Synthesis of 11-Deoxy-8-azaprostaglandin E_1

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Received February 16, 1977

In two recent communications, Bolliger and Muchowski[2] and DeKoning and co-workers[3] reported the synthesis of 11-deoxy-8-aza-PGE_1. A similar route to that of Bollinger and Muchowski has also been reported in a patent by Himizu and co-workers.[4] We would like to report herein an alternative synthetic sequence to 8-aza-PGE_1 (**8a**) and 8-aza-15-*epi*-PGE_1 (**8b**) as outlined in Scheme I.

Reaction of pyroglutamic acid (1) with 2-amino-2-methyl-1-propanol in refluxing $PhCH_3$ containing HMPA afforded the oxazoline **2**[5] (64%; mp 92–95 °C). Methylation of **2** with methyl iodide in refluxing nitromethane and subsequent reduction of the resulting oxazolinium iodide with sodium borohydride[6] in methanol yielded the oxazolidines **3** (54%; mp 93–96 °C).

Alkylation of the sodium salt of the oxazolidines **3** with methyl 7-bromoheptanoate in refluxing THF and subsequent chromatography on silica gel G and elution with ether–hexane solutions afforded the esters **4** (49%). Hydrolysis of **4** with an aqueous trifluoroacetic acid–THF solution at room temperature for 3.5 h yielded the aldehyde **5** (77%). The aldehyde proved to be relatively stable, if chromatographed immediately on silica gel G with ether–hexane solutions and stored at −5 °C.

Reaction of the aldehyde **5** with the lithium salt of dimethyl (2-oxo-heptyl)phosphonate in THF at 0 °C and subsequent chromatography on silica gel G with ether–hexane solutions afforded the enone **6** (76%). The enone **6** was allowed to react with an ethanolic sodium borohydride solution at −40 °C for a 2.5-h period. The excess $NaBH_4$ was destroyed with a 10% ethanolic hydrochloric acid solution at −40 °C and the crude reaction product was passed through a short column of silica gel G to afford a 1:1 mixture of the ester alcohols **7a** and **7b** (82%). A more extensive column chromatography of the epimeric C-15 alcohols **7a** and **7b** on silica gel G and elution with ether–hexane solutions yielded a faster moving (less polar) diastereoisomer and a diastereoisomeric mixture of **7a** and **7b** enriched in **7a** as determined by TLC analysis. The less polar compound was tentatively assigned to the 15β-epimer **7b**, in analogy with the characteristic TLC behavior of methyl 11-deoxy-15-*epi*-PGE_1 and methyl 11-deoxy-PGE_1.

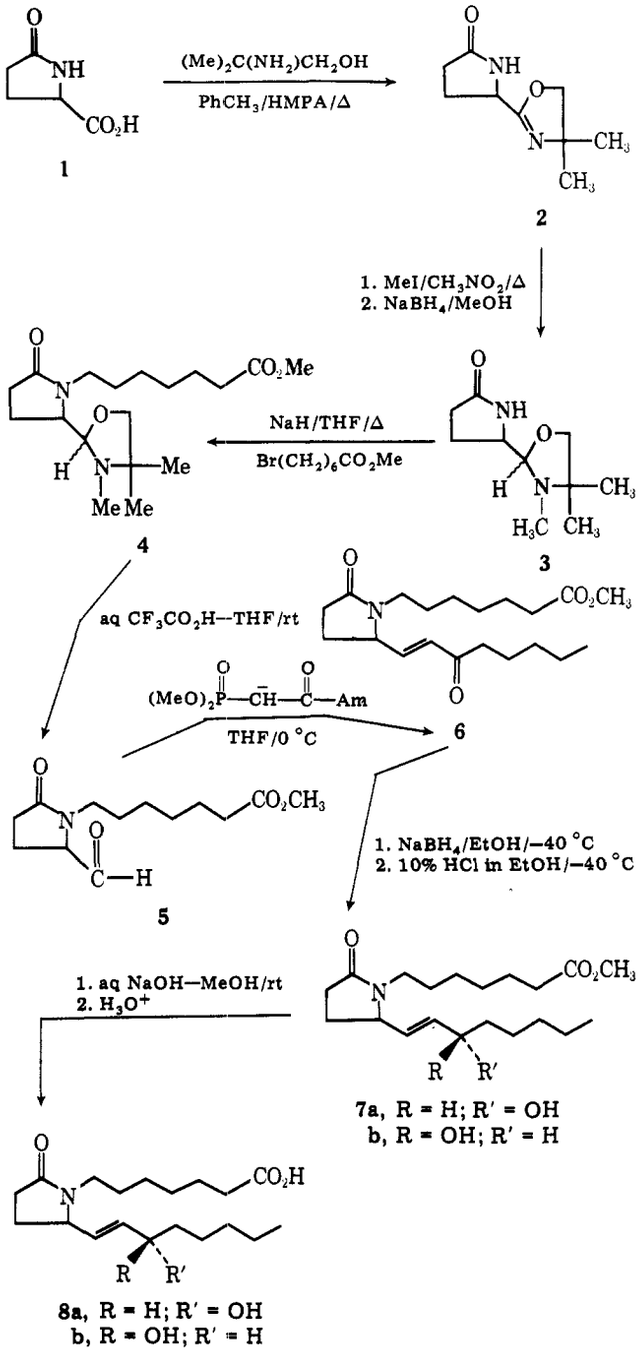
Reaction of the ester alcohol **7b** with an aqueous methanolic sodium hydroxide solution at room temperature and subsequent acidification afforded 8-aza-11-deoxy-15-*epi*-PGE_1 (**8b**) (mp 89–90 °C).

Hydrolysis of the diastereoisomeric mixture of **7a** and **7b** (enriched in **7a** via column chromatography) with an aqueous methanolic sodium hydroxide solution at room temperature and subsequent acidification yielded a C-15 epimeric mixture of acids. Trituration of these acids with a hot ether–hexane solution afforded the higher melting diastereoisomer, 8-aza-11-deoxy-PGE_1 (**8a**) (mp 108.5–110 °C).

Saponification of the 1:1 mixture of the ester alcohols **7a** and **7b** with an aqueous methanolic sodium hydroxide solution at room temperature followed by acidification yielded a C-15 epimeric mixture of acids **8a** and **8b** [72%; mp 82.5–85 °C].

The acid alcohols were found[7] to be active in inhibiting gastric acid secretion.

Scheme I



Experimental Section

2-(5-Oxo-2-pyrrolidinyl)-4,4-dimethyl-2-oxazoline (2). *dl*-Pyroglutamic acid (1) (25.0 g, 0.194 mol) was dissolved in 70 mL of hexamethylphosphoramide (HMPA). 2-Amino-2-methylpropanol (17.3 g, 0.194 mol) and 250 mL of toluene were added and the resulting mixture was heated to reflux for 72 h utilizing a Dean–Stark trap. After cooling, toluene was removed with a rotary evaporator and the remaining toluene and unreacted amino alcohol were removed by distillation at 12 mm, and the HMPA at 0.15 mm. Distillation of the resulting residue afforded 22.9 g (64%) of the oxazoline **2**: bp 140–147 °C (0.15 mm); mp 92–95 °C (washed with hexanes); NMR ($CDCl_3$) δ 7.0 (s, 1 H), 4.10–4.33 (m, 1 H), 3.95 (s, 2 H), 2.15–2.52 (m, 4 H), 1.30 (s, 6 H); IR (CCl_4) 1670 and 1711 cm^{-1}.

Anal. Calcd for $C_9H_{14}N_2O_2$: C, 59.32; H, 7.74; N, 15.37. Found: C, 59.06; H, 7.75; N, 15.34.

2-(5-Oxo-2-pyrrolidinyl)-3,4,4-trimethyloxazolidines (3). The oxazoline **2** (53.0 g, 0.29 mol) was dissolved in 175 mL of dry CH_3NO_2. Methyl iodide (82.7 g, 0.58 mol) was added to the above solution and the resulting mixture was heated at 70 °C for 2 days with stirring. Additional methyl iodide was added to maintain a decent CH_3I reflux rate over a 2-day period. Excess methyl iodide and nitromethane were removed by distillation at 12 mm, thus affording 89 g (94%) of the oxazolinium iodide, a viscous brown syrup which turned to a glassy solid on standing at room temperature: NMR [CH_3NO_2 (δ 4.33) and

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Publication Date: September 1, 1977 | doi: 10.1021/jo00439a021

CH_3I (δ 2.15), standards] δ 7.25 (s, br, 1 H), 4.95–5.25 (m, 1 H), 4.85 (s, 2 H), 3.39 (s, 3 H), 2.20–2.60 (m, 4 H), 1.58 (s) and 1.62 (s) (6 H).

Since the oxazolinium iodide is very hygroscopic, the salt was reduced directly to the oxazolidines **3**.

A solution of $NaBH_4$ (6.5 g, 0.17 mol) dissolved in 250 mL of absolute MeOH was cooled at 0 °C. A solution of the oxazolinium iodide (20 g, 0.062 mol) dissolved in 82 mL of MeOH was added dropwise over a 30-min period with stirring. The reaction was stirred at 0 °C for 45 min and then between 0 and 20 °C for an additional 45 min. The reaction was concentrated on a rotary evaporator, poured into 150 mL of H_2O, and extracted with three 250-mL portions of $CHCl_3$. The chloroform extracts were washed with NaCl solution, dried ($MgSO_4$), and filtered, and concentration of the chloroform solution with a rotary evaporator yielded an oil which solidified on standing in a freezer. The crude solid was chromatographed with silica gel G and elution with ether afforded 6.6 g (54%) of the pure oxazolidines **3**: NMR (CCl_4) δ 7.35 (s, br, 1 H), 3.90–3.95 (truncated peak, 1 H), 3.52 (s) and 3.30–3.70 (m) (3 H), 2.22 (s) and 1.80–2.30 (m) (7H), 1.13 (s, 3 H), and 0.97 (s, 3 H): IR (CCl_4) 3455, 3215, 3100, and 1710 cm^{-1}; mp 93–96 °C.

Anal. Calcd for $C_{10}H_{18}N_2O_2$: C, 60.58; H, 9.15; N, 14.13. Found: C, 60.68; H, 9.17; N, 13.96.

2-[5-Oxo-1-(6-carbomethoxyhexyl)-2-pyrrolidinyl)]-3,4,4-trimethyloxazolidines (4). The oxazolidine **3** (7.94 g, 0.04 mol) was dissolved in 100 mL of dry THF. A 50% suspension of sodium hydride in mineral oil (1.92 g, 0.04 mol) was added and the resulting mixture was stirred for 1.4 h at room temperature under N_2. Methyl 7-bromoheptanoate (8.92 g. 0.04 mol) dissolved in 20 mL of dry THF was added dropwise over a 5-min period, and the addition funnel was rinsed with an additional 10 mL of THF. The resulting reaction mixture was refluxed for 91 h and then allowed to cool. The solvent was removed and the resulting oil was poured into 150 mL of H_2O and extracted with three 200-mL portions of CH_2Cl_2. The dried methylene chloride extracts were concentrated to give 14.1 g of crude **4**. The crude oil was chromatographed with silica gel G, and elution with ether–hexane solutions yielded 6.7 (49%) of the ester oxazolidines **4**: NMR (CCl_4) δ 4.17 (d, 1 H, methine of oxazolidine), 3.61 (s, $-CO_2CH_3$), 3.54 (s, $-OCH_2-$), 3.0–3.75 (m, methine of pyrrolidinone) (6 H), 2.19 and 2.22 (singlets, two *N*-methyls of oxazolidine), 2.50–1.80 (multiplets, buried, $-CH_2C(O)N$, $-CH_2N$, $-CH_2CO_2Me$, $-CH_2CHN$), 1.80–1.20 (m, $-(CH_2)_4$ of side chain), 0.99 and 1.10, and 1.03 and 1.14 (singlets, *gem*-dimethyls) (25 H); IR (neat) 1741 and 1684 cm^{-1}.

Anal. Calcd for $C_{18}H_{32}O_4N_2$: C, 63.50; H, 9.47; N, 8.23. Found: C, 63.64; H, 9.45; N, 8.14.

Methyl 7-(2-Formyl-5-oxo-1-pyrrolidinyl)heptanoate (5). The ester oxazolidine (500 mg, 0.001 47 mol) was dissolved in an aqueous THF–CF_3CO_2H solution [0.5 mL of THF, 0.5 mL of H_2O and trifluoroacetic acid (0.24 g, 0.0021 mol)] and stirred for 3.5 h at room temperature. The reaction was poured into 20 mL of H_2O and extracted with three 50-mL portions of CH_2Cl_2. The methylene chloride extracts were combined, washed with 40 mL of a 5% $NaHCO_3$ solution, and dried. Concentration of the CH_2Cl_2 solution with a rotary evaporator and pumping the resulting oil at 0.1 mm with heat afforded 0.29 g (77%) of the aldehyde **5**: NMR (CCl_4) δ 9.54 (d, 1 H, J = 3 Hz), 3.75–4.15 (m), 3.60 (s), and 2.55 and 3.50 (m) (6 H), 1.90–2.50 (br, m) and 1.0–2.80 (br, m) (8 H); IR (neat) 2860, 2715, 1740 and 1730 (saw tooth) and 1670 cm^{-1}. The aldehyde proved to be stable, if chromatographed immediately and stored in a freezer at −5 °C. TLC analysis showed **5** as one spot; however, after Kugelrohr distillation [200 °C (0.08 mm)] TLC analysis indicated a less polar top spot (~20%) present in distilled **5**. The aldehyde **5** was therefore committed directly, after column chromatography, to the Wadsworth–Emmons reaction.

Methyl 8-Aza-9,15-dioxo-13,14-dehydroprostanoate (6). A three-neck flask fitted with a condenser, nitrogen inlet tube, magnetic stirring bar, and serum cap was flamed and deaerated with nitrogen. Dimethyl (2-oxoheptyl)phosphonate (627 mg, 0.0028 mol) dissolved in 25 mL of THF was placed in the reaction vessel under N_2 and cooled to 0 °C. A hexane solution of 2.5 M BuLi (1.12 mL, 0.0028 mol) was added with a syringe and the reaction was allowed to stir at 0 °C for 20 min. The ester aldehyde **5** (800 mg, 0.003 14 mol) dissolved in 25 mL of dry THF was added to the reaction all at once at 0 °C and the resulting reaction mixture was allowed to stir at 0 °C for 2.5 h. The milky white reaction was poured into an ice–water mixture and extracted with CH_2Cl_2. The dried extracts were concentrated to give 1.25 g of an oil. The oil (1.25 g) was chromatographed immediately using silica gel G and elution with ether–hexane solutions yielded 750 mg (76%) of pure enone **6**: NMR (CCl_4) δ 6.60 (q, J_{12-13} = 8, J_{13-14} = 16 Hz) and 6.11 (d, J_{13-14} = 16 Hz) (2 H), 4.85–4.30 (m), 3.60 (s), and 3.55–2.63 (m) (6 H), 2.00–2.55 (m), 1.08–1.92 (br peak), and 0.95 (t, distorted) (25 H); IR (neat) 1735, 1690, and 1680 (shoulder) cm^{-1}; mass spectrum *m/e* 351 (M), 320 (M − OCH_3), 252 (M − COC_5H_{11}), 222 [M − $(CH_2)_5CO_2CH_3$].

Anal. Calcd for $C_{20}H_{33}NO_4$: C, 68.34; H, 9.46; N, 3.99. Found: C, 68.39; H, 9.55; N, 3.83.

Methyl 15α- and 15-*epi*-11-Deoxy-8-aza-PGE$_1$ (7a and 7b). A three-neck flask fitted with two addition funnels, a magnetic stirring bar, and a nitrogen inlet tube was flamed and deaerated with nitrogen. $NaBH_4$ (180 mg, 0.0048 mol) was placed in the reaction vessel and the vessel was cooled to −40 °C. Dry ethanol was added to obtain a clear ethanolic $NaBH_4$ solution at −40 °C. The enone **6** (820 mg, 0.0023 mol) dissolved in 30 mL of absolute ethanol was added all at once and the reaction mixture was allowed to stir for 2.5 h at −40 °C. Excess $NaBH_4$ was killed with a 10% ethanolic HCl solution at −40 °C and the reaction mixture was concentrated with a rotary evaporator. The resulting residue was poured into 50 mL of H_2O and extracted with three 150-mL portions of CH_2Cl_2. The dried methylene chloride extracts were concentrated; chromatography with a short silica gel column and elution with ether–hexane solutions yielded 800 mg of a 1:1 epimeric mixture of the ester alcohols **7a** and **7b**: NMR (CCl_4) δ 5.15–5.80 (m, 2 H), 3.75–4.15 (m), 3.60 (s), and 2.55–3.45 (m) (8 H), 1.90–2.50 (br peak), 1.15–1.85 (br peak), and 0.90 (t, distorted) (25 H); IR (CCl_4) 1745 and 1680 cm^{-1}; mass spectrum *m/e* 353 (m), 336 (M − OH), 335 (M − H_2O), 322 (M − OCH_3), 278 [M − OH and $(CH_2)_3CH_3$], 252 (M − $C_5H_{11}CHOH$), 226 (M − CH=CHCHOHC_5H_{11}), 224 [M − $(CH_2)_5CO_2Me$], 194 (M − CH=CHCHOHC_5H_{11} and CH_3OH or M − CH_2=CH$(CH_2)_4CO_2CH_3$ and OH), 178 (M − $C_5H_{11}CHOH$ and $CH_3CO_2CH_3$).

Anal. Calcd for $C_{20}H_{35}NO_4$: C, 67.95; H, 9.98; N, 3.96. Found: C, 67.77; H, 10.03; N, 3.79.

Chromatography of the 1:1 epimeric mixture of ester alcohols **7a** and **7b** on silica gel G and elution with ether–hexane solutions afforded 200 mg of a faster moving (less polar) diastereoisomer and 510 mg of a diastereoisomeric mixture of **7a** and **7b** which was enriched in **7a** as determined by TLC analysis. The less polar compound was tentatively assigned to the 15β epimer **7b** in analogy with the characteristic TLC behavior of methyl 11-deoxy-15-*epi*-PGE_1 and methyl 11-deoxy-PGE_1. The less polar diastereoisomer **7b** was not characterized further, but was subjected directly to basic hydrolysis.

15-*epi*-11-Deoxy-8-aza-PGE$_1$ (8b). Methyl 15-*epi*-11-deoxy-8-aza-PGE_1 (**7b**) (0.20 g, 0.000 567 mol) was dissolved in 2.6 mL of methanol. An aqueous sodium hydroxide solution [NaOH (0.026 g, 0.000 65 mol) and 1.04 mL of H_2O] was added to the above solution and the resulting mixture was stirred at room temperature for 20 h.

The reaction mixture was poured into 10 mL of H_2O and extracted with ether. The aqueous layer was acidified with concentrated HCl and extracted with methylene chloride. The dried extracts were concentrated to give approximately 200 mg of the acid (**8b**).

An ether–hexane solution was added to the acid (**8b**) and the resulting solid was filtered with suction and triturated with hot Et_2O to afford 80 mg (42%) of pure 15-*epi*-11-deoxy-8-aza-PGE_1 (**8b**): mp 89–90 °C (Et_2O); IR (KBr) 3550–3150 (br), 1735 and 1665 cm^{-1}; mass spectrum *m/e* 339 (M), 322 (M − OH), 321 (M − H_2O), 268 (M − C_5H_{11}), 264 [M − H_2O and $(CH_2)_3CH_3$], 250 (M − C_5H_{11} and H_2O), 238 (M − $C_5H_{11}CHOH$), 225 [M − CH_2=CH$(CH_2)_4CO_2H$], 224 [M − $(CH_2)_5CO_2H$], 212 (M − CH=CHCHOHC_5H_{11}), 210 [M − $(CH_2)_6CO_2H$].

Anal. Calcd for $C_{19}H_{33}NO_4$: C, 67.22; H, 9.80; N, 4.13. Found: C, 67.09; H, 9.78; N, 4.04.

11-Deoxy-8-aza-PGE$_1$ (8a). The diastereoisomeric mixture **7a** and **7b**, enriched in **7a** (400 mg, 0.001 13 mol), was dissolved in 6 mL of methanol. An aqueous sodium hydroxide solution [NaOH (0.052 g, 0.00130 mol) and 2.5 mL of H_2O] was added to the above solution and the resulting mixture was stirred at room temperature for 23 h.

The reaction mixture was poured into 15 mL of H_2O and extracted with two 25-mL portions of Et_2O. The aqueous layer was acidified with concentrated HCl and extracted with three 60-mL portions of CH_2Cl_2; 390 mg of the acids **8a** and **8b** was obtained.

Addition of an ether–hexane solution to the epimeric acids **8a** and **8b** afforded a solid. Repeated trituration of the solid with a hot ether–hexane solution afforded the higher melting diastereoisomer, 11-deoxy-8-aza-PGE_1 **8a**: mp 108.5–110 °C; IR (KBr) 3500–3100 (br), 1735 and 1665 cm^{-1}; mass spectrum *m/e* 339 (M), 322 (M − OH), 321 (M − H_2O), 268 (M − C_5H_{11}), 264 [M − H_2O and $(CH_2)_3CH_3$], 250 (M − C_5H_{11} and H_2O), 238 (M − $C_5H_{11}CHOH$), 225 [M − CH_2=CH$(CH_2)_4CO_2H$], 224 [M − $(CH_2)_5CO_2H$], 212 (M − CH=CHCHOHC_5H_{11}), 210 [M − $(CH_2)_6CO_2H$].

Anal. Calcd for $C_{19}H_{33}NO_4$: C, 67.22; H, 9.80; N, 4.13. Found: C, 67.56; H, 9.64; N, 4.03.

A 1:1 Epimeric Mixture of 15α- and 15-*epi*-11-Deoxy-8-aza-

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Publication Date: September 1, 1977 | doi: 10.1021/jo00439a021

PGE_1 (8a and 8b). The 1:1 mixture of epimeric ester alcohols **7a** and **7b** (1.15 g, 0.003 26 mol) was dissolved in 15 mL of methanol. An aqueous sodium hydroxide solution [NaOH (150 mg, 0.00375 mol) and 6 mL of H_2O] was added to the above solution and the resulting mixture was stirred at room temperature for 20 h.

The reaction mixture was poured into 50 mL of H_2O and extracted with two 50-mL portions of ether. The aqueous layer was acidified with concentrated HCl at 0 °C and extracted with three 200-mL portions to CH_2Cl_2. The dried methylene chloride extracts were concentrated to give 1.0 g (90%) of an oil, crude **8**, which solidified on standing at −5 °C. The solid was chromatographed using silica gel G and elution with hexane–ether and ether–CH_2Cl_2 solutions yielded 800 mg (72%) of a pure 1:1 epimeric mixture of 15α- and 15-*epi*-11-deoxy-8-aza PGE_1: mp 82.5–85 °C; NMR ($CDCl_3$) δ 0.87 (t, distorted, 3 H), 1.10–1.90 (br hump), 2.0–2.60 (m) and 2.8–3.70 (m) (24H), 4.28–3.86 (m, 1 H), 5.48–5.75 (m, 2 H) and 6.37 (s, 2 H). After addition of D_2O the resonance peak at δ 6.37 disappeared: IR (KBr) 3400 (shoulder), 3200, 2910, 2600 (shoulder), 1715 and 1650 cm^{-1}; mass spectrum *m/e* 339 (M), 322 (M − OH), 321 (M − H_2O), 268 (M − C_5H_{11}), 264 [M − H_2O and $(CH_2)_3CH_3$], 250 (M − C_5H_{11} and H_2O), 238 (M − $C_5H_{11}CHOH$), 225 [M − CH_2=$CH(CH_2)_4CO_2H$], 224 [M − $(CH_2)_5CO_2H$], 212 (M − CH=$CHCHOHC_5H_{11}$), 210 [M − $(CH_2)_6CO_2H$)].

Anal. Calcd for $C_{19}H_{33}NO_4$: C, 67.22; H, 9.80; N, 4.13. Found: C, 67.08; H, 9.91; N, 4.08.

Acknowledgment. We would like to thank the A. H. Robins Co. for a grant in support of this work, Mr. John Forehand for mass spectra data, Mr. Malcolm Stone for microanalysis, and Mr. Ashby F. Johnson, Jr., for coordinating the data obtained from the Robins Co.

Registry No.—**1**, 149-87-1; **2**, 62842-02-8; **2** methiodide, 62861-45-4; **3** isomer 1, 62861-46-5; **3** isomer 2, 62842-03-9; **4** isomer 1, 62861-47-6; **4** isomer 2, 62861-48-7; **5**, 57740-57-5; **6**, 57740-58-6; **7a**, 57740-59-7; **7b**, 57740-60-0; **8a**, 57740-61-1; **8b**, 57740-62-2; 2-amino-2-methylpropanol, 124-68-5; methyl 7-bromoheptanoate, 54049-24-0; dimethyl (2-oxoheptyl)phosphonate, 36969-89-8.

References and Notes

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(7) We would like to thank Dr. W. J. Welstead, Jr., and Dr. C. Lunsford of the A. H. Robins Pharmaceutical Company, Richmond, Va., for making these results known to us.

Use of Insoluble Polymer Supports in Organic Synthesis. 9. Synthesis of Unsymmetrical Carotenoids on Solid Phases[1]

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Received February 16, 1977

Carotenoids have been synthesized by many routes.[2] One of the most attractive routes to *symmetrical* carotenoids, such as β-carotene, is the $C_{15} + C_{10} + C_{15}$ approach,[3] whereby 2 mol of a suitable C_{15} Wittig reagent reacts with the *symmetrical* C_{10} dialdehyde, 2,7-dimethyl-2,4,6-octatrien-1,8-dial (**1**).[4] This approach has also been used in the synthesis of *unsymmetrical* carotenoids such as γ-carotene, whereby the symmetrical dialdehyde **1** first reacts with one C_{15} Wittig reagent to yield the product from reaction at just one end of the aldehyde, namely an apocarotenal.[3,5,6] All these cases give apocarotenals or their analogues <60% yield and in some cases under 5% yield.[6] Subsequent reaction of the apocarotenal with a second C_{15} Wittig reagent yields the unsymmetrical carotenoid. Alternatively, the symmetrical dialdehyde **1** can react with a 1:1 mixture of two different C_{15} Wittig reagents to give unsymmetrical carotenoids contaminated with large quantities of symmetrical carotenoids.[6] The unsymmetrical carotenoids are formed in moderate to poor yields by solution methods due to the formation of substantial amounts of symmetrical products and recovery of unreacted reagents. The pure products are then obtained only after careful chromatography.

Table I. Yields of Apocarotenals and Analogues Prepared on Solid Phases

Apocarotenal or analogue	Registry no.	Quantity of 1 bound to 3, mmol/g	Quantity of apocarotenal or analogue, mmol/g	Yield, %
6a	62930-48-7	0.26	0.182	70
6b	62930-49-8	0.26	0.22	86
6c	62948-59-8	0.195	0.195	100[a]
6d	1638-05-7	0.195	0.056	29
6e	1071-52-9	0.195	0.140	72[a]

[a] The literature yields[3] by solution methods were 45 and 52% for **6c** and **6e**, respectively.

In our laboratory, we have shown that insoluble polymer supports[7] can be used as monoblocking groups for symmetrical diols and have applied this advantage to the synthesis of insect sex attractants.[8] Similarly, polymer-bound 1,2- and 1,3-diols have been used as monoblocking agents of symmetrical aromatic dialdehydes,[9,10] although attempted monoprotection of symmetrical aliphatic dialdehydes failed.[10] In any event, the completely conjugated symmetrical dialdehyde **1** reacted with the previously prepared 2% cross-linked divinylbenzene–styrene copolymer **2**,[9] containing vicinal diol groups, in anhydrous dioxane containing *m*-benzenedisulfonic acid as catalyst. This product gave the monoblocked polymer-bound aldehyde **3**, which exhibited an absorption in its IR spectrum at 1680 cm^{-1}. Cleavage of the aldehyde from the polymer in 0.5 N HCl in wet tetrahydrofuran (THF) led to recovered **1** and **2**, the latter exhibiting no absorption in the carbonyl region of its IR spectrum. Based on recovered **1**, the capacity of **3** was 0.2–0.3 mmol of 1/g. Condensation of **3** with the Wittig reagent prepared from *m*-nitrobenzyltriphenylphosphonium bromide (**4a**) and base[11] yielded the polymer-bound Wittig product **5a**, exhibiting IR absorption bands at 1530 and 1350 cm^{-1} typical of the nitro group. Indeed, as IR spectroscopy remains one of the few tools by which reactions can be followed on polymer supports, the nitro-Wittig reagent was carefully selected in the first instance in order to follow the progress of this synthetic route. Thus, in this reaction a polymer-bound product **5a** containing a diagnostic IR absorption band was obtained. Acid hydrolysis of **5a** gave the mono Wittig adduct, 2,7-dimethyl-9-(*m*-nitrophenyl)-2,4,6,8-nonatetraen-1-al (**6a**) in good yield (Table I). Similarly, the Wittig reagent, prepared from benzyltriphenylphosphonium bromide (**4b**)[11] gave the polymer-bound product **5b**, which on acid cleavage yielded 2,7-dimethyl-9-phenyl-2,4,6,8-nonatetraen-1-al (**6b**) in high yield (Table I).

The Wittig reagents, prepared from α[3], β[12], and ψ-ionylideneethyltriphenylphosphonium bromides[3] and *n*-butyllithium, respectively, reacted with polymer-bound aldehyde **3** in anhydrous dioxane to give the polymer-bound apocarotenals **5c**, **5d**, and **5e**, respectively. Cleavage of **5c–e** under acidic conditions led to α-apo-12′-carotenal (**6c**),[3] β-apo-12′-carotenal (**6d**),[13] and apo-12′-lycopenal (**6e**)[3] in good yields (Table I). The formation of **6d** was accompanied by the recovery of 64% of unreacted dialdehyde **1**, but no dialdehyde

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Publication Date: September 1, 1977 | doi: 10.1021/jo00439a021