Acknowledgment.** We thank Professor David A. Evans (Harvard University) for a preprint of his work[3c] and for helpful discussions. Financial support from the Natural Sciences and Engineering Research Council of Canada and from the National Institutes of Health (GM29826) is gratefully acknowledged.

**Registry No.** **1**, 2144-45-8; **3a** (isomer 1), 103422-96-4; **3a** (isomer 2), 103423-02-5; **3b**, 103422-97-5; **3c** (isomer 1), 103423-00-3; **3c** (isomer 2), 103422-98-6; (±)-**3d**, 103422-99-7; **3e**, 103423-03-6; (±)-**3f**, 103423-04-7; **4a**, 103422-95-3; **4b**, 80697-93-4; **4c**, 95798-31-5; **4d**, 451-40-1; **5**, 72223-17-7; **6**, 17510-46-2; (±)-**7**,

(24) Marshall, J. R.; Walker, J. *J. Chem. Soc.* **1952**, 467–475.
(25) Evans, D. A.; Ennis, M. D.; Mathre, D. J. *J. Am. Chem. Soc.* **1982**, *104*, 1737–1739.
(26) *Beilsteins Handbuch der Organischen Chemie* Springer-Verlag: Berlin; Vol. 10, p 194.

579-44-2; 8, 94-02-0; $ClCO_2CH_2Ph$, 501-53-1; $H_2O_2$, 7722-84-1; $PhCH_2COCl$, 103-80-0; (±)-$PhCH(OH)CO_2H$, 611-72-3; (±)-$PhCH(CO_2H)OCO_2CH_2Ph$, 103423-01-4; (*R*)-$PhCH(OH)CO_2H$, 611-71-2; (±)-$PhCH(COCl)OCO_2CH_2Ph$, 103423-05-8; (*R*)-4-isopropyloxazolidin-2-one, 95530-58-8.

## Carbonylation in Strong Acid. Lactones from Allylic Derivatives

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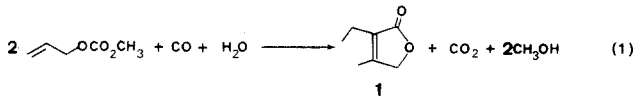
The carbonylation of organic compounds with carbon monoxide in the presence of a soluble transition-metal catalyst, particularly of group VIII, has been an area of great interest and has provided access to many valuable products.[2] However, carbonylation in strong acid has received much less attention even though it is practiced in the commercial production of pivalic and other alkanoic acids.[3] In the Koch modification, the substrate is mixed with a strong acid under a moderate carbon monoxide pressure in the absence of water to generate an intermediate acylium ion which is then carefully hydrolyzed.[4] The reaction conditions are surprisingly mild in comparison to metal-catalyzed reactions. Typically, temperatures between −20 and 80 °C and pressures less than 10 MPa are employed. Strong acids such as $H_2SO_4$, $H_3PO_4$, HF, and $BF_3$ are used as the catalysts as well as the solvents. Under these conditions, nearly all olefins and a number of dienes, unsaturated esters, alcohols, diols, reactive alicyclic compounds, halogenated compounds, certain amines, and esters react to form the corresponding carboxylic acids.[5]

In general, the products of the Koch reaction are determined by the relative stabilities of the carbenium ions from protonation of the substrates. With higher olefins and alcohols, rearrangement, disproportionation, and dimerization can occur leading to mixtures of products. Only a very limited number of examples of substituted olefins have been reported, and the products observed are predictable. β-Citronellyl chloride and methallyl chloride gave 2,2,6-trimethyl-8-chloro-1-octanoic acid and chloropivalic acid, respectively.[6] Our effort has been focused on the carbonylation of oxysubstituted allylic compounds, the results of which are reported herein.

The gradual introduction of allyl methyl carbonate into a pressure vessel containing concentrated sulfuric acid and pressurized with CO (6.9 MPa) maintained at 50 °C followed by cautious discharge of the solution into ice–water gave 3-ethyl-4-methyl-2(5*H*)-furanone (**1**) in 48% distilled yield and a considerable amount of tar (eq 1).

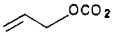
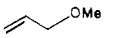
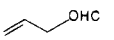
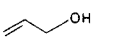
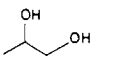
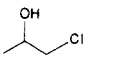
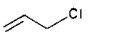



(1)

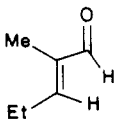
**1**

Other allylic compounds also provided **1**, albeit in lower yields (Table I). When 1,2-propanediol, 1-chloro-2-propanol, or allyl chloride were used, additional products (11.4% of **2** from the diol and 30% of a mixture of **3** and **4** from the others) were isolated along with **1**.

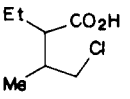
**Table I. Yield of 1 from Carbonylation of $C_3$ Derivatives[a]**

| $C_3$ derivative | product 1, % | product other (%) |
|---|---|---|
|  | 48 | |
|  | 28 | |
|  | 18.5 | |
|  | 20 | |
|  | 19 | 2 (11.4) |
|  | 10 | 3 + 4 (30) |
|  | 10 | 3 + 4 (30) |

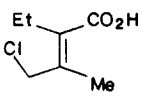
[a] Substrate:$H_2SO_4$ = 1:6.




**2**




**3**




**4**

The identities of **1** and **2** were established by comparison with authentic samples[7,8] and those of **3** and **4** by inference from their solubility in base, spectral data, and their conversion to **1** in hot aqueous acid.

The $C_7$ skeleton common to all the products can only be satisfied by a dimerization of allylic fragments and CO incorporation, in a manner similar to the formation of $C_9$ and $C_{13}$ acids from isobutylene via acid-catalyzed dimerization and trimerization.[9] In our case, the product is more complex, and its formation cannot be readily rationalized on the basis of the known reaction sequence. The observation of the same product from all the $C_3$ derivatives and the isolation of **2-4**, which we believe are closely related and are intermediates to **1**, suggest that the pathway outlined in Scheme I is operative. The formation of allyl carbenium ion from the starting materials in concentrated sulfuric acid is expected.[10] Addition of an allyl cation to another allylic molecule followed by proton loss and rearrangement gives the conjugated diene **5**. The $C_6$ allyl cation, from the protonation of **5**, reacts with CO to yield an acylium complex **7**[11] which upon hydrolysis gives the acid **8**. The final product, **1**, results from the acid-catalyzed ring closure of **8**. It can be seen that **5** is equivalent to the enol form of **2** and that **8** is identical with **3** and **4** when Y = Cl, thus accounting for all the products observed. The intermediacy of **2** is supported by the observation that it was the sole product when the carbonylation of 1,2-propanediol was conducted at 20 °C.

The difference in yields from the various allylic compounds is difficult to explain and may be related to their relative stabilities in sulfuric acid. The predominance of **3** and **4** in the reaction products of 1-chloro-2-propanol and allyl chloride is probably due to the slower rate at which they cyclize to **1** as compared to the rate for the oxygen analogues. To confirm the fast cyclization of the latter, **1** was hydrolyzed by sodium hydroxide to **9**, and the pH of the solution was the adjusted to 3 and 5.6 with aqueous HCl or ammonium sulfate at room temperature. Moni-

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