The product was further purified by column chromatography: mp 110-111 °C (lit.[26] mp 110-111 °C); mass spectrum, m/z 251 (M^+); NMR 2.90-3.02 (m, 8, CH_2), 7.16 (dd, 2, $H_{6,8}$, $J_{6,7}$ = 7.7 Hz), 7.25 (d, 1, H_7), and 7.97 ppm (s, 2, $H_{1,3}$).

2-Nitro-4,5,7,8,9,10,11,12-octahydrobenzo[*a*]pyrene (IIa). The nitration of II was completed in 20 min, giving the product IIa in a 98% yield: mp 152-153 °C; mass spectrum, m/z 305 (M^+); NMR 1.69-1.90 (m, 4, $H_{8,9}$), 2.63-3.10 (m, 8, $H_{4,5,7,10,11,12}$), 6.88 (s, 1, H_6), and 7.95 ppm (s, 2, $H_{1,3}$).

2-Nitro-9,10-dihydrophenanthrene (IIIa). The nitration of III was accomplished by reaction of a two-fold excess of N_2O_4 to 0.55 mmol (100 mg) of III in 50 mL of methylene chloride for 4.5 h. Determined by NMR spectral analysis, the crude reaction mixture contained 95% IIIa, 2.5% III, and 2.5 of an isomer of IIIa. Upon chromatography of the crude product followed by recrystallization from ethyl ether, pure IIIa was obtained as pink prisms: mp 80-82 °C (lit.[27] mp 81-82 °C); mass spectrum, m/z 225 (M^+); NMR 2.89-3.03 (m, 4, $H_{9,10}$), 7.32-7.40 (m, 3, H_{6-8}), 7.92 (dd, 1, H_5, $J_{5,6}$ = 6.8 Hz), 8.05 (dd, 1, H_4, $J_{3,4}$ = 8.1 Hz), 8.14 (s, 1, H_1), and 8.15 ppm (d, 1, H_3).

2-Nitro-7,8,9,10,11,12-hexahydrochrysene (IVa). The nitration of IV was complete within 1 h. Purification of IVa (75% yield) was accomplished by column chromatography: mp 123-124 °C; mass spectrum, m/z 279 (M^+); NMR 1.73-1.87 (m, 4, $H_{8,9}$), 2.71-2.99 (m, 8, $H_{7,10-12}$), 7.08 (d, 1, H_6, $J_{5,6}$ = 8.6 Hz), 7.69 (d, 1 H_5), 7.98 (d, 1, H_4, $J_{3,4}$ = 9.4 Hz), 8.11 (d, 1, H_1), and 8.12 ppm (d, 1, H_3).

3-Nitro-5,6,12,13-tetrahydrodibenz[*a*,*h*]anthracene (Va). The nitration of V was complete within 1 h. Compound Va (70% yield) was separated from Va′ and Va″ by preparative TLC on silica gel eluting with methylene chloride/hexane (1:1): mp 137-139 °C; mass spectrum, m/z 327 (M^+); NMR 2.86-3.10 (m, 8, $H_{5,6,12,13}$), 7.23-7.38 (m, 3, $H_{9,10,11}$, $J_{8,9}$ = 7.6 Hz), 7.81 (s, 1, H_7), 7.87 (s, 1, H_{14}), 7.89 (d, 1, H_8), 8.11 (d, 1 H_1, $J_{1,2}$ = 8.3 Hz), 8.16 (s, 1 H_4), and 8.21 ppm (d, 1, H_2).

General Procedure for Dehydrogenation with DDQ. Compounds Ia-Va were aromatized by DDQ in benzene or dioxane with refluxing temperature under an argon atmosphere. The resulting reaction mixture was filtered through Celite, and the filtrate was chromatographed on neutral alumina eluting with benzene. The yellow band that eluted from the column was stripped of solvent and recrystallized from methylene chloride/hexane (1:1).

2-Nitropyrene (Ib). A solution of 50 mg (0.2 mmol) of Ia and 180 mg of DDQ (0.8 mmol) in 50 mL of benzene was refluxed for 48 h. After workup and chromatography, the residue was recrystallized, yielding pure Ib (48 mg, 98%): mp 201-203 °C (lit.[26] mp 201-202.5 °C); mass spectrum, m/z 247 (M^+); NMR 8.23 (d, 1, H_7), 8.37 (d, 2, $H_{4,10}$), 8.41 (d, 2, $H_{5,9}$), 8.44 (d, 2, $H_{6,8}$), and 9.12 ppm (s, 2, $H_{1,3}$).

2-Nitrobenzo[*a*]pyrene (IIb). A solution of 50 mg (0.16 mmol) of IIa and 446 mg of DDQ (1.97 mmol) in 50 mL of benzene was refluxed for 15 h. Upon chromatography and recrystallization, compound IIb was obtained (46 mg, 98%): mp 142-144 °C; mass spectrum, m/z 297 (M^+); NMR 7.92 (dd, 1, H_8), 7.97 (dd, 1, H_9), 8.22 (d, 1, H_4), 8.29 (d, 1, H_5), 8.45 (d, 1, H_7), 8.69 (d, 1, H_{12}), 8.83 (s, 1, H_6), 8.96 (s, 1, H_3), 9.20 (s, 1, H_1), 9.24 (d, 1, H_{11}), and 9.27 ppm (s, 1, H_{10}). Anal. Calcd for $C_{20}H_{11}NO_2$: C, 80.80; H, 3.73; N, 4.71. Found: C, 80.72; H, 3.79; N, 4.78.

2-Nitrophenanthrene (IIIb). A solution of 50 mg (0.22 mmol) of IIIa and 101 mg (0.44 mmol) of DDQ in 50 mL of dioxane was refluxed 48 h. After chromatography and recrystallization, pure compound IIIb was obtained (47 mg, 96%): mp 100-101 °C (lit.[28] mp 100-101 °C); mass spectrum, m/z 223 (M^+); NMR 7.75-7.83 (m, 2, $H_{6,7}$), 7.99-8.09 (m, 3, H_{8-10}), 8.42 (d, 1, H_5, $J_{5,6}$ = 7.7 Hz), 8.89 (s, 1, H_1), 8.91 (d, 1, H_3, $J_{3,4}$ = 9.2 Hz), and 9.04 ppm (d, 1 H_4).

2-Nitrochrysene (IVb). A solution of 20 mg (0.07 mmol) of IVa and 97 mg of DDQ (0.43 mmol) in 50 mL of dioxane was refluxed for 6 days. The resulting reaction mixture was chromatographed, and further purification by recrystallization provided pure compound IVb in a 75% yield: mp 138-139 °C; mass spectrum, m/z 273 (M^+); NMR 7.76 (dd, 1, H_8, $J_{7,8}$ = 8.6 Hz), 7.82 (dd, 1, H_9, $J_{9,10}$ = 8.6 Hz), 8.14 (d, 1, H_7), 8.22 (d, 1, H_6, $J_{5,6}$ = 9.1 Hz), 8.39 (d, 1, H_{12}, $J_{11,12}$ = 9.3 Hz), 8.48 (d, 1, H_4, $J_{3,4}$ = 9.1 Hz), 8.93 (d, 1, H_5), 9.00 (dd, 1, H_{10}), 9.03 (s, 1, H_1), 9.09 (d, 1, H_{11}), and 9.17 ppm (d, 1, H_4). Anal. Calcd for $C_{18}H_{12}NO_2$: C, 79.11; H, 4.06; N, 5.13. Found: C, 79.02; H, 4.17; N, 5.19.

3-Nitrodibenz[*a*,*h*]anthracene (Vb). A solution of 30 mg (0.09 mmol) of Va and 83 mg of DDQ (0.36 mmol) in 50 mL of dioxane was refluxed for 15 h. The reaction mixture was chromatographed and recrystallization of the product yielded Vb (28 mg, 98%): mp 151-153 °C; mass spectrum, m/z 323 (M^+); NMR 7.74 (dd, 1, H_{10}, $J_{10,11}$ = 7.7 Hz), 7.79 (dd, 1, H_9, $J_{8,9}$ = 8.6 Hz), 7.93 (d, 1, H_{12}, $J_{12,13}$ = 9.5 Hz), 8.04 (d, 1, H_{11}), 8.10 (d, 1, H_6, $J_{5,6}$ = 8.6 Hz), 8.14 (d, 1, H_{13}), 8.30 (d, 1, H_5), 8.52 (d, 1, H_2, $J_{1,2}$ = 8.6 Hz), 8.92 (s, 1, H_4), 9.07 (d, 1, H_8), 9.27 (d, 1, H_1), 9.52 (s, 1, H_7), and 9.55 ppm (s, 1, H_{14}). Anal. Calcd for $C_{22}H_{13}NO_2$: C, 81.72; H, 4.05; N, 4.33. Found: C, 81.62; H, 4.12; N, 4.32.

Acknowledgment. We gratefully acknowledge P. Fleischer for typing this manuscript.

(26) Allinger, N. L.; DaRooge, M. A.; Hermann, R. B. *J. Am. Chem. Soc.* **1961**, *83*, 1974-1978.
(27) Krueger, J. W.; Mosettig, E. *J. Org. Chem.* **1938**, *3*, 340-346.
(28) Hallas, G.; Wada, B. T. *Chem. Ind.* **1978**, 630-631.

Enzymatic Halohydration of Glycals

Kevin K.-C. Liu and Chi-Huey Wong*

Department of Chemistry, The Scripps Research Institute, 10666 North Torrey Pines Road, La Jolla, California 92037

Received February 19, 1992

Haloperoxidase-catalyzed halogenation reactions are important biological processes. They are, for example, involved in the biosynthesis of the hormone thyroxine and in many biological defense systems.[1] They catalyze the following general reaction (eq 1):

$$AH + X^- + H_2O_2 + H^+ \xrightarrow{\text{haloperoxidase}} AX + 2H_2O \quad (1)$$

X = Cl, Br, or I

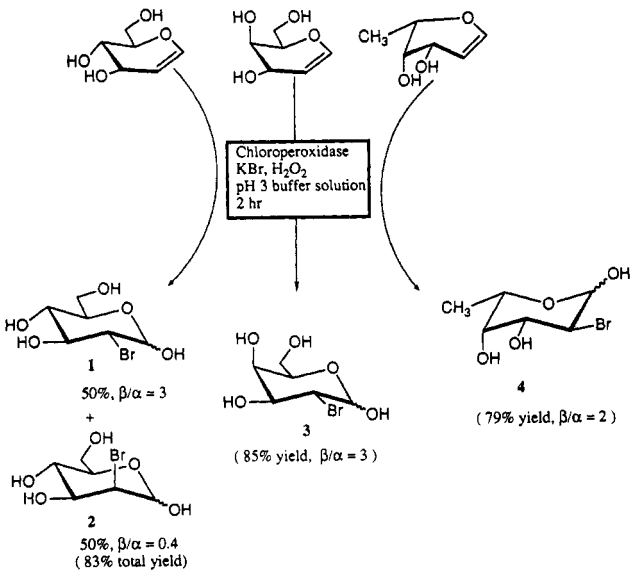
Chloroperoxidase (EC 1.11.1.10) can utilize chloride, bromide, and iodide ions as donors for the enzymatic halogenation reactions.[2-3] The enzyme also possesses the catalase activity for the disproportionation of hydrogen peroxide.[4] The chloroperoxidase-catalyzed halogenation seems to involve a hypohalous acid (HOX) as halogenating reagent, but the mechanism is not well understood. A mechanism involving an enzyme-bound electrophilic halogenating species was proposed for chloroperoxidase;[5] another mechanism involving free hypohalous acid as the halogenating species was proposed for myeloperoxidase.[6] Both reactions seem to proceed through a reactive "iron-oxo" intermediate. Previous studies indicate that chloroperoxidase showed poor stereoselectivity in reactions with a series of substrates.[7]

Chloroperoxidase catalyzes the oxidative formation of the carbon-halogen bond in a large number of substrates,[8]

(1) Neidleman, S. L.; Geigert, J. *Biohalogenation: Principles, Basic Roles and Applications*; Ellis Horwood Ltd.: Chichester, 1986.
(2) Morrison, M.; Schonbaum, G. R. *Annu. Rev. Biochem.* **1972**, *45*, 935-988.
(3) Neidleman, S. L. *CRC Crit. Rev. Microbiol.* **1975**, *5*, 333-358.
(4) Frew, J. E.; Jones, P. *Adv. Inorg. Bioorg. Mech.* **1984**, *3*, 176.
(5) Libby, R. D.; Thomas, J. A.; Hager, J. P. *J. Biol. Chem.* **1982**, *257*, 5030.
(6) Harrison, J. E.; Shultz, J. *J. Biol. Chem.* **1976**, *251*, 1371. de Montellano, P. R. O.; Choe, Y. S.; DePillis, G.; Catalano, C. E. *J. Biol. Chem.* **1987**, *262*, 11641.
(7) Remarkishnan, K.; Oppenhuizen, M. E.; Saunder, S.; Fisher, J. *Biochemistry* **1983**, *22*, 3271.

0022-3263/92/1957-3748$03.00/0 © 1992 American Chemical Society

Scheme I

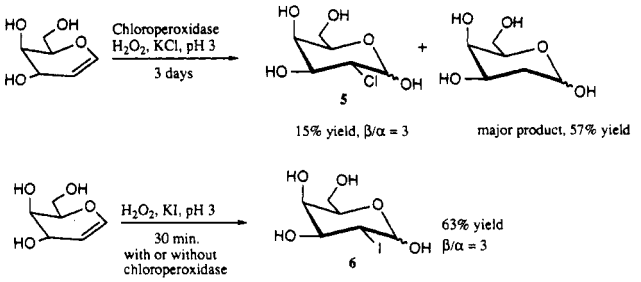


including β-keto acids, steroids, substituted phenol,[5] thiols, thiazole, alkynes, cyclopropanes,[9] alkenes,[10] and sulfides.[11]

We report here the first enzymatic synthesis of 2-deoxy-2-halo sugars using glycals as substrates and chloroperoxidase as a catalyst. These halogenated sugars are biologically important compounds or useful synthons. 2′-Halo-substituted anthracycline glycosides, for example, showed some antitumor activity.[12] 2-Deoxy-2-halo-glycosides are useful intermediates for the synthesis of carbohydrates, such as 2-deoxy glycosides,[13-15] C_2-isotopically labeled glycosides,[16] and other derivatives.[17] Chemically, 2-deoxy-2-halo glycosides have been synthesized via halogenations[18-21] or halogenoalkoxylations.[14,21-23] However, unprotected glycals have not been subjected to halohydration in aqueous solution. The chloroperoxidase-catalyzed halohydration of unprotected glycals described in this paper provides an alternative route to 2-deoxy-2-halo glycosides.

The halohydrations of three glycals, D-galactal, D-glucal, and L-fucal, with hydrogen peroxide and potassium halide in the presence of chloroperoxidase, were investigated in a buffered aqueous solution at pH 3. Enzymatic bromohydrations of D-galactal and L-fucal stereoselectively gave 2-bromo-2-deoxy-D-galactose (β/α = 3) and 2-bromo-2-deoxy-L-fucose (β/α = 2), respectively. When D-glucal was

Scheme II



subjected to the same reaction, a mixture of 2-bromo-2-deoxy-D-mannose (β/α = 0.4) and 2-bromo-2-deoxy-D-glucose (β/α = 3) was obtained (Scheme I). The enzymatic reaction was completed in less than 3 h. The control reaction, however, showed less than 5% formation of halogenated products during the same period of time, and the major product 2-deoxy sugar was isolated in 62–69% yield after 4 days of reaction.

The enzymatic reactions with D-galactal and L-fucal tend to form the thermodynamically favored products, i.e., 2-equatorially substituted halo sugars. The unfavorable 1,3-diaxial interaction may preclude the formation of 2-axially substituted product. In contrast, the lack of 1,3-diaxial interaction may lead to the formation of a mixture of products observed in the case of D-glucal.[14,22]

D-Galactal was further investigated for the enzymatic chlorohydration and iodohydration reactions. In the enzymatic chlorohydration, the same galacto configuration was obtained stereoselectively; the reaction was, however, much slower than the bromohydration reaction and a substantial amount of simple hydration product was formed (Scheme II). On the other hand, iodohydration of galactal was very fast, and in the absence of enzyme, a significant nonenzymatic halohydration was observed.

In summary, chloroperoxidase-catalyzed bromohydration and iodohydration of glycals gave good yields of the corresponding 2-halo-2-deoxy sugars. The enzyme also catalyzes chlorohydrations with a much slower rate. A single isomer can be obtained in the halohydration of D-galactal or L-fucal in aqueous solution.

Experimental Section

General Procedure for Chloroperoxidase-Catalyzed Halohydration. To a reaction mixture containing 20 mL of citric–phosphate buffer (pH 3), 1 mmol of glycal, 5 mmol of potassium halide, and 600 units of the enzyme was added 400 μL of H_2O_2 (30%). After 15 min, another 200 μL of H_2O_2 (30%) was added, and the reaction was continued for 30 min (iodohydration), 2 h (bromohydration), or 3 days (chlorohydration) at room temperature. The solvent was removed under reduced pressure, and methanol was added to the residue. The insoluble material was filtered off, and the solvent was removed under reduced pressure. The residue was purified with silica gel column chromatography to yield 2-deoxy-2-halo sugars. The products were converted to peracetates by a standard method (pyridine, acetic anhydride, 1 day) and purified by silica gel column chromatography for characterization.

Peracetate of compound 1: ^{1}H-NMR ($CDCl_3$) δ, α-isomer, 2.04 (3 H, s), 2.08 (3 H, s), 2.10 (3 H, s), 2.21 (3 H, s), 4.05 (1 H, dd, J = 2.5, 12.5 Hz, H-6), 4.08 (1 H, dd, J = 3.5, 11 Hz, H-2), 4.28 (1 H, ddd, J = 2, 4, 10 Hz, H-5), 4.31 (1 H, dd, J = 4, 12.5 Hz, H-6), 5.09 (1 H, dd, J = 9, 10 Hz, H-3), 5.52 (1 H, dd, J = 9, 11 Hz, H-4), 6.36 (1 H, d, J = 3.5 Hz, H-1) ppm; β-isomer, 2.03 (3 H, s), 2.09 (3 H, s), 2.11 (3 H, s), 2.18 (3 H, s), 3.88 (1 H, ddd, J = 2.4, 4.5, 10.5 Hz, H-5), 3.90 (1 H, dd, J = 9, 10.5 Hz, H-2), 4.11 (1 H, dd, J = 2.5, 12.5 Hz, H-6), 4.32 (1 H, dd, J = 4.5, 12.5 Hz, H-6), 5.03 (1 H, dd, J = 9, 10 Hz, H-3), 5.34 (1 H, dd, J = 9, 10.5 Hz), 5.81 (1 H, d, J = 9 Hz, H-1) ppm; ^{13}C-NMR ($CDCl_3$) δ 20.52–20.67 (4 × C), 47.50, 62.10, 68.46, 72.85, 74.36, 93.11,

(8) Yamada, H.; Itoh, N.; Izumi, Y. *J. Biol. Chem.* **1985**, *260*, 11962 and references cited therein.
(9) Geigert, J.; Neidleman, S. L.; Dalietos, D. J. *J. Biol. Chem.* **1983**, *258*, 2273.
(10) Neidleman, S. L.; Geigert, L. *Trends Biotech.* **1983**, *21*.
(11) Colonna, S.; Gaggero, N.; Manfredi, A.; Gullotti, M.; Casella, L.; Carrea, G.; Pasta, P. *Biochemistry* **1990**, *29*, 10465.
(12) Horton, D.; Priebe, W. In *Anthracycline Antibiotics*; El Khadem, H. S., Ed.; Academic Press: New York, 1982; p 192.
(13) Lemieux, R. U.; Morgan, A. R. *Can. J. Chem.* **1964**, *43*, 2190.
(14) Tatsuta, K.; Fujimoto, K.; Kinoshita, M.; Umezawa, S. *Carbohydr. Res.* **1977**, *54*, 85.
(15) Binkley, R. W.; Bankaitis, D. *J. Carbohydr. Res.* **1982**, *1*, 1.
(16) Lemieux, R. U.; Levine, S. *Can. J. Chem.* **1964**, *64*, 1473.
(17) Horton, D.; Priebe, W.; Sznaidman, M. *Carbohydr. Res.* **1989**, *187*, 149–153.
(18) Igarashi, K.; Honna, T.; Imagawa, T. *J. Org. Chem.* **1969**, *35*, 610.
(19) Hall, L. D.; Manville, J. F. *Can. J. Chem.* **1969**, *47*, 361.
(20) Horton, D.; Priebe, W.; Varela, O. *J. Org. Chem.* **1986**, *51*, 3479.
(21) Lemieux, R. U.; Fraser-Reid, B. *Can. J. Chem.* **1965**, *43*, 1460.
(22) Horton, D.; Priebe, W.; Sznaidman, M. *Carbohydr. Res.* **1990**, *205*, 71 and references cited therein.
(23) Monneret, C.; Choay, P. *Carbohydr. Res.* **1981**, *96*, 299.

167.91–172.10 (4 × C) ppm; HRMS (M + Na^+) calcd 433.0110/435, found 433.0112/435.

Peracetate of compound 2: ^{1}H-NMR ($CDCl_3$) δ, α-isomer, 2.07 (3 H, s), 2.10 (3 H, s), 2.11 (3 H, s), 2.17 (3 H, s), 4.19 (1 H, ddd, J = 2.5, 4.5, 10.5 Hz, H-5), 4.17 (1 H, dd, J = 2.5, 10.5 Hz, H-6), 4.23 (1 H, dd, J = 4.5, 12.5 Hz, H-6), 4.43 (1 H, dd, J = 2, 4 Hz, H-2), 5.21 (1 H, dd, J = 4, 9.5 Hz, H-4), 5.45 (1 H, t, J = 10 Hz, H-4), 6.32 (1 H, d, J = 2 Hz, H-1) ppm; ^{13}C-NMR ($CDCl_3$) δ 20.60, 20.66, 20.75, 20.86, 47.77, 61.82, 65.54, 68.75, 71.25, 93.11, 167.20–171.90 (4 × C) ppm; β-isomer, 2.07 (3 H, s), 2.10 (3 H, s), 2.12 (3 H, s), 2.18 (3 H, s), 3.82 (1 H, ddd, J = 2.5, 5, 9.5 Hz, H-5), 4.13 (1 H, dd, J = 2.5, 12.5 Hz, H-6), 4.27 (1 H, dd, J = 5, 10.5 Hz, H-6), 4.60 (1 H, dd J = 3.5, 1.5 Hz, H-2), 5.00 (1 H, dd, J = 4, 9.5 Hz, H-3), 5.43 (1 H, t, J = 9.5 Hz, H-4), 5.74 (1 H, d, J = 1.5 Hz, H-1) ppm; ^{13}C-NMR ($CDCl_3$) δ 20.60–20.85 (4 × C), 51.05, 61.82, 65.27, 71.01, 73.04, 90.01, 167.20–171.90 (4 × C) ppm; HRMS (M + Na^+) calcd 433.0110/435, found 433.0115.435.

Peracetate of compound 3: ^{1}H-NMR ($CDCl_3$) δ, β-isomer, 2.04 (3 H, s), 2.07 (3 H, s), 2.16 (3 H, s), 2.19 (3 H, s), 4.08 (1 H, dd, J = 9, 11.5 Hz, H-2), 4.10–4.15 (3 H, m, 2 × H-6 and H-5), 5.15 (1 H, dd, J = 3, 11.5 Hz, H-3), 5.35 (1 H, d, J = 3 Hz, H-4), 5.84 (1 H, d, J = 9 Hz, H-1) ppm; ^{13}C-NMR ($CDCl_3$) δ 20.42, 20.52, 20.61, 20.66, 46.35, 60.89, 67.03, 71.94, 72.78, 93.43, 168.31–170.90 (4 × C) ppm; α-isomer, ^{13}C-NMR ($CDCl_3$) δ 20.42–20.66 (4 × C), 44.39, 67.04, 67.69, 68.64, 69.39, 91.05, 167.01–170.86 (4 × C) ppm; HRMS (M + Na^+) calcd 433.0110/435, found 433.0119.435.

Compound 4: ^{1}H-NMR ($CDCl_3$) δ, β-isomer, 1.12 (3 H, d, J = 6.5, CH_3), 3.45 (1 H, dd, J = 1, 3 Hz, H-4), 3.52 (1 H, dd, J = 3, 10.5 Hz, H-3), 3.58 (1 H, qd, J = 1, 6.5 Hz, H-5), 3.69 (1 H, dd, J = 8.5, 10.5 Hz, H-2), 4.45 (1 H, d, J = 8.5 Hz, H-1); ^{13}C-NMR ($CDCl_3$) δ, β-isomer 16.71, 58.04, 72.13, 73.56, 76.03, 98.78 ppm; α-isomer, 16.71, 54.71, 67.25, 71.13, 74.55, 94.20 ppm; HRMS (M + Na^+) calcd 248.9738/251, found 248.9730/251.

Peracetate of compound 5: ^{1}H-NMR ($CDCl_3$) δ, β-isomer, 2.05 (3 H, s), 2.08 (3 H, s), 2.16 (3 H, s), 2.18 (3 H, s), 4.06 (1 H, dd, J = 9, 11.5 Hz, H-2), 4.07–4.15 (3 H, m, 2 × H-6 and H-5), 5.09 (1 H, dd, J = 3, 11.5 Hz), 5.39 (1 H, d, J = 3 Hz, H-4), 5.75 (1 H, d, J = 9 Hz, H-1) ppm; ^{13}C-NMR ($CDCl_3$) δ, β-isomer, 20.21–22.55 (4 × C), 55.30, 60.87, 66.84, 71.86, 72.74, 93.53, 168.20–180.21 (4 × C) ppm; α-isomer, 20.1–22.55 (4 × C), 53.46, 61.04, 67.44, 68.67, 69.51, 90.94, 168.20–180.21 (4 × C) ppm; HRMS (M + Na^+) calcd 389.0615/391, found 389.0610/391.

Peracetate of compound 6: ^{1}H-NMR ($CDCl_3$) δ, β-isomer, 2.04 (3 H, s), 2.07 (3 H, s), 2.12 (3 H, s), 2.17 (3 H, s), 4.06–4.17 (4 H, m, H-2, 2 × H-6 and H-5), 5.13 (1 H, dd, J = 3.5, 10 Hz, H-3), 5.25 (1 H, d, J = 3.5 Hz, H-4), 5.91 (1 H, d, J = 9.5 Hz, H-1) ppm; ^{13}C-NMR ($CDCl_3$) δ, β-isomer, 20.5–22.50 (4 × C), 24.98, 60.94, 67.10, 72.16, 74.10, 94.15, 168.20–179.36 (4 × C) ppm; α-isomer, 20.5–22.50 (4 × C), 29.87, 60.63, 67.68, 68.31, 69.42, 92.16, 168.20–179.36 (4 × C) ppm; HRMS (M + Na^+) calcd 480.9972, found 480.9999.

Acknowledgment. This research was supported by the NIH (GM44154).

Supplementary Material Available: ^{1}H NMR spectra of **1–6** (6 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

Additions and Corrections

Vol. 56, 1991

Shubh D. Sharma, Geza Toth, and Victor J. Hruby*. A Simple General Method for (Radio)iodination of a Phenylalanine Residue in Peptides: Preparation of [D-Pen^2,4′-^{125}I-Phe^4,D-Pen^5]Enkephalin, a Peptide with Extraordinary Selectivity for δ-Opioid Receptors.

Page 4981. Since publication of our results, two other recent examples of radioiodination of phenylalanine residues using an alternative method have come to our attention. These include radioiodination of angiotensin and [D-Ala^2]Enk by Bossé et al. [Bossé, R.; Neugelbauer, W.; Escher, E. In *Synthesis and Applications of Isotopically Labelled Compounds 1988*; Baillie, T. A., Jones, J. R., Eds.; Elsevier Sci. Publ.: Amsterdam, 1989; pp 761–766] and a second paper on the radioiodination of Phe-containing opioid peptides by Bossé and Escher [Bossé, R.; Escher, E. In *Peptides 1990*; Giralt, E., Andreu, D., Eds.; ESCOM Science Publishers: Leiden, 1991; pp 632–634].

Ronald P. W. Kesselmans, Joannes B. P. A. Wijnberg,* and Aede de Groot*. Synthesis of All Stereoisomers of Eudesm-11-en-4-ol. 1. Stereospecific Synthesis of the Trans- and Cis-Fused Octahydro-8-hydroxy-4a,8-dimethyl-2(1*H*)-naphthalenones. Conformational Analysis of the Cis-Fused Compounds.

Page 7234, column 2, line 32, should read "**9d(A)** is reduced to less than 0.1%, ...".