Table 1. Carbonylation of Benzal Chloride to Alkyl Phenylacetates using $Co_2(CO)_8$[a]

Entry	Base (5 meq.)	Alcohol ROH	Yield of[b] $C_6H_5CH_2COOR$	C_6H_5CHO
1	K_2CO_3	C_2H_5OH	92(85)	6
2	None	C_2H_5OH	11	49
3	$Ca(OH)_2$	C_2H_5OH	59	19
4	KOH	C_2H_5OH	43	39
5	NEt_3	C_2H_5OH	32	trace
6	K_2CO_3	CH_3OH	36(32)	54
7	K_2CO_3	$n-C_3H_7OH$	34(31)	10
8	K_2CO_3	$i-C_3H_7OH$	45(43)	5
9	K_2CO_3	$n-C_4H_9OH$	69(48)	6
10	K_2CO_3	$t-C_4H_9OH$	trace	4

[a]Benzal chloride (0.325g, 2 mmol) base (5 meq), alkanol (10 m*l*), and $Co_2(CO)_8$ (0.034g, 0.1 mmol) at 80 °C for 24 h under 30 atm of CO. [b]GLC yield, phenyl ether as internal standard; parentheses are isolated yields.

carbonylation reaction is being currently used for the production of large volume chemicals.[1] Many applications are reported on the carbonylation of benzyl halides with carbon monoxide using cobalt,[2] iron,[3] ruthenium,[4] rhodium,[5] and palladium.[6] However, there are few reports on the carbonylation of benzal halides as the geminal dihalide compound to give alkyl phenylacetates[7] and phenylacetic acids.[8] The alkyl phenylacetates are used as a perfume in waxes and honey.

We herein wish to report a simple method for the carbonylation of benzal chloride leads to alkyl phenylacetates in good yield.

$$C_6H_5CHCl_2 + CO + ROH \xrightarrow[80\ ^\circ C]{Co_2(CO)_8,\ K_2CO_3} C_6H_5CH_2COOR$$
(30 atm)

A typical procedure is illustrated as follows: In a 100 m*l* stainless steel autoclave, a mixture of benzal chloride (0.325 g, 2.0 mmol), potassium carbonate (0.345g, 2.5 mmol), ethanol (10 m*l*), and dicobalt octacarbonyl (0.034 g, 0.1 mmol) is placed under an argon atmosphere. Carbon monoxide is charged up to 30 atm at room temperature, and then the mixture is stirred at 80 °C for 24 h. After cooling, the carbon monoxide is vented out in fume hood. The mixture is filtered, concentrated, and then separated by column chromatography (SiO_2, ethyl acetate–hexane). The products are analyzed by means of ^1H, ^{13}C-NMR, mass, and IR spectra.

Table 1 shows that dicobalt octacarbonyl in alkanol medium can be used for selective monocarbonylation of benzal chloride. The optimum condition is found as 80 °C and 30 atm of carbon monoxide. Potassium carbonate, calcium hydroxide, triethylamine, and potassium hydroxide are used both as acid scavenger and catalyst activator in alkanol medium. Potassium carbonate is superior for the selective monocarbonylation to others (Entry 1). In the absence of base, formation of the carbonylated product is reduced and benzaldehyde is formed in considerable amount (Entry 2). With potassium hydroxide, ethyl phenylacetate and benzaldehyde are formed almost equally (Entry 4). The use of other alcohols–potassium carbonate system leads to lower yields of carbonylated products (Entries 6–10). Application of the present procedure to other substituted benzal chlorides and elucidation of reaction mechanism are now in progress and will be reported in due time.

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Enantiospecific Synthesis of (+)-Coriolic Acid, A Self-Defensive Substance against Rice Blast Disease[1]

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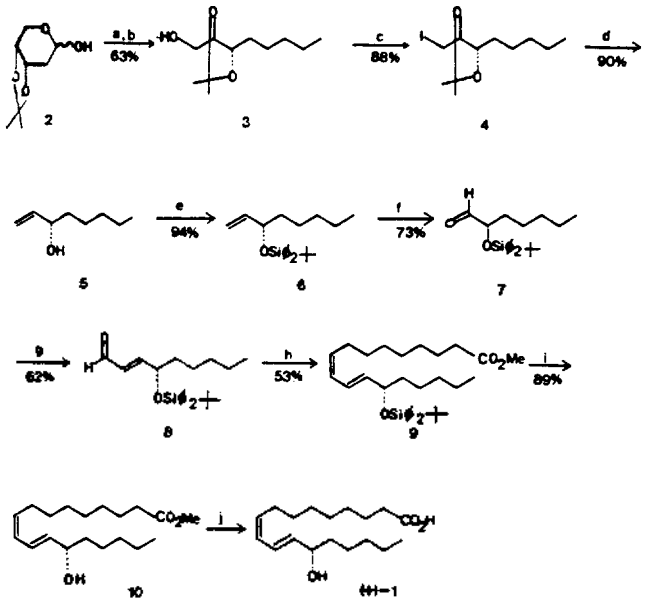
Coriolic acid **1**[2] is an oxygenated unsaturated fatty acid which has the structure of 13-hydroxy-9Z,11E-octadecadienoic acid. This metabolite of linoleic acid in vegetable oils or in bovine heart mitochondria, exhibits unique calcium-specific ionophoric activity.[3] Recently (+)-**1** has been



[a](a) $(C_6H_5)_3P^+(CH_2)_2CH_3Br^-$, n-BuLi, THF, -30 °C→rt, 24h (b) H_2 Pd/C, EtOAc, 1 atm, rt, 36 h (c) I_2, $(C_6H_5)_3P$, imidazole, toluene, 60 °C, 3h (d) Zn, EtOH, reflux, 6 h (e) $tBuPh_2SiCl$, imidazole, DMF, rt, 24 h (f) THF-H_2O (4:1), 0 °C, 20 min then $NaIO_4$, °C, 1 h (g) $(C_6H_5)_3P$=CHCHO, benzene, reflux, 8 h (h) $(C_6H_5)_3P^+(CH_2)_8CO_2$-MeBr$^-$, n-BuLi, THF-HMPA, 0 °C→-78 °C then add 8, -78 °C→rt, 5 h (i) n-Bu_4NF, THF, 25 °C, 3 h (j) ref. 7f.

Scheme 1.

isolated from the resistant cultivar of rice plant and shown to act as self-defensive substance against rice blast disease.[4] In addition, recent studies have demonstrated that this metabolite stimulates prostacyclin production by cultured bovine endothelial cells and inhibits platelet adhesion to cultured human enothelium.[5] Thus, this acid may have significant effects on the adhesive events involved in the pathogenesis of thrombosis, inflammation and metastasis.[6] Several chiral syntheses of this metabolite have been reported in the literature.[7]

Here we report an enantiospecific synthesis of (+)-coriolic acid, (+)-**1**, from (-)-2-deoxy-D-ribose via chiral α-hydroxyaldehyde **7** as the intermediate, which is shown in Scheme 1.

Acetonide **2**, prepared[8] as an anomeric mixture in ~60% yield from commercial (-)-2-deoxy-D-ribose[9] was condensed with n-propylidenetriphenylphosphorane in a Wittig reaction, followed by catalytic hydrogenation on Pd/C at atmospheric pressure to provide the saturated alcohol **3**,[10] $[\alpha]_D^{21} = +30.36°$ (c = 0.20, $CHCl_3$) in 63% overall yield. The alcohol **3** was directly converted[11] to the iodide **4** by reacting with iodine and triphenylphosphine in the presence of imidazole. The iodide **4** on treatment[12] of activated zinc in refluxing ethanol underwent a facile reductive elimination to afford (S)-matsutake alcohol,[13,14] (S)-1-octene-3-ol (**5**),[10] $[\alpha]_D = +9.0°$ (c = 4.0, $CHCl_3$) [lit.[13] $[\alpha]_D^{26} = +8.1°$ (c = 1.46, $CHCl_3$) in 90% yield. This alcohol was protected with t-butyldiphenylsilyl chloride to give **6**, $[\alpha]_D^{24} = +28.0°$ (c = 4.0, $CHCl_3$) in 94% yield. Dihydroxylation of the olefin **6** followed by oxidative cleveage with $NaIO_4$ afforded O-protected α-hydroxylaldehyde **7**, $[\alpha]_D^{25} = +6.3°$ (c = 1.2, benzene) [lit.[15] $[\alpha]_D = +6.1°$ (c = 1.44, benzene)], which is an important building block for the synthesis of biologically active compounds such as arachidonic acid metabolites etc.. Wittig reaction of **7** with formylmethylenetriphenylphosphorane resulted in the formation of (E)-unsaturated aldehyde **8**,[10,7d] $[\alpha]_D^{25} = -1.90°$ (c = 0.4, $CHCl_3$)[lit.[7d] $[\alpha]_D^{25} = -1.89°$ (c = 1.67, $CHCl_3$)]. Condesation of **8** with the yilde derived from 8-carbomethoxyoctyltriphenylphosphonium bromide[16] provided the (Z)-isomer **9** $[\alpha]_D^{25} = -16°$ (c = 0.07, $CHCl_3$), and its (E)-isomer in the ratio of 4:1. The separation of (Z)-isomer was carried out by HPLC chromatography through a μ-PORASIL(7.9 mm × 30 cm, eluent: EtOAc/hexanes = 1:20, Rt of Z isomer: 4.0 min; E isomer: 5.1 min) in 53% yield. Deprotection of the silylgroup gave coriolic acid methyl ester **10**, $[\alpha]_D^{25} = +6.4°$ (c = 1.0, $CHCl_3$)[lit.[7h] $[\alpha]_D^{23} = +6.1°$ (c = 0.98, $CHCl_3$). The saponification leading to (+)-coriolic acid, (+)-**1**, has already been described.[7f]

In conclusion, we have synthesized (+)-coriolic acid methyl ester enantiospecifically from (-)-2-deoxy-D-ribose in ten steps via α-hydroxyaldehyde as the key intermediate.

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10. Satisfactory spectral and physical data were obtained for

the compounds in accord with the structure. Selected physical and spectral data are as follows. (2R, 3S)-2,3-Isopropylidenedioxy-1-octanol (3): ^{1}H-NMR(80 MHz, $CDCl_3$) δ 0.92 (t, 3H), 1.38(s, 3H), 1.48(s, 3H), 1.22-1.59(m, 8H), 3.62(d, 2H), 4.13(m, 2H). IR(neat) 3450, 1045 cm^{-1}, $[\alpha]_D^{21} = +30.36°$ (c = 0.20, $CHCl_3$). TLC, SiO_2, R_f = 0.72 (hexanes/EtOAc 1:1). (2S, 3S)-2,3-Isopropylidenedioxy-1-iodooctane (4): ^{1}H-NMR(80 MHz, $CDCl_3$) δ 0.89(t, 3H), 1.18-1.78(m, 14H), 3.26(d, 2H, J = 5 Hz), 3.49-3.80(m, 2H). IR(neat) 1380, 1230, 1045cm^{-1}. TLC, SiO_2, R_f = 0.72 (hexanes/EtOAc 3:1). (S)-1-Octen-3-ol(5): ^{1}H-NMR(80 MHz, $CDCl_3$) δ 0.90(t, 3H), 1.09-1.83(m, 8H), 4.36(m, 1H), 5.16(d, 1H, J = 6 Hz), 5.32(d, 1H, J = 12 Hz), 5:82(ddd, 1H, J_1 = 12 Hz, J_2 = 9 Hz, J_3 = 5 Hz). IR(neat) 3450 cm^{-1} $[\alpha]_D^{24} = +9.0°$ (c = 4.0, $CHCl_3$). TLC, SiO_2, R_f = 0.49 (hexanes/EtOAc 3:1). (S)-[(1,1-Dimethyl)ethyldiphenylsilyloxy]-1-octene (6): ^{1}H-NMR (100 MHz, $CDCl_3$) δ 0.90(t, 3H), 1.10-1.50(m, 17H), 4.10(m, 1H), 4.92(d, 1H, J = 6 Hz), 5.05(d, 1H, J = 12 Hz), 5.80(ddd, 1H, J_1 = 12 Hz, J_2 = 9 Hz, J_3 = 5 Hz). $[\alpha]_D^{24} = +28.0°$ (c = 4.0, $CHCl_3$). TLC, SiO_2, R_f = 0.69(hexanes/EtOAc 3:1). (S)-2-[(1,1-Dimethyl)ethyldiphenylsilyloxy]-1-heptanol (7): ^{1}H-NMR (100 MHz, $CDCl_3$) δ 0.80(t, 3H), 1.10(s, 9H), 1.20-1.60(m, 8H), 4.00(m, 1H), 7.40(m, 5H), 7.65(m, 5H), 9.60(d, 1H). IR(neat) 2962, 2873, 1715 cm^{-1}. $[\alpha]_D^{25} = +6.3°$ (c = 1.2, benzene). TLC, SiO_2 R_f = 0.59 (hexanes/EtOAc 4:1). (2E)-4-[(1,1-Dimethyl) ethyldiphenylsilyloxy]-2-nonen-1-al (8): ^{1}H-NMR(100 MHz, $CDCl_3$) δ 0.82(t, 3H, J = 6.7 Hz), 1.09(s, 9H), 1.30-2.00(m, 8H), 4.00(q, 1H), 6.22(ddd, 1H, J_1 = 15 Hz, J_2 = 7.5 Hz, J_3 = 1.4 Hz), 6.70(dd, 1H, J_1 = 15 Hz, J_2 = 5.0 Hz), 7.33(m, 5H) 7.68(m, 5H), 9.50(d, 1H, J = 8.0 Hz). IR(neat) 3060, 3040, 2960, 2940, 2840, 1675 cm^{-1}. $[\alpha]_D^{25} = -19°$ (c = 0.4, $CHCl_3$). TLC, SiO_2 R_f = 0.50(hexanes/EtOAc 5:1). Methyl-(13S)-[(1,1-dimethyl)ethyldiphenylsilyloxyl]-(9Z, 11E)-9,11-octadecadienoate (9): ^{1}H-NMR(270 MHz, $CDCl_3$) δ 0.90(t, 3H), 1.00-1.90(m, 18H), 2.02(q, 2H), 2.32(t, 2H), 3.67(s, 3H), 4.18(q, 1H), 5.35 (dt, 1H, J_1 = 8.5 Hz, J_2 = 7.5 Hz), 5.56(dd, 1H, J_1 = 15 Hz, J_2 = 7.5 Hz), 5.87(t, 1H, J = 10 Hz), 6.20(dd, 1H, J_1 = 15 Hz, J_2 = 10 Hz), 7.33(m, 5H), 7.70(m, 5H), IR(neat) 3050, 3020, 1740cm^{-1}. $[\alpha]_D^{25} = -16°$ (c = 0.07, $CHCl_3$). TLC, SiO_2, R_f = 0.50 (hexanes/EtOAc 5:1). Methyl-(13S)-hydroxy-(9Z), (11E)-octadecadienoate(10): ^{1}H-NMR(270 MHz, $CDCl_3$) δ 0.90(t, 3H), 1.10-1.50(m, 3H), 1.60-1.90(m, 6H), 2.10(q, 2H, J = 7Hz), 2.42(t, 2H, J = 7Hz), 3.71(s, 3H), 4.20(q, 1H), 5.40(dt, 1H, J_1 = 8.5Hz, J_2 = 7.5Hz), 5.60(dd, 1H, J_1 = 15Hz, J_2 = 7.5Hz), 5.90(t, 1H, J = 10Hz), 6.30(dd, 1H, J_1 = 15Hz, J_2 = 10Hz). IR(neat) 3400, 1735cm^{-1}, $[\alpha]_D^{25} = +6.4°$ (c = 10, $CHCl_3$). TLC, SiO_2, R_f = 0.30(hexanes/EtOAc 5:1).

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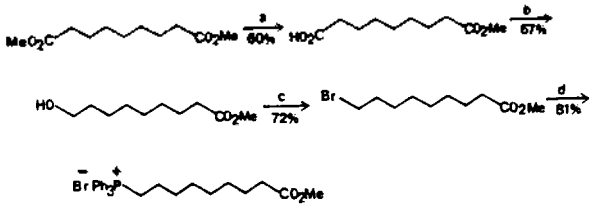

(a) KOH, EtCH, rt, 4h, (b) $ClCO_2Et$, Et_3N, THF, 0°C, 1h, then $NaBH_4$, MeOH, rt, 2h, (c) PBr_3, ether, pyridine, rt, 12h (d) Ph_3P, CH_3CN, reflux, 48 h.

Solvent Effects on the Reactions of 1-Benzyl-1,4-dihydronicotinamide in Ethanol/Water Mixed Solvent

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1,4-Dihydronicotinamides like 1-benzyl-1,4-dihydronicotinamide (BNAH) have been the subject of intense study as model compounds of coenzyme reduced nicotinamide adenine dinucleotide (NADH).[1] The net change of NADH and NADH model compound in the reduction reaction is the transfer of a hydride (H^-) equivalent from dihydronicotinamide moiety to the substrate. However, the detailed mechanism of the reduction is still much of the controversy whether the reaction is an one-step hydride transfer[2-5] or a three-step electron-proton-electron transfer mechanism.[6-9] For oxidation of NADH model compounds by cupric ion[10] and ferrocenium salts[4], the possibility of the mechanism in which the reactants was proposed.

The effects of reaction medium on the reaction rate gives information about the reaction mechanism.[11] In biomimetic transformation such as reactions of NADH analogs, the medium effect is particularly important with respect to the reaction environment in biochemical systems. It has been noted that the rates of the reduction of acridinium ions[2,12] and trifluoroacetophenone[13,14] by 1,4-dihydronicotinamides are sensitive to the polarity of medium. In this communication, we wish to report the solvent effects on the acid (HCl)-catalyzed hydration reaction as well as cupric, ferricyanide, and acridinium ion oxidation reactions of BNAH.