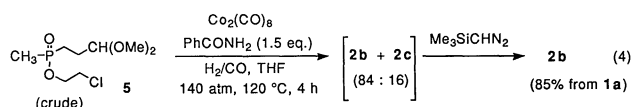


a) Rh 0.01 mg-atom, **1a** 10 mmol, solvent 9 ml, 100 °C, CO/H₂=1/1, 100 atm at room temperature, 5–19 h, linear-sel.=100×3/(3+4). b) Rh complex 0.05 mmol, **1a** 5.7 mmol, P(OPh)₃ 0.13 mmol, benzene 1.4 ml, CO/H₂=1/1, 1 atm, 45 °C, 2 h. acac: acetylacetonate.

the hydroformylation of **1a** with cobalt or rhodium catalysts, respectively, are similar to those reported for the hydroformylation of an α,β -unsaturated carboxylate with $\text{Co}_2(\text{CO})_8$ or $\text{Rh}_4(\text{CO})_{12}$.⁶ On the other hand, Trzeciak et al. have reported an unusually high linear selectivity in the rhodium-catalyzed hydroformylation of ethyl acrylate with the $\text{Rh-P}(\text{OPh})_3$ system.⁷ The catalytic system was successfully applied to the hydroformylation of **1a** to achieve a high linear selectivity under mild conditions (Table 2).⁸

Since a high linear selectivity and a high yield have been achieved in the hydroformylation of **1a** with $\text{Co}_2(\text{CO})_8$ in MeOH (Eq. 3), we next investigated the amidocarbonylation⁹ of the resulting acetal (**5**) (Eq. 4). Although examples of amidocarbonylation of acetals have been rare,¹⁰ the reaction of **5** proceeded smoothly to give a mixture of the methyl ester (**2b**) and presumably the free carboxylic acid (**2c**);¹¹ the latter could be quantitatively converted to the former via the treatment with trimethylsilyldiazomethane.¹² The amidocarbonylation proceeded in various solvents such as benzene, ethyl acetate, dioxane, and tetrahydrofuran; the last one gave the highest reaction rate. Since the amidocarbonylation is slow in methanol, the solvent should be exchanged after the hydroformylation.



The hydrolysis of **2b** was easily carried out under acidic conditions to give glufosinate quantitatively. Thus, glufosinate can be efficiently synthesized via successive hydroformylation–amidocarbonylation of the methylvinylphosphinate. The resolution of racemic glufosinate and the conversion of the optical isomer to its racemate have already been established.¹³

Experimental

¹H and ¹³C NMR signals were referred to tetramethylsilane as an internal standard. Chemical shift in ³¹P NMR was referred to H_3PO_4 .

$\text{Co}_2(\text{CO})_8$ was recrystallized from toluene at a low temperature. $\text{Rh}(\text{acac})[\text{P}(\text{OPh})_3]_2$ was synthesized according to the literature.¹⁴ The methylvinylphosphinate (**1a**) was obtained from Nissan Chemical Industries Ltd.

Hydroformylation of 1a. Octacarbonyldicobalt (0.1 mmol), the methylvinylphosphinate (10 mmol), and methanol (9 ml) were added to a 27 ml Hastelloy-C autoclave under nitrogen. Synthesis gas ($\text{H}_2/\text{CO}=1/1$) was charged up to 100 atm at room temperature. The autoclave was heated in an oil bath at 120°C for 2 h. The reaction mixture was analyzed by capillary GC (OV-1701 and PEG-20M, 25 m) using tridecane as an internal standard. Rhodium catalyzed reactions were conducted similarly; see Table 2 for reaction conditions.

Amidocarbonylation of 5. Hydroformylation of **1a** was carried out in methanol as stated above. The reaction mixture was concentrated. The resulting oil, octacarbonyldicobalt (0.2 mmol), benzamide (15 mmol) and tetrahydrofuran (10 ml) were added to a 27 ml Hastelloy-C autoclave under nitrogen. Synthesis gas ($\text{H}_2/\text{CO}=1/1$) was charged up to 140 atm. The autoclave was heated in an oil bath at 120°C for 3.8 h. The reaction mixture was analyzed by HPLC (ODS, meth-

anol: $\text{H}_2\text{O}=1/1$) using benzene as an internal standard after the esterification of the free amino acid with trimethylsilyldiazomethane.¹⁰

The products were isolated by distillation (Kugelrohr) or preparative thin-layer chromatography (silica gel, CHCl_3 : $\text{MeOH}=15:1$). Spectral data were listed below.

2-Chloroethyl Methylvinylphosphinate (1a). ¹H NMR (CDCl₃) $\delta=1.57$ (d, $J=14$ Hz, 3H, CH_3P), 3.70 (t, $J=6$ Hz, 2H, CH_2Cl), 4.0–4.4 (m, 2H, OCH_2), 6.0–6.5 (m, 3H, $\text{CH}=\text{CH}_2$); ¹³C NMR (CDCl₃) $\delta=14.9$ (d, $J=102$ Hz, CH_3P), 43.1 (d, $J=7$ Hz, CH_2Cl), 63.8 (d, $J=6$ Hz, OCH_2), 129.6 (d, $J=121$ Hz, $\text{CH}=\text{CH}_2$), 135.8 (s, $\text{CH}=\text{CH}_2$); MS m/z (%) 171 ($\text{M}^{+37}\text{Cl}+\text{H}$, 0.3), 169 ($\text{M}^{+35}\text{Cl}+\text{H}$, 1.0), 153 ($\text{M}^{+35}\text{Cl}-\text{Me}$, 4), 133 ($\text{M}^{+}-\text{Cl}$, 100), 119 (15), 107 (24), 91 (20). Found: m/z 133.0407 ($\text{M}^{+}-\text{Cl}$). Calcd for $\text{C}_5\text{H}_{10}\text{O}_2\text{P}$: M, 133.0418.

2-Chloroethyl Ethylmethylphosphinate. Bp $80\text{--}90^\circ\text{C}/0.5 \text{ mmHg}$ (1 mmHg $\approx 133.3 \text{ Pa}$); ¹H NMR (CDCl₃) $\delta=1.19$ (dt, $J=19$ and 8 Hz, 3H, CH_3CH_2), 1.50 (d, $J=14$ Hz, 3H, CH_3P), 1.80 (dq, $J=15$ and 8 Hz, 2H, CH_2CH_3), 3.70 (t, $J=6$ Hz, 2H, CH_2Cl), 4.1–4.3 (m, 2H, OCH_2); ¹³C NMR (CDCl₃) $\delta=6.1$ (d, $J=5$ Hz, CH_2CH_3), 13.2 (d, $J=90$ Hz, CH_3P), 22.8 (d, $J=95$ Hz, CH_2P), 43.4 (d, $J=7$ Hz, CH_2Cl), 63.7 (d, $J=6$ Hz, OCH_2); MS m/z (%) 173 ($\text{M}^{+37}\text{Cl}+\text{H}$, 0.1), 171 ($\text{M}^{+35}\text{Cl}+\text{H}$, 0.3), 155 ($\text{M}^{+35}\text{Cl}-\text{Me}$, 2), 141 ($\text{M}^{+35}\text{Cl}-\text{Et}$, 9), 135 (100), 121 (16), 115 (14), 107 (17), 91 (54). Found: m/z 171.0336 ($\text{M}^{+}+\text{H}$). Calcd for $\text{C}_5\text{H}_{13}\text{ClO}_2\text{P}$: M, 171.0341.

2-Chloroethyl Methyl(3-oxopropyl)phosphinate (3). Bp $150\text{--}180^\circ\text{C}/0.4 \text{ mmHg}$; IR (neat) 1730 cm^{-1} (CO); ¹H NMR (CDCl₃) $\delta=1.56$ (d, $J=14$ Hz, 3H, CH_3P), 2.10 (dt, $J=14$ and 8 Hz, 2H, CH_2P), 2.7–3.0 (m, 2H, CH_2CHO), 3.71 (t, $J=5$ Hz, 2H, CH_2Cl), 4.1–4.3 (m, 2H, OCH_2), 9.83 (s, 1H, CHO); ¹³C NMR (CDCl₃) $\delta=14.5$ (d, $J=92$ Hz, CH_3P), 21.8 (d, $J=96$ Hz, CH_2P), 36.1 (d, $J=3$ Hz, CH_2CHO), 43.3 (d, $J=7$ Hz, CH_2Cl), 64.0 (d, $J=6$ Hz, OCH_2), 199.1 (d, $J=13$ Hz, CHO); MS m/z (%) 201 ($\text{M}^{+37}\text{Cl}+\text{H}$, 0.3), 199 ($\text{M}^{+35}\text{Cl}+\text{H}$, 1.0), 163 ($\text{M}^{+}-\text{Cl}$, 21), 144 (17), 142 (48), 135 (100), 127 (24), 119 (86), 107 (100). Found: m/z 199.0279 ($\text{M}^{+}+\text{H}$). Calcd for $\text{C}_6\text{H}_{13}\text{ClO}_3\text{P}$: M, 199.0289.

2-Chloroethyl Methyl(1-methyl-2-oxoethyl)phosphinate (4). Bp $140\text{--}160^\circ\text{C}/0.35 \text{ mmHg}$; IR (neat) 1720 cm^{-1} (CO); ¹H NMR (CDCl₃) (diastereomer) $\delta=1.407$ and 1.423 (dd, $J=16$ and 7 Hz, 3H, PCHCH_3), 1.547 and 1.569 (d, $J=14$ Hz, 3H, CH_3P), 3.0–3.5 (m, 1H, CHCHO), 3.73 (t, $J=5$ Hz, 2H, CH_2Cl), 4.2–4.4 (m, 2H, OCH_2), 9.80 and 9.87 (d, $J=2$ Hz, 1H, CHO); ¹³C NMR (CDCl₃) (diastereomer) $\delta=7.61$ (s, CHCH_3), 7.67 (d, $J=1.5$ Hz, CHCH_3), 12.77 and 12.94 (d, $J=93$ Hz, CH_3P), 43.06 and 43.10 (d, $J=7$ Hz, CH_2Cl), 50.33 and 50.39 (d, $J=79$ Hz, CHCH_3), 64.51 and 64.63 (d, $J=6$ Hz, OCH_2), 197.77 (d, $J=3$ Hz, CHO), 197.89 (s, CHO); MS m/z (%) 200 (M^{+37}Cl , 3), 198 (M^{+35}Cl , 11), 163 ($\text{M}^{+}-\text{Cl}$, 55), 149 ($\text{M}^{+}-\text{CH}_2\text{Cl}$, 15), 137 (15), 136 (26), 135 (100), 119 (59), 117 (13), 115 (17), 109 (42), 107 (61), 97 (24), 91 (44). Found: m/z 198.0222 (M^{+}). Calcd for $\text{C}_6\text{H}_{12}\text{ClO}_3\text{P}$: M, 198.0212.

2-Chloroethyl (3,3-Dimethoxypropyl)methylphosphinate (5). Bp $100^\circ\text{C}/5.6\times 10^{-4} \text{ mmHg}$; ¹H NMR (CDCl₃) $\delta=1.52$ (d, $J=14$ Hz, 3H, CH_3P), 1.7–2.0 (m, 4H, PCH_2CH_2), 3.34 (s, 6H, OCH_3), 3.70 (t, $J=6$ Hz, 2H, CH_2Cl), 4.1–4.3 (m, 2H, OCH_2), 4.3–4.5 (m, 1H, CH_2CH); ¹³C NMR (CDCl₃) $\delta=14.0$ (d, $J=92$ Hz, CH_3P), 24.4 (d, $J=70$ Hz, CH_2P), 25.4 (d, $J=21$ Hz, PCH_2CH_2), 43.3 (d, $J=6$ Hz, CH_2Cl), 53.4 (d, $J=3$ Hz, CH_3O), 63.8 (d, $J=6$ Hz, OCH_2), 104.0 (d, $J=17$ Hz, CH); MS m/z (%) 245 ($\text{M}^{+37}\text{Cl}-\text{H}$, 0.3), 243 ($\text{M}^{+37}\text{Cl}-\text{H}$, 1.0), 231 ($\text{M}^{+37}\text{Cl}-\text{CH}_3$, 6), 229 ($\text{M}^{+35}\text{Cl}-\text{CH}_3$, 18), 215 ($\text{M}^{+37}\text{Cl}-\text{OCH}_3$, 52), 214 (17), 213 ($\text{M}^{+35}\text{Cl}-\text{OCH}_3$, 100), 199 (16), 197 (38), 193 (11), 177 (28), 165 (35), 161 (10), 151 (11), 149 (39), 141 (12), 135 (44), 133 (39), 131 (20), 121 (36), 119 (59), 107 (17), 101 (15), 93 (17). Found: m/z 243.0566 ($\text{M}^{+}-\text{H}$). Calcd for $\text{C}_8\text{H}_{17}\text{ClO}_4\text{P}$: M, 243.0553; Found: m/z 229.0398 ($\text{M}^{+}-\text{CH}_3$). Calcd

for $C_7H_{15}ClO_4P$: M, 229.0396.

2-Chloroethyl (2,2-Dimethoxy-1-methylethyl)methylphosphinate (6). This minor product formed in hydroformylation in methanol was identified only by GCMS. MS m/z (%) 245 ($M^{+}(^{37}Cl)-H$, 0.6), 243 ($M^{+}(^{35}Cl)-H$, 1.5), 231 ($M^{+}(^{37}Cl)-CH_3$, 8), 229 ($M^{+}(^{35}Cl)-CH_3$, 24), 215 ($M^{+}(^{37}Cl)-OCH_3$, 24), 213 ($M^{+}(^{35}Cl)-OCH_3$, 67), 199 (14), 197 (31), 177 (11), 173 (17), 165 (27), 149 (64), 143 (29), 141 (82), 135 (30), 133 (13), 125 (17), 123 (11), 117 (19), 115 (35), 111 (16), 107 (15), 102 (69), 93 (55), 79 (67), 76 (18), 75 (100). Found: m/z 243.0560 ($M^{+}-H$). Calcd for $C_8H_{17}ClO_4P$: M, 243.0553. Found: m/z 229.0413 ($M^{+}-CH_3$). Calcd for $C_7H_{15}ClO_4P$: M, 229.0396.

2-Chloroethyl [3-Benzoylamino-3-(methoxycarbonyl)propyl]methylphosphinate (2b). IR (neat) 3450 cm^{-1} (NH), 1740 cm^{-1} (CO_2Me), 1660 cm^{-1} (PhCO); 1H NMR ($CDCl_3$) (diastereomer) $\delta=1.525$ and 1.546 (d, $J=14\text{ Hz}$, 3H, CH_3P), $1.75-2.05$ (m, 2H, PCH_2), $2.05-2.4$ (m, 2H, CH_2CH), $3.6-3.75$ (m, 2H, CH_2Cl), 3.79 (s, 3H, CO_2CH_3), $4.1-4.3$ (m, 2H, OCH_2), $4.75-5.0$ (m, 1H, NCH), $7.35-8.0$ (m, 6H, Ph and NH); ^{13}C NMR ($CDCl_3$) (diastereomer) $\delta=14.2$ (d, $J=94\text{ Hz}$, CH_3P), 24.5 (s, CH_2CH), 26.01 and 26.11 (d, $J=93\text{ Hz}$, PCH_2), 43.27 and 43.32 (d, $J=7\text{ Hz}$, CH_2Cl), 52.8 (s, CO_2CH_3), 52.8 (d, $J=21\text{ Hz}$, CH), 64.1 (d, $J=7\text{ Hz}$, OCH_2), 127.4 (s, Ph, meta), 128.6 (s, Ph, ortho), 129.9 (s, Ph, para), 133.4 (s, Ph, C1), 167.4 (d, $J=2.5\text{ Hz}$, CO_2), 172.3 (s, PhCO); ^{31}P NMR ($CDCl_3$) $\delta=55$ (s); MS m/z (%) 363 ($M^{+}(^{37}Cl)$, 0.5), 361 ($M^{+}(^{35}Cl)$, 1.4), 304 ($M^{+}(^{37}Cl)-CO_2CH_3$, 19), 302 ($M^{+}(^{35}Cl)-CO_2CH_3$, 48), 284 (8), 256 (12), 105 (100). Found: m/z 361.0865 (M^{+}). Calcd for $C_{15}H_{21}ClNO_5P$: M, 361.0845 . Anal. ($C_{15}H_{21}ClNO_5P$) C, H, N, Cl.

Hydrolysis of 2b. The methyl ester **2b** (182 mg) was dissolved in 6 mol dm^{-3} hydrochloric acid (4 ml) and refluxed overnight. The resulting mixture was washed with benzene to remove benzoic acid. The water layer was concentrated to dryness in vacuo to give pure glufosinate (**2a**) (96 mg, 100%). 1H NMR²⁰⁾ (D_2O) $\delta=1.42$ (d, $J=14\text{ Hz}$, 3H, CH_3P), $1.7-2.2$ (m, 4H, PCH_2CH_2), 4.06 (t, $J=6\text{ Hz}$, 1H, $CHCO_2$); ^{13}C NMR^{2d,i)} (D_2O) $\delta=14.4$ (d, $J=92\text{ Hz}$, CH_3P), 23.5 (d, $J=2\text{ Hz}$, PCH_2CH_2), 26.0 (d, $J=93\text{ Hz}$, PCH_2), 53.6 (d, $J=17\text{ Hz}$, CH), 172.0 (s, CO_2H).

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