Preparation of 9-Hydroxy-14-azaprostanoic Acids

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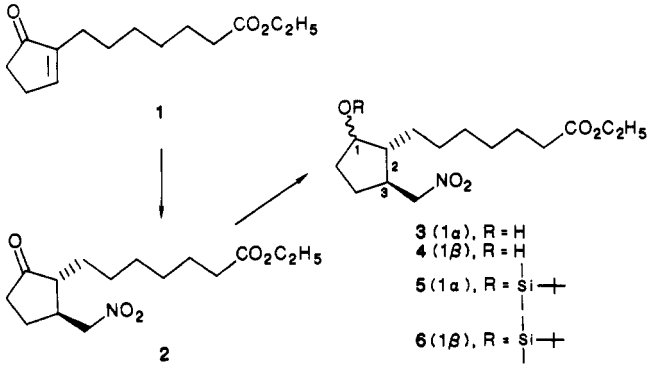
The title compounds **13**, **14**, **19**, and **20** were prepared from 2-(6-carbethoxyhexyl)cyclopent-2-en-1-one (**1**). Conjugate addition of nitromethane and subsequent stereoselective reduction of the ketone **2** with lithium tri-*sec*-butyl hydride provided the desired natural prostaglandin stereochemistry on the five-membered ring. Protection of the hydroxyl group and ozonolysis of the nitronate salt gave the aldehyde **7** of the same stereochemistry. Unfortunately, condensation of this aldehyde with *n*-hexylamine and in situ $NaBH_4$ reduction resulted in epimerization of the lower side chain and loss of stereochemical control. However, the natural prostaglandin stereochemistry could be retained by first reducing the nitro group, before proceeding with condensation (hexanal) and metal hydride reduction. Stereochemical assignments were in part established through intramolecular hydrogen-bonding experiments.

Lower side-chain azaprostanoids have proven to be interesting and specific modulators of prostaglandin action (TXA_2 antagonists).[1-6] Consequently, we were intersted in extending this work to include $PGF_{2\alpha}$-like azaprostanoids (lacking the 11α-hydroxyl group) in search of specific antagonists of this biologically important prostaglandin.

The present paper describes a stereoselective synthesis of 9α-hydroxy-14-azaprostanoic acid (**19**), possessing the natural prostaglandin stereochemistry. Preparation of the other three possible diastereomers (**13**, **14**, **20**) of this molecule is also described.

Results and Discussion

Syntheses and Stereochemical Analysis of 9-Hydroxy-14-azaprostanoic Acids 13, 14, 19, and 20. Michael addition[7-10] of excess nitromethane to the starting α,β-unsaturated derivative **1** proceeded smoothly within



12–24 h without solvent to give the desired trans nitro derivative **2**. The nitro ketone **2** was reduced with lithium tri-*sec*-butyl hydride to provide the desired cis relationship between the hydroxyl group (i.e., α orientation) and the alkyl ester side chain.[11] The reduction was found to give exclusively (>97%) the desired C-1α isomer **3** in 50% isolated yield.

In contrast, reduction of this same nitro ketone **2** with sodium borohydride gave a 1:1 mixture of the C-1α (**3**) and C-1β (**4**) isomers, which could be separated by column chromatography. Using APT and heteronuclear and homonuclear correlation NMR spectroscopy, the C_1–C_3 and nitromethylene carbons in the two isomers **3** and **4** were assigned.

On comparison, the α isomer **3** was found to have all four of these resonances shifted a few ppm upfield when compared to the same carbons of the β isomer **4**. Roberts and co-workers had previously concluded that such upfield ^{13}C shifts are caused by steric compression and that the shifts could be used to establish stereochemical relationships in simple cyclopentane derivatives.[12] This original work has been extended to the assignment of cis/trans stereochemistry in other more complicated five-membered rings.[13] Application of these techniques in the present work indicates that the shifts observed for the more sterically crowded isomer **3** are in agreement with the stereochemistry of **3** as assigned on the basis of the anticipated stereoselectivity of lithium tri-*sec*-butyl hydride.

Corey and co-workers have been instrumental in the development of protecting groups that suppress side reactions and act as directing groups to affect the stereochemical outcome of a reaction.[14] It seemed reasonable that this type of group might assist the desired stereochemical outcome in the present situation. Both nitro esters **3** and **4**, when treated with TMBDSCl in the usual manner, provided the α and β siloxy nitro esters **5** and **6** in good yield.

The protected nitro esters were converted to the corresponding aldehydes by ozonolysis of the nitronate salt,[15]

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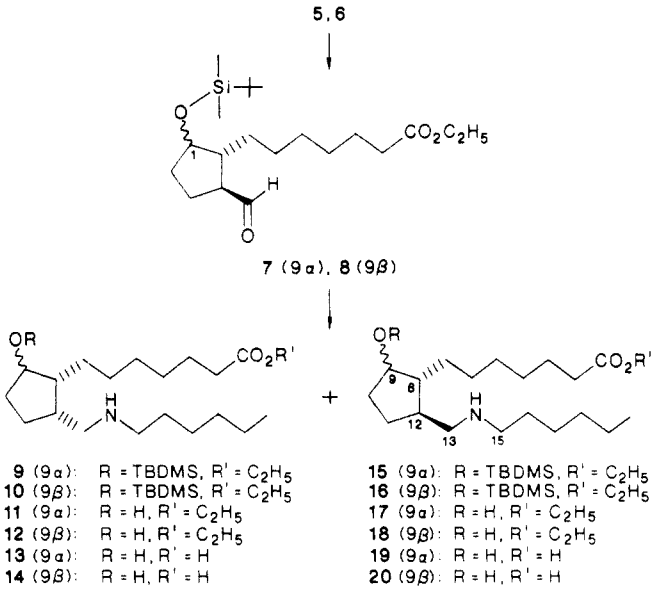
which was found preferable to the $KMnO_4$ procedure.[16] Conventional homonuclear decoupling experiments on freshly prepared material were used to assign the proton resonances at the three chiral centers in the two isomers. Important to the following discussion, these spectra indicate that both α (**7**) and β (**8**) isomers had a trans relationship of the aldehyde and the alkyl ester side chain and there was no indication in either case of cis contamination (^1H NMR <5%).

Condensation of the crude α-trans and β-trans siloxy aldehydes **7** and **8** with *n*-hexylamine was essentially complete in 4–6 h as judged by TLC. Surprisingly, TLC



9 (9α):	R = TBDMS, R' = C_2H_5	**15** (9α):	R = TBDMS, R' = C_2H_5
10 (9β):	R = TBDMS, R' = C_2H_5	**16** (9β):	R = TBDMS, R' = C_2H_5
11 (9α):	R = H, R' = C_2H_5	**17** (9α):	R = H, R' = C_2H_5
12 (9β):	R = H, R' = C_2H_5	**18** (9β):	R = H, R' = C_2H_5
13 (9α):	R = H, R' = H	**19** (9α):	R = H, R' = H
14 (9β):	R = H, R' = H	**20** (9β):	R = H, R' = H

analysis of each reaction mixture, after $NaBH_4$ reduction, revealed two distinct products, which turned out to be the side-chain cis and trans isomers. Thus, four compounds (**9**, **15**, **10**, **16**), two each from the α-trans and β-trans isomers, were isolated by medium-pressure chromatography and gave essentially identical EI and DCI MS. It was found that the isolated yield of the fast-moving, less polar compound (**9**, α-cis) and the slower moving, polar residue (**15**, α-trans) was in a 1 to 6 ratio. On the other hand, the corresponding β-trans isomer yielded a 1 to 2 ratio of **16** (β-trans) and **10** (β-cis). Unexpectedly, isomerization had occurred during the condensation and/or reduction of the intermediate Schiff's bases in both cases.

With the possible exception of C_8, resonances for C_9, C_{12}, C_{13}, and C_{15} showed, by application of the aforementioned steric arguments of Roberts, the expected upfield shifts when the aza derivative **9** (most steric crowding) was compared with **15** (least crowding). However, assignment of stereochemistry based on the ^{13}C NMR spectra for the other two isomers **16** and **10** in this series did not at first glance agree with that as determined by other methods. Stereochemical assignment based on high-field ^1H NMR analysis of the four isomers was also ambiguous (NOE experiments were not attempted). Surprisingly, IR analysis of the four isomers, after removal of the TBDMS groups, provided the strongest spectroscopic evidence for the assigned stereochemistry (see following discussion).

Attempts to cleave the siloxyl groups of all four diastereomers (**9**, **10**, **15**, **16**) with standard fluoride reagents such as tetra-*n*-butylammonium fluoride resulted in only very slow cleavage (60% in 2 days at room temperature).

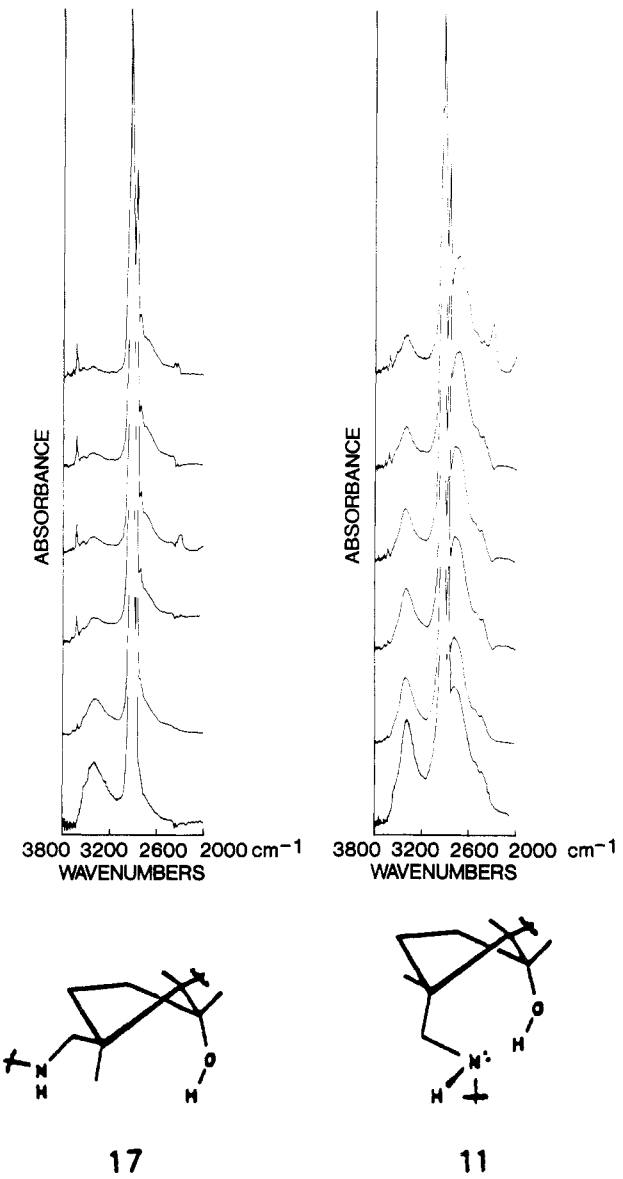


Figure 1. Hydrogen bonding in ethyl 9α-hydroxy-14-azaprostanoates **11** and **17**. Stacked IR spectra (CCl_4) for both compounds have the following molarity (M)/cell thickness (μm) ratios (bottom to top): 0.05/50, 0.03/100, 0.012/200, 0.008/300, 0.006/400, 0.005/500. For further details see the Experimental Section.

The yield of the reaction was not greatly improved by elevated temperature. However, deblocking of the TBDMS derivatives with boron trifluoride etherate proceeded smoothly at room temperature in about 5 h.[17]

The most likely position for the aforementioned isomerization to have occurred is at the C_3 (C_{12} prostaglandin numbering) position. Therefore, if the stereochemical relationship of the C_1 (C_9 prostaglandin numbering) hydroxyl group to that of the lower chain in each of the four isomers could be determined, the overall stereochemistry of the three chiral centers would be established.

If one examines models of the four diastereomers of ethyl 9-hydroxy-14-azaprostanoate, it can be readily seen that two of these derivatives, the 9α-cis (**11**) and 9β-trans (**18**) isomers, can undergo intramolecular hydrogen bonding, whereas their counterparts, the 9α-trans (**17**) and 9β-cis (**12**) cannot. As such, demonstration of intramolecular hydrogen bonding in each of the two sets of dia-

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stereomers, i.e. 9α-cis/trans (**11**, **17**) and 9β-cis/trans (**12**, **18**), would define the relative stereochemistry.

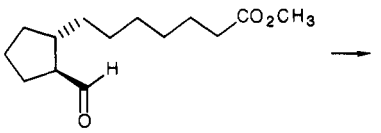
The results of a dilution IR experiment for the 9α-cis (**11**) and 9α-trans (**17**) derivatives are shown in Figure 1. Whereas the α-trans derivative **17** exhibits only intermolecular hydrogen bonding, that of the α-cis **11** exhibits intramolecular hydrogen bonding as well, as evidenced by retention of the broad band at 3400 cm^{-1} upon dilution. Therefore, this compound (α-cis, **11**) must have the hydroxyl group and lower side chain on the same side of the molecule. Consequently, the other compound must be the α-trans isomer.

An analogous set of experiments was performed for the 9β-hydroxy compounds **18** and **12**. As expected, the compound assigned as the 9β-cis derivative (**12**) did not show intramolecular hydrogen bonding whereas that of the 9β-trans did.

Examination of a high-field (360-MHz) ^1H NMR spectra of the unstable aldehydes **7** and **8** showed no indication of doubling for isolated protons near the three chiral centers. That such an analysis is sensitive to stereochemistry at the centers in question is indicated by comparison of the ^1H NMR spectra of aldehydes **7** and **8**, which differ only in stereochemistry about the C_1 position. Change in chirality at C_1 results in a shift of approximately 0.4 ppm for the resonance position of the aldehyde proton and somewhat more than a 0.3 ppm for the proton at the C_1 position. In addition, the individual preparations were homogeneous by capillary GC and TLC.

Since the nitro and aldehyde precursors (**5**–**8**) appear isomerically pure, we conclude that isomerization must be occurring via an imine–enamine type tautomerization.[18] Examination of the relative yields of the four isomers (**9**, **10**, **15**, **16**) suggests that the TBDMS group is playing a role in the stereochemical outcome of the products. Thus, the trans relationship for the side chains is favored in the case where the TBDMS group is in the α position, as would be expected on steric grounds. In addition, the relatively greater proportion of the cis orientation for the β-TBDMS derivative is also consistent with such an argument.

However, the mechanism and driving force for this epimerization must be more complex than suggested by this simple ground-state analysis. Thus, when the aldehyde **21**,[19] lacking the TBDMS group, is condensed with *n*-hexylamine and subsequently reduced with sodium borohydride under the same conditions, the only detectable isomer (^1H NMR >96%) is methyl 14-azaprostanoate (**22**) in 77% yield.



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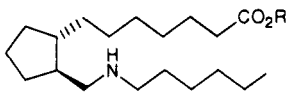
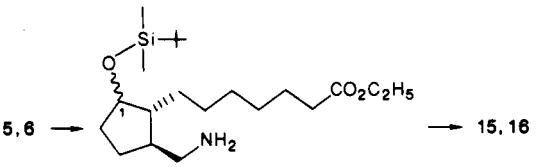


22, R = CH_3
23, R = H

The four 9-hydroxy-14-azaprostanoates **11**, **12**, **17**, and **18** and 14-azaprostanoate **22** were hydrolyzed and the amino acids brought to their isoelectric points in the usual manner. Spectra (^1H NMR, ^{13}C NMR, CIMS, EIMS, IR) were consistent with the four diastereomeric azaprostanoids **13**, **14**, **19**, and **20** and the deoxy derivative **23** as assigned.

Stereoselective Synthesis of 9α-Hydroxy-14-azaprostanoic Acid. Unexpected isomerization at the Schiff's base stage (or during its in situ reduction) resulted in isomeric mixtures and loss of stereochemical control. Since it appeared that the nitro derivative **5** possessed the natural prostaglandin stereochemistry, one way to avoid this problem was to fix the stereochemistry at the C_3 (C_{12} prostaglandin numbering) position by reducing the nitro group to an amine. Subsequent condensation with hexanal and metal hydride reduction could then be used to extend the lower side chain, avoiding the epimerization problem.

Attempts to reduce the nitro group using Al-Amalgam were not successful.[20] However, hydrogenation with Raney Nickel in absolute ethanol proceeded smoothly and was complete in a few hours at room temperature for both the α-trans and β-trans nitro derivatives **5** and **6**.[21] The corresponding amines (**24**, **25**) were successfully used for the coupling reactions without further purification.



24 (1α)
25 (1β)

The α-trans amine **24** was condensed with hexanal in absolute ethanol and subsequently reduced with $NaBH_4$. Analysis of the crude reaction mixture showed a single amine (nitroprusside spray detectable),[22] which was identical in all respects with the α-trans siloxy compound **15** prepared by the previous aldehyde route. Similarly, reaction of the β-trans amine **25** with hexanal and subsequent reduction produced a product found to be identical with **16** prepared by the aldehyde route. Thus, a direct synthesis of the desired target 9α-hydroxy-14-azaprostanoic acid possessing the natural prostaglandin stereochemistry was in hand.

Biological evaluation of the four 9-hydroxy-14-azaprostanoic acids is to be presented elsewhere.

Experimental Section

Melting points were determined in open capillaries with a Thomas-Hoover apparatus and are uncorrected. IR spectra were recorded on a Nicolet MX-1 FT IR spectrometer. Proton and carbon NMR spectra were recorded on a Nicolet NT-360 spectrometer. CIMS (NH_3, 0.4 mmHg, 50 °C) were obtained on a Finnigan 4510 spectrometer in either the direct-insertion (oils) or direct chemical ionization (DCI, solids) modes. The GC/CI/MS data were obtained on the same equipment with a 15-m DB-1 (0.25-mm) fused silica capillary column (J&W Scientific). GC analyses were carried out on a Perkin-Elmer Sigma 2000 GC fitted with a methyl silicone capillary column (10 m × 0.25 mm, 1.5–2.0 mL/min He, programmed from 200 to 250 °C at 5 °C/min.). Medium-pressure chromatography refers to silica gel (Sigma type H, 10–40 μm) using a low-pressure pump. TLC was performed on Merck silica gel 60-F-254 (0.2 mm, precoated on TLC aluminum sheet), and spots were visualized by UV light, iodine vapor, and nitroprusside–acetaldehyde spray reagent,[22] when appropriate.

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Elemental analyses were performed by Micro-Tech Laboratories Inc., Skokie, IL.

3β-(Nitromethyl)-2α-(6-carbethoxyhexyl)-1α-cyclopentanol (3). The precursor nitro derivative **2** was prepared by a method similar to that reported for the methyl ester.[7] A mixture of nitromethane (42.7 g, 0.7 mol), the ester **1** (33.3 g, 0.14 mol), and 1,1,3,3-tetramethylguanidine (3.23 g, 0.028 mol) was stirred at room temperature for 24 h. The reaction mixture was dissolved in ether (500 mL), washed with ice-cold 5% aqueous HCl (2 × 300 mL) and brine (300 mL), and dried ($MgSO_4$). Removal of the solvent in vacuo and column chromatography (ether:hexane = 4:6) gave 3β-(nitromethyl)-2α-(6-carbethoxyhexyl)-1-cyclopentanone (**2**): 30.6 g (73%); TLC (ether:hexane = 1:1) R_f 0.26; GC t_R 4.07 min (92%); IR (neat, cm^{-1}) 1553 (NO_2), 1383 (NO_2); ^1H NMR ($CDCl_3$) δ 4.62 (AB, 1, CH_2NO_2, J_{gem} = 12.2 Hz, J_{vic} = 5.2 Hz), 4.42 (AB, 1, CH_2NO_2, J_{gem} = 12.2 Hz, J_{vic} = 8.7 Hz), 2.71 (m, 1, H_3), 2.44 (m, 1, H_5), 2.24 (m, 1, H_5), 1.91 (m, 1, H_2); ^{13}C NMR ($CDCl_3$) δ 217.15 (>C=O, ketone), 173.63 (>C=O, ester), 79.08 (CH_2NO_2), 51.67 (C_2), 39.82 ($CHCH_2NO_2$), 37.12 (C_5); EIMS, m/e 299 (M^+, 2), 157 (side-chain cleavage, 100%).

A. Sodium Borohydride Method. Sodium borohydride (2.12 g, 0.056 mol) in absolute ethanol (150 mL) was added dropwise to a solution of **2** (13.7 g, 0.046 mol) in absolute ethanol (350 mL) and the mixture stirred for 5 h at room temperature. Acetone (2 mL) was added to the reaction mixture to decompose any remaining hydride, and solvents were removed, in vacuo. The residue was dissolved in ether (300 mL), washed with ice-cold 5% aqueous HCl (2 × 200 mL), water (200 mL), and brine (200 mL), and dried ($MgSO_4$). Evaporation of the solvent gave a crude mixture of α- and β-hydroxy nitro esters **3** and **4**: 12.9 g (94%); column chromatography (ether:hexane = 1:1), **3** (5.04 g, 37%) as a first elutent; TLC (ether:hexane = 7:3) R_f 0.45; GC t_R 4.24 min (97%); IR (neat, cm^{-1}) 3450 (br, OH); ^1H NMR ($CDCl_3$) δ 4.48 (AB, 1, CH_2NO_2, J_{gem} = 11.7 Hz, J_{vic} = 4.7 Hz), 4.25 (AB, 1, CH_2NO_2, J_{gem} = 11.7 Hz, J_{vic} = 9.9 Hz), 4.27 (m, 1, H_1), 2.51 (m, 1, H_3), 2.13 (m, 1, H_2), 1.80 (m, 1, H_5), 1.7 (m, 1, H_5); ^{13}C NMR ($CDCl_3$) δ 174.04 (>C=O), 79.98 (CH_2NO_2), 73.24 (C_1), 48.75 (C_2), 40.97 (C_3), 33.26 (C_5); CIMS, m/e 302 (M + 1), 319 (M + NH_4). Anal. Calcd for $C_{15}H_{27}NO_5$: C, 59.78; H, 9.03; N, 4.65. Found: C, 59.37; H, 9.10; N, 4.58.

B. Selectride Method. A solution of nitro keto ester **2** (0.50 g, 1.67 mmol) in dry THF was cooled to −78 °C, and a 1 M solution of lithium tri-*sec*-butyl hydride (L-Selectride; 2.34 mL, 2.34 mmol) in THF was slowly added. The solution was stirred at −78 °C for 4.5 h (the color of the solution immediately changed to yellow upon addition of the metal hydride), and then 3 N NaOH (2.2 mL) was added, followed by 30% H_2O_2 (1.7 mL). The peroxide was added slowly so that the reaction did not become too vigorous. The solution was allowed to stand at room temperature for 18 h. The reaction mixture was neutralized by 5% HCl and extracted with ether (5 × 50 mL). The organic extracts were washed with water and brine and dried ($MgSO_4$). Removal of the solvent under reduced pressure gave the crude alcohol **3**, 0.5 g. This residue contained the corresponding acid, which presumably was formed during the workup procedure, as evidenced by TLC (a tailing spot near the origin) and reduced integration for the ethyl ester protons. The mixture was reesterified overnight with absolute ethanol (15 mL) containing a catalytic amount of *p*-TsOH to give the alcohol **3** (0.23 g, 50%) after the usual workup: TLC and spectroscopic data (^1H NMR, ^{13}C NMR, MS) were identical with the sample that was prepared by the sodium borohydride method. Coinjection of this product with the authentic α isomer also gave a single peak on the GC (>97%), t_R 4.27 min.

3β-(Nitromethyl)-2α-(6-carbethoxyhexyl)-1β-cyclopentanol (4). Further elution of the column used to separate the α isomer (**3**) furnished the β isomer **4** (5.46 g, 40%) as a colorless oil: TLC (ether:hexane = 6:4) R_f 0.36; GC t_R 4.09 min (~100%); IR (neat, cm^{-1}) 3433 (br, OH); ^1H NMR ($CDCl_3$) δ 4.49 (AB, 1, CH_2NO_2, J_{gem} = 11.9 Hz, J_{vic} = 6.1 Hz), 4.38 (AB, CH_2NO_2, J_{gem} = 11.9 Hz, J_{vic} = 8.6 Hz), 4.01 (m, 1, H_1), 2.31 (m, 1, H_3), 1.87 (m, 1, H_2); ^{13}C NMR ($CDCl_3$) δ 174.05 (>C=O), 80.61 (CH_2NO_2), 78.16 (C_1), 51.30 (C_2), 42.67 (C_3); CIMS, m/e 302 (M + 1). Anal. Calcd for $C_{15}H_{27}NO_5$: C, 59.78; H, 9.03; N, 4.65. Found: C, 59.40; H, 9.15; N, 4.58.

3β-(Nitromethyl)-2α-(6-carbethoxyhexyl)-1α-[(*tert*-butyldimethylsilyl)oxy]cyclopentane (5). The α-hydroxy nitro ester **3** (4.16 g, 13.8 mmol), imidazole (2.31 g, 34 mmol), and *tert*-butyldimethylsilyl chloride (TBDMSCl, 2.86 g, 19 mmol) were dissolved in DMF (35 mL), and the mixture was stirred at 50 °C under nitrogen for 24 h. After cooling to room temperature, brine (100 mL) was added and the mixture extracted with ether (3 × 200 mL). The ether extracts were washed with ice-cold 1 N HCl (2 × 200 mL), water (2 × 200 mL), and brine (200 mL) and dried ($MgSO_4$). Evaporation of the solvent gave the crude silylated product containing a small amount of unreacted starting material (TLC). Medium-pressure chromatography gave the unreacted starting material **3** (0.40 g) and the siloxy ester **5** (4.78 g, 83%): TLC (ethyl acetate:hexane = 1:8) R_f 0.58; GC t_R 8.26 min (97%); ^1H NMR ($CDCl_3$) δ 4.47 (AB, 1, CH_2NO_2, J_{gem} = 11.6 Hz, J_{vic} = 4.69 Hz), 4.22 (AB, 1, CH_2NO_2, J_{gem} = 11.6 Hz, J_{vic} = 9.7 Hz), 4.19 (m, 1 H_1), 2.49 (m, 1, H_3), 2.08 (m, 1, H_2), 0.88 (s, 9, *t*-Bu), 0.047 (s, 3, CH_3Si), 0.036 (s, 3, CH_3Si); ^{13}C NMR ($CDCl_3$) δ 80.08 (CH_2NO_2), 73.85 (C_1), 49.42 (C_2), 41.03 (C_3), 25.76 (*t*-Bu), 18.00 (quaternary carbon), −5.08 (CH_3Si), −4.20 (CH_3Si); EIMS, m/e 400 ($M^+ - CH_3$, 1.5), 358 (M^+ − *t*-Bu, 98), 75 ($HOSi(CH_3)_2$, 100); CIMS, m/e 416 (M + 1). Anal. Calcd for $C_{21}H_{41}NSiO_5$: C, 60.68; H, 9.94; N, 3.37. Found: C, 60.90; H, 10.32; N, 3.30.

3β-(Nitromethyl)-2α-(6-carbethoxyhexyl)-1β-[(*tert*-butyldimethylsilyl)oxy]cyclopentane (6). By the same procedure as for the silylation of the α isomer **3**, β-hydroxy nitro ester **4** (4.29 g, 14.25 mmol) gave unreacted starting material (0.62 g) and **6** (4.35 g, 74%): TLC (ethyl acetate:hexane = 1:8) R_f 0.62; GC t_R 6.59 min (97%); ^1H NMR ($CDCl_3$) δ 4.46 (AB, 1, CH_2NO_2, J_{gem} = 11.9 Hz, J_{vic} = 6.9 Hz), 4.35 (AB, 1, CH_2NO_2, J_{gem} = 11.9 Hz, J_{vic} = 8.7 Hz), 3.92 (m, 1, H_1), 2.35 (m, 1, H_3), 1.89 (m, 1, H_2), 0.87 (s, 9, *t*-Bu), 0.044 (s, 3, CH_3Si), 0.039 (s, 3, CH_3Si); ^{13}C NMR ($CDCl_3$) δ 80.92 (CH_2NO_2), 78.55 (C_1), 51.65 (C_2), 42.02 (C_3), 25.78 (*t*-Bu), 17.89 (quaternary carbon), −4.81 (CH_3Si), −4.60 (CH_3Si); EIMS, m/e 400 ($M^+ - CH_3$, 1), 358 (M^+ − *t*-Bu, 88), 75 ($HOSi(CH_3)_2$, 100); CIMS, m/e 416 (M + 1). Anal. Calcd for $C_{21}H_{41}NSiO_5$: C, 60.68; H, 9.94; N, 3.37. Found: C, 60.97; H, 9.70; N, 3.19.

Ozonolysis of 5. The silyl nitro ester **5** (4.4 g, 10.6 mmol) in dry methanol (40 mL) was added to a methanolic solution of sodium methoxide [60 mL, prepared from 0.25 g (11 mmol) of Na] and the mixture stirred for 15 min at 0 °C. The solution was then cooled to −78 °C and a stream of O_3–O_2 bubbled through until the solution turned light blue (5 h). After the flask was flushed with O_2, dimethyl sulfide (5 mL, 0.08 mol) was added at −78 °C. The mixture was allowed to come to room temperature over a period of 5 h. Solvents were removed in vacuo, and the resulting residue was extracted with ethyl acetate (3 × 100 mL). The organic layer was washed with water (2 × 200 mL) and brine (2 × 200 mL) and dried ($MgSO_4$). Removal of the solvent in vacuo, using a water bath (<30 °C), afforded the crude aldehyde **7** (3.8 g). GC/CI/MS analysis of this material indicated that it contained ~76% aldehyde **7**. The preparation was used without further purification because of its instability but apparently contains small amounts of starting material (IR: 1553 cm^{-1}, NO_2), transesterified methyl ester [^1H NMR δ 3.66 (OCH_3)], and other minor impurities as seen spectroscopically as well as by GC analysis. TLC also shows one single major spot along with fast-moving impurities that were identified as starting material and transesterified methyl ester by GC/CI/MS. The following spectral data are on the crude product: TLC R_f 0.24 (ether:hexane = 1:7); GC t_R 3.75 min (~76%); IR (neat, cm^{-1}) 2795 (CHO); ^1H NMR ($CDCl_3$) δ 9.17 (d, 1, CHO, J = 3.4 Hz), 4.21 (m, 1, H_1), 2.62 (m, 1, H_3), 2.02 (m, 1, H_2); EIMS, m/e 383 (M^+ − 1), 327 (M^+ − *t*-Bu, 2), 75 ($HOSi(CH_3)_2$, 100); CIMS, m/e 385 (M + 1), 402 (M + 18).

Ozonolysis of 6. The silyl ester **6** (4.21 g, 10.1 mmol) was converted to the aldehyde by ozonolysis in a manner similar to the previous preparation of α-siloxy aldehyde **7**. The crude aldehyde (**8**; 3.28 g), containing similar impurities to those in the preparation of **7**, was used without further purification: TLC (ether:hexane = 1:7) R_f 0.26; GC t_R 3.84 min (>97%). The following spectral data are of the crude product: IR (neat, cm^{-1}) 2708 (CHO); ^1H NMR ($CDCl_3$) δ 9.57 (d, 1, CHO, J = 2.9 Hz), 3.89 (m, 1, H_1), 2.28 (t, 3, CH_2CO_2, J = 7.6 Hz, H_3 overlapping triplet), 2.04 (m, 1, H_2), 1.80 (m, 1); EIMS, m/e 339 (M^+ − OEt, 2), 327 (M^+ − *t*-Bu, 70), 75 ($HOSi(CH_3)_2$, 100); CIMS, m/e 385 (M + 1), 402 (M + 18).

9α-Hydroxy-14-aza-12-isoprostanoic Acid (13). To a solution of the aldehyde **7** (3.84 g, 10 mmol) and molecular sieves (3 g, 4-Å) in absolute ethanol (60 mL) was added dropwise *n*-hexylamine (1.02 g, 10.1 mmol). The solution was stirred under nitrogen at room temperature for 5 h. After cooling (ice bath), $NaBH_4$ (0.42 g, 11 mmol, 98%) was added, and the mixture stirred for an additional 30 min. The excess borohydride was decomposed by the addition of acetone (2 mL). The molecular sieves were filtered, and the solvent was removed in vacuo. The residue was dissolved in ethyl acetate (200 mL), washed with water (2 × 200 mL) and brine (200 mL), and dried ($MgSO_4$). Removal of the solvent gave a mixture of the crude amines as a yellow residue (4.17 g). Medium-pressure chromatography (chloroform:methanol = 9:1) gave 9α-[(*tert*-butyldimethylsilyl)oxy]-14-aza-12-isoprostanoate (**9**): 0.4 g (8%); TLC (chloroform:methanol = 85:15) R_f 0.53 (homogeneous); ^1H NMR ($CDCl_3$) δ 4.15 (m, 1, H_9), 3.00–2.82 (m, 3, H_{13}, H_{15}), 2.76 (dd, 1, H_{13}, $J_{gem} \simeq J_{vic} \simeq$ 12.3 Hz), 2.13 (m, 2, H_8, H_{12}); ^{13}C NMR ($CDCl_3$) δ 73.73 (C_9), 51.80 (C_{13}), 50.52 (C_8), 47.40 (C_{15}), 38.60 (C_{12}); EIMS, *m/e* 469 (M^+, 1), 114 ($M^+ - CH_2{=}NH(CH_2)_5CH_3$, 100); CIMS, *m/e* 470 (M + 1).

The siloxy amino ester **9** (0.3 g, 0.64 mmol) was dissolved in $CHCl_3$ (30 mL) and magnetically stirred under nitrogen. To this was added $BF_3{\cdot}Et_2O$ (0.8 mL, 5.6 mmol). After stirring for 8 h, the reaction mixture was poured into 5% aqueous Na_2CO_3 (50 mL) and extracted with $CHCl_3$ (3 × 50 mL). The combined extracts were washed with water (2 × 100 mL) and brine (100 mL) and dried ($MgSO_4$). After solvent removal, purification by column chromatography gave ethyl 9α-hydroxy-14-aza-12-isoprostanoate (**11**; 0.15 g, 66%) as an oil: TLC (chloroform:methanol = 85:15) R_f 0.4 (homogeneous); ^1H NMR ($CDCl_3$) δ 4.21 (m, 1, H_9), 3.05 (dd, 1, H_{13}, J_{gem} = 12.1 Hz, J_{vic} = 2.3 Hz), 2.94 (t, 2, H_{15}, J = 8.3 Hz), 2.71 (dd, 1, H_{13}, $J_{gem} \simeq J_{vic} \simeq$ 11.2 Hz), 2.27 (m, 1, H_{12}); ^{13}C NMR ($CDCl_3$) δ 73.10 (C_9), 52.29 (C_{13}), 49.98 (C_8), 48.23 (C_{15}), 39.01 (C_{12}); EIMS, *m/e* 355 (M^+, 1), 114 ($M^+ - CH_2{=}NH(CH_2)_5CH_3$, 100); CIMS, *m/e* 356 (M + 1).

The hydroxy amino ester **11** (0.71 g, 2 mmol) was refluxed with aqueous NaOH (2.5%, 12 mL) until a homogeneous solution was obtained (3–4 h). After cooling, the solution was acidified by the dropwise addition of 5% aqueous HCl, made strongly basic by addition of excess concentrated NH_4OH, and then gently heated to expel excess NH_3 until neutral to pH paper. The solution was passed through an amberlite XAD-2 column (polystyrene, Alltech Associate, 50 g) to remove excess salts. The column was first eluted with water and then with methanol. The methanol fractions were combined, evaporated (to about 1 mL), and trituated with cold acetonitrile to give **13** (0.15 g, 31%), which was spectroscopically (IR, ^1H NMR, CIMS) the same as the analytical sample obtained by three recrystallizations from methanol/acetonitrile: mp 133–135 °C; ^1H NMR (methanol-d_4) δ 4.17 (m, 1, H_9), 3.04 (dd, 1, H_{13}, J_{gem} = 12.3 Hz, J_{vic} = 2.5 Hz), 2.92 (t, 2, H_{15}, J = 7.6 Hz), 2.74 (dd, 1, H_{13}, $J_{gem} \simeq J_{vic}$ = 11.2), 0.92 (t, 3, H_{20}, J = 6.1 Hz); ^{13}C NMR (methanol-d_6) δ 182.35 (CO_2H), 74.86 (C_9), 54.02 (C_{13}), 50.78 (C_8), 49.55 (C_{15}), 40.92 (C_{12}), 14.32 (C_{20}); CIMS, *m/e* 328 (M + 1). Anal. Calcd for $C_{19}H_{37}NO_3$: C, 69.68; H, 11.39; N, 4.28. Found: C, 69.38; H, 11.44; N, 4.10.

9α-Hydroxy-14-azaprostanoic Acid (19). Further elution of the column used to separate the α-cis isomer **9** gave ethyl 9α-[(*tert*-butyldimethylsilyl)oxy]-14-azaprostanoate (**15**): 2.28 g (46%); TLC (chloroform:methanol = 85:15) R_f 0.48 (homogeneous with a trace of **9**, estimated to be less than 5% by TLC); ^1H NMR ($CDCl_3$) δ 4.15 (m, 1, H_9), 2.79 (dd, 1, H_{13}, J_{gem} = 11.6 Hz, J_{vic} = 3.6 Hz), 2.70 (m, 2, H_{15}), 2.49 (dd, 1, H_{13}, $J_{gem} \simeq J_{vic} \simeq$ 11 Hz), 2.00 (m, 2, H_8, H_{12}); ^{13}C NMR ($CDCl_3$) δ 74.40 (C_9), 55.04 (C_{13}), 50.20 (C_8), 50.12 (C_{15}), 41.96 (C_{12}); EIMS, *m/e* 469 (2), 114 ($M^+ - CH_2{=}NH(CH_2)_5CH_3$, 100); CIMS, *m/e* 470 (M + 1).

The siloxy ester **15** (1.49 g, 3.18 mmol) in $CHCl_3$ (120 mL) was desilylated with $BF_3{\cdot}Et_2O$ (3.94 mL) in the same manner as for the iso compound **9** to give ethyl 9α-hydroxy-14-azaprostanoate (**17**): 0.61 g (54%); TLC (chloroform:methanol = 85:15) R_f 0.34 (homogeneous); IR (neat, cm^{-1}) 3410 (br, OH); ^1H NMR ($CDCl_3$) δ 4.21 (m, 1, C_9 H), 2.73 (dd, 1, H_{13}, J_{gem} = 11.2 Hz, J_{vic} = 4.5 Hz), 2.60 (m, 2, H_{15}), 2.38 (dd, 1, H_{13}, J_{gem} = 11.2 Hz, J_{vic} = 9.8 Hz), 2.05 (m, 1, H_{12}); ^{13}C NMR ($CDCl_3$) δ 74.23 (C_9), 55.24 (C_{13}), 50.35 (C_{15}), 49.54 (C_8), 42.25 (C_{12}); EIMS, *m/e* 355 (M^+, 2), 114 ($M^+ - CH_2{=}NH(CH_2)_5CH_3$, 100); CIMS, *m/e* 356 (M + 1).

The amino ester **17** (0.61 g, 1.72 mmol) was hydrolyzed and brought to its isoelectric point in a manner similar to **13**. The precipitate was collected by filtration, washed with cold water, and air-dried to give the target compound as a white, microcrystalline powder (**19**; 183 mg, 33%) that was spectroscopically (IR, ^1H NMR, MS) identical with the analytical sample prepared by two recrystallizations from aqueous methanol: mp 143–145 °C; ^1H NMR (methanol-d_4) δ 4.19 (m, 1, H_9), 3.09 (dd, 1, H_{13}, J_{gem} = 12.3 Hz, J_{vic} = 3.2 Hz), 2.97 (m, 2, H_{15}), 2.80 (dd, 1, H_{13}, $J_{gem} \simeq J_{vic} \simeq$ 12.3 Hz), 2.15 (t, 2, CH_2CO_2, J = 7.2 Hz), 0.93 (t, 3, H_{20}, J = 6.9 Hz); EIMS, *m/e* 327 (M^+, 0.5), 114 ($M^+ - CH_2{=}NH(C-H_2)_5CH_3$, 100); CIMS, *m/e* 328 (M + 1). Anal. Calcd for $C_{19}H_{37}NO_3$: C, 69.68; H, 11.39; N, 4.28. Found: C, 69.38; H, 11.31; N, 4.02.

9β-Hydroxy-14-azaprostanoic Acid (20). The β-aldehyde **8** (3.07 g, 8 mmol) was condensed with *n*-hexylamine (0.97 g, 9.6 mmol) in a manner similar to the previous preparation of α isomers **15** and **9** to give a crude, viscous oil, 3.60 g. Medium-pressure chromatography (chloroform:methanol = 9:1) gave **16**: 0.53 g (14%); TLC (chloroform:methanol = 85:15) R_f 0.38 (homogeneous); ^1H NMR ($CDCl_3$) δ 3.85 (m, 1, H_9), 3.05–2.80 (m, 4, H_{13}, H_{15}), 2.04 (m, 2, H_8, H_{12}); ^{13}C NMR ($CDCl_3$) δ 78.28 (C_9), 53.11 (C_{13}), 52.81 (C_8), 48.28 (C_{15}), 40.53 (C_{12}); EIMS, *m/e*, fragmentations identical with that of the α isomer, 469 (M^+, 1), 114 (100); CIMS, *m/e* 470 (M + 1).

The β-silyl ester **16** (1.28 g, 2.73 mmol) was desilylated in a manner similar to that for the α isomers **9** and **15** to give a crude oil, 0.90 g. Purification by column chromatography gave ethyl 9β-[(*tert*-butyldimethylsilyl)oxy]-14-azaprostanoate (**18**): 0.78 g (81%); TLC (chloroform:methanol = 85:15) R_f 0.32 (homogeneous); IR (neat, cm^{-1}) 3545 (br, OH); ^1H NMR ($CDCl_3$) δ 4.02 (m, 1, H_9), 3.19 (dd, 1, H_{13}, J_{gem} = 12.6 Hz, J_{vic} = 4.3 Hz), 2.93 (m, 3, H_{13}, H_{15}), 2.09 (m, 1, H_8); ^{13}C NMR ($CDCl_3$) δ 77.59 (C_9), 52.25 (C_{13}), 51.92 (C_8), 48.88 (C_{15}), 41.58 (C_{12}); CIMS, *m/e* 356 (M + 1).

The β-amino ester **18** (0.43 g, 1.21 mmol) was hydrolyzed by the usual method to give the amino acid **20** (109 mg, 28%), which gave spectroscopic data identical with that of the analytical sample prepared by two recrystallizations from methanol/acetonitrile: mp 147–149 °C; ^1H NMR (methanol-d_4) δ 4.01 (m, 1, H_9), 3.12 (dd, 1, H_{13}, J_{gem} = 12.6 Hz, J_{vic} = 3.8 Hz), 2.98 (t, 2, H_{15}, J = 7.6 Hz), 2.94 (dd, 1, H_{13}, J_{gem} = 12.6 Hz, J_{vic} = 10.1 Hz), 2.25 (t, 2, CH_2CO_2, J = 7.2 Hz), 0.92 (t, 3, H_{20}, J = 6.9 Hz); CIMS, *m/e* 328 (M + 1). Anal. Calcd for $C_{19}H_{37}NO_3$: C, 69.68; H, 11.39; N, 4.28. Found: C, 69.80; H, 11.15; N, 4.35.

9β-Hydroxy-14-aza-12-isoprostanoic Acid (14). Further elution of the column used to separate the siloxy ester **16** gave ethyl 9β-[(*tert*-butyldimethylsilyl)oxy]-14-aza-12-isoprostanoate (**10**): 1.18 g (31%); TLC (chloroform:methanol = 85:15) R_f 0.29 (homogeneous); ^1H NMR ($CDCl_3$) δ 3.80 (m, 1, H_9), 2.72 (dd, 1, H_{13}, J_{gem} = 11.7 Hz, J_{vic} = 4.7 Hz), 2.61 (m, H_{15}), 2.51 (dd, 1, H_{13}, J_{gem} = 11.7 Hz, J_{vic} = 9.0 Hz); ^{13}C NMR ($CDCl_3$) δ 78.76 (C_9), 55.40 (C_{13}), 51.95 (C_8), 49.81 (C_{15}), 42.84 (C_{12}); EIMS, *m/e*, fragmentation pattern identical with that of the α isomers **9** and **15**, *m/e* 469 (M^+, 2), 114 (100); CIMS, *m/e* 470 (M + 1).

The amino ester **10** (270 mg, 0.58 mmol) was desilylated in the usual manner to give ethyl 9β-hydroxy-14-aza-12-isoprostanoate (**12**): 170 mg (83%); TLC (chloroform:methanol = 85:15) R_f 0.20 (homogeneous); IR (neat, cm^{-1}) 3395 (br, OH); ^1H NMR ($CDCl_3$) δ 3.87 (m, 1, H_9), 2.85 (dd, 1, H_{13}, J_{gem} = 12.3 Hz, J_{vic} = 3.6 Hz), 2.68 (m, 2, H_{15}), 2.57 (dd, 1, H_{13}, J_{gem} = 12.3 Hz, J_{vic} = 5.1 Hz); ^{13}C NMR ($CDCl_3$) δ 77.71 (C_9), 53.58 (C_{13}), 52.54 (C_8), 50.11 (C_{15}), 43.41 (C_{12}); EIMS, the same fragmentation pattern as the α isomers **11** and **17**, *m/e* 355 (M^+, 1), 114 (100); CIMS, *m/e* 356 (M + 1).

The amino ester **12** (160 mg, 0.45 mmol) was hydrolyzed in the usual manner and recrystallized from aqueous methanol to give **14** (70 mg, 48%) as a white crystalline powder that shows ^1H NMR and CIMS spectra essentially identical with that of the analytical sample obtained (54 mg, 76% recovery) after two more recrystallization using the same solvent: mp 146–148 °C; ^1H NMR (methanol-d_4) δ 3.88 (m, 1, H_9), 3.09 (dd, 1, H_{13}, J_{gem} = 12.3 Hz, J_{vic} = 3.6 Hz), 2.95 (m, 3, H_{13}, H_{15}), 2.16 (t, 2, CH_2CO_2, J = 7.2 Hz), 0.92 (t, 3, C_{20} H, J = 6.9 Hz); ^{13}C NMR (MeOH-d_4) δ 182.48 (COOH), 78.53 (C_9), 54.26 (C_{13}), 53.10 (C_8), 49.57 (C_{15}), 42.76 (C_{12}), 14.30 (C_{20}); CIMS, *m/e* 328 (M + 1). Anal. Calcd for $C_{19}H_{37}NO_3$:

C, 69.68; H, 11.39; N, 4.28. Found: C, 69.30; H, 11.68; N, 4.05.

Ethyl 9α-[(*tert*-Butyldimethylsilyl)oxy]prostanoate (15) via Reduction of the Nitro Derivative 5. To a solution of **5** (145 mg, 0.35 mmol) in absolute ethanol (100 mL) was added Raney nickel (ca. 200 mg) and the mixture hydrogenated in Parr hydrogenator (50 psi at room temperature). After 2 h, the mixture was filtered through a Celite bed and the solvent removed in vacuo to give a viscous oil. Purification by column chromatography gave the amino ester **24**: 101 mg (75%); TLC (chloroform:methanol = 85:15) R_f 0.33 (homogeneous); GC t_R 4.22 min; IR (neat, cm^{-1}) 3438, 3325 (br, NH_2); ^1H NMR ($CDCl_3$) δ 4.15 (m, 1, C_1), 2.80 (m, 1, CH_2NH_2), 2.46 (m, 1, CH_2NH_2); EIMS, *m/e* 328 ($M^+ - t$-Bu, 100); CIMS, *m/e* 386 (M + 1). The crude amine **24** (77 mg, 0.20 mmol) in absolute ethanol (25 mL) was stirred with freshly distilled hexanal (77 mg, 0.18 mmol) in the presence of molecular sieves (3 Å) under nitrogen. After 2 h, the reaction mixture was cooled by ice bath and $NaBH_4$ (7.6 mg, 0.20 mmol) added. After 30-min stirring, the solvent was removed in vacuo and the crude product dissolved in ethyl acetate (100 mL), washed with water (2 × 100 mL) and brine (100 mL), and dried ($MgSO_4$). Column chromatography gave the siloxy ester **15**, 61 mg (65%). The ester **15**, so obtained, cochromatographed (TLC) with an authentic sample of **15** prepared by the aldehyde method and showed identical spectroscopic data (CIMS, ^1H NMR, ^{13}C NMR, IR).

Ethyl 9β-[(*tert*-Butyldimethylsilyl)oxy]prostanoate (16) via Reduction of the Nitro Derivative 6. Nitro derivative **6** (160 mg, 0.40 mmol) was reduced with Raney nickel (ca. 200 mg) in a manner similar to that for the preparation of the amine **24** to give the 1β isomer **25**: 132 mg (86%); TLC (chloroform:methanol = 85:15) R_f 0.28; GC t_R 3.98 min (single major peak); IR (neat, cm^{-1}) 3400 (br, NH_2); ^1H NMR ($CDCl_3$) δ 3.79 (m, 1, C_1), 2.79 (m, 1, CH_2NH_2), 2.60 (m, 1, CH_2NH_2); CIMS, *m/e* 386 (M + 1). This preparation was used without further purification. The crude amine **25** (96.3 mg, 0.25 mmol) in absolute ethanol was condensed with hexanal (20 mg, 0.2 mol) as previously described for the 9α isomer **24**. The crude oil was purified by column chromatography (chloroform:methanol = 99:1) to give **16**, 64 mg (68%). The product was chromatographically and spectroscopically (^1H NMR, ^{13}C NMR, CIMS) identical with that prepared by the ozonolysis procedure.

14-Azaprostanoic Acid (23). To a mixture of potassium *tert*-butoxide (12.5 g, 112 mmol) and anhydrous diglyme (100 mL) was added powdered methoxymethyltriphenylphosphonium chloride (38.3 g, 112 mmol) in one portion and the mixture allowed to stir under nitrogen at 10 °C for 5 min before 2-(6-carbomethoxyhexyl)cyclopentanone (11 g, 48.7 mmol) was added. The reaction mixture was stirred for 4 h at room temperature and then poured into water (100 mL) and extracted with petroleum ether (6 × 100 mL). The organic layer was washed with water (6 × 100 mL) and dried ($MgSO_4$). Removal of the solvents in vacuo gave a light yellow oil (12.7 g) that was chromatographed (silica gel, 250 g). Elution with hexane/ether (1 L, 95:5) gave the *E* and *Z* isomers of 1-(methoxymethylene)-2-(6-carbomethoxyhexyl)-cyclopentane[19] (8.5 g, 69%) as a colorless oil: TLC (hexane:ether = 80:20) R_f 0.55 (two overlapping spots); ^1H NMR ($CDCl_3$) δ 3.67 (s, 3, $COOCH_3$), 3.57 and 3.52 [m, 1 = $CHOCH_3$ (*E* and *Z* isomers)]; CIMS, *m/e* 272 (M + 18).

Under a nitrogen atmosphere, perchloric acid (7.2 mL, 70%) was added dropwise to a solution of the 1-(methoxymethylene)-2-(6-carbomethoxyhexyl)cyclopentanes (8 g, 31.5 mmol) in ether (100 mL) and the mixture allowed to stir for 13 min. The aqueous layer was separated and extracted with ether (2 × 25 mL). The combined organic layers were washed with sodium bicarbonate (15 mL, 5%) and brine and dried ($MgSO_4$). Removal of the solvents in vacuo gave *trans*-1-formyl-2-(6-carbomethoxyhexyl)cyclopentane[19] (**21**) as a colorless oil: 6.81 g (90%); ^1H NMR ($CDCl_3$) δ 9.57 (d, 1, CHO).

To a solution of **21** (3 g, 12.5 mmol) in anhydrous methanol (50 mL) containing molecular sieves (3 Å, 2 g) was added hexylamine (1.89 g, 18.7 mmol) and the mixture stirred at room temperature for 28 h. After the mixture was cooled to ice bath temperature, sodium borohydride (0.47 g, 12.7 mmol) was added and the reaction allowed to stir for 1 h. After decomposition of the excess borohydride (0.5 mL acetone), the reaction mixture was filtered and solvents were removed in vacuo. The residue was dissolved in ether (300 mL), washed with brine (2 × 30 mL), and dried ($MgSO_4$). Removal of solvent in vacuo gave methyl 14-azaprostanoate (**22**; 3.1 g, 77%) as the only detectable product with no indication (TLC and ^1H NMR <5%) of the iso isomer: TLC (ethyl acetate) R_f 0.20 (homogeneous); ^1H NMR ($CDCl_3$) δ 3.67 (s, 3, OCH_3), 2.67 (dd, 1, H_{13}), 2.58 (AB, 2, H_{15}), 2.37 (dd partially overlapping CH_2CO_2, 1, H_{13}); CIMS, *m/e* 326 (M + 1).

The methyl 14-azaprostanoate (2 g, 6.15 mmol) was hydrolyzed and brought to its isoelectric point in a manner similar to **13**. The gum that formed was washed with water by decanting, dissolved in $CHCl_3$, and again washed with water. Removal of the solvent in vacuo gave a residue that was chromatographed on silica gel (methanol:ether = 1:9) to give 14-azaprostanoic acid (**23**; 1.3 g, 68%) as a semisolid. Recrystallization (ether/chloroform) gave the analytical sample, 1.1 g; mp 86–88 °C; ^1H NMR (methanol-d_4) δ 3.05 (dd, 1, H_{13}), 2.96 (m, 2, H_{15}), 2.78 (dd, 1, H_{13}), 2.15 (t, 2, CH_2CO_2), 0.92 (m, 3, H_{20}); CIMS, *m/e* 312 (M + 1). Anal. Calcd for $C_{19}H_{37}NO_2$: C, 73.26; H, 11.97; N, 4.49. Found: C, 73.23, H, 12.15; N, 4.32.

Intramolecular Hydrogen-Bonding Study of Ethyl 9-Hydroxy-14-azaprostanoate Derivatives 11, 12, 17, and 18. A Wilmad VR-6 variable path length cell with NaCl window was used for the hydrogen-bonding studies. The cell was calibrated by the interface fringe method prior to use. Spectroscopic grade CCl_4 was used for the serial dilution experiments. The samples were serially diluted as follows [molarity (M)/cell thickness (μm)]: 0.05/50, 0.03/100, 0.012/200, 0.008/300, 0.006/400, 0.005/500. Reference spectra (CCl_4) for each thickness were obtained and used for subtraction. The intense band at 1551 cm^{-1} was used as null number. Twenty-seven scans were summed for each dilution.

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Registry No. 1, 40098-44-0; **2**, 103693-53-4; **3**, 103693-54-5; **4**, 103773-05-3; **5**, 103693-55-6; **6**, 103773-06-4; **7**, 103693-56-7; **8**, 103773-07-5; **9**, 103693-57-8; **10**, 103773-08-6; **11**, 103693-58-9; **12**, 103773-09-7; **13**, 103693-59-0; **14**, 103773-10-0; **15**, 103773-11-1; **16**, 103773-12-2; **17**, 103773-13-3; **18**, 103773-14-4; **19**, 103773-15-5; **20**, 103773-16-6; **21**, 54482-69-8; **22**, 103693-60-3; **24**, 103693-61-4; **25**, 103773-17-7; $H_3C(CH_2)_5NH_2$, 111-26-2; $H_3C(CH_2)_4CHO$, 66-25-1; $CH_3OCH_2PPH_3^+Cl^-$, 4009-98-7; 2-(6-carbomethoxyhexyl)-cyclopentanone, 37617-17-7; (*E*)-1-(methoxymethylene)-2-(6-carbomethoxyhexyl)cyclopentanone, 103693-62-5; (*Z*)-1-(methoxymethylene)-2-(6-carbomethoxyhexyl)cyclopentanone, 103693-63-6.