Synthesis of Carbocycles via Intramolecular Conjugate Additions: Total Syntheses of Axane Sesquiterpenoids

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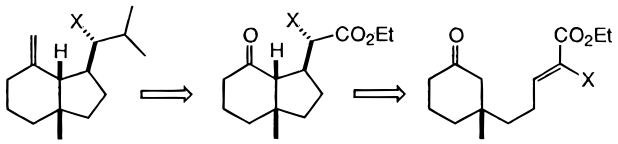
Syntheses of (±)-axamide-1 (**2**) and (±)-axisonitrile-1 (**1**) are described. The syntheses require 12 steps and 13 steps, respectively, from vinylogous ester **8** and feature the diastereoselective cyclization of unsaturated ester **7** to perhydroindan **5**. Some interesting reactions of the organometallic derived from [(trimethylsilyl)methyl]magnesium chloride and cerium trichloride are also described.

A variety of sesquiterpenoid isonitriles have been isolated from marine sponges.[1,2] These compounds are often found, along with their isothiocyanate and formamide counterparts, in nudibranchs that feed on these sponges. The axanes are one family of such sesquiterpenoids, first isolated from the sponge *Axinella cannabina* in the mid 1970s.[3,4] During studies on the chemical defense systems of Mediterranean nudibranchs, axisonitrile-1 (**1**) was found to be a potent ichthyotoxin toward the marine fish *Chromis chromis* and the fresh water fish *Carassius carassius*.[5,6] Indeed, at a concentration as low as 8 ppm, ingestion by the fish was followed by sedation and death occurred within 24 h. Moreover, axisonitrile-1 was also present in ethereal extracts of the digestive glands, mantles, and secretion of the nudibranch *Phyllidia pulitzeri* which feeds on *Axinella cannabina*. This led to the suggestion that the nudibranch uses the sponge as its source of a chemical substance used as a form of defense against predators.

Along with these interesting biological properties, the rather unusual skeleton of the axane family of sesquiterpenoids has attracted some attention and only a few other compounds having the same perhydroindan skeleton have been discovered.[7] From the standpoint of synthesis, a challenging feature of axisonitrile-1 (**1**), and its congeners axamide-1 (**2**) and axisothiocyanate-1 (**3**), is the presence of a side chain appended to the perhydroindan by a stereogenic carbon. This article describes total syntheses of racemic axanes **1**−**3** using an intramolecular conjugate addition to establish the four contiguous stereogenic centers in these natural products.[8,9,10]

Scheme 1



1 X = N=C
2 X = NHCHO
3 X = N=C=S

4 X = NHAc
5 X = NHCHO

6 X = NHAc
7 X = NHCHO

Our approach revolved around preparation of an α-amino acid derivative such as **4** or **5** via cyclization of an unsaturated ester such as **6** or **7** (Scheme 1). The carbethoxy group was to serve as a functional handle for construction of the side chain isopropyl group, and the stereochemical course of the cyclization was predicted on the basis of earlier studies in our laboratory.[11] The preparation of cyclization substrates **6** and **7** is outlined in Scheme 2. Addition of (4-methyl-3-pentenyl)magnesium bromide[12] to vinylogous ester **8** was followed by an acidic workup to provide cyclohexenone **9** in 70% yield. Treatment of **9** with lithium dimethylcuprate gave **10** in 89% yield.[13] Protection of the ketone and ozonolysis of the olefin gave aldehyde **11** (87%). Treatment of **11** with ethyl α-acetamidomalonate gave **12** (64%), and ketal hydrolysis provided cyclization substrate **6** in 82% yield.[14] In a similar manner, **11** was converted to **13** (80%) and ketal hydrolysis provided **7** in 94% yield.[15] The olefin geometry in **6** and **7** was assigned on the basis of the chemical shift of their vinyl protons.[16]

[⊗] Abstract published in *Advance ACS Abstracts,* January 1, 1996.

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(2) Also see: Burreson, B J.; Christophersen, C.; Scheuer, P. J. *Tetrahedron* **1975**, *31*, 2015. Ciminiello, P.; Magno, S.; Mayol, L.; Piccialli, V. *J. Nat. Prod.* **1987**, *50*, 217. Ciminiello, P.; Fattorusso, E.; Magno, S.; Mayol, L. *J. Nat. Prod.* **1985**, *48*, 64.

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(4) For other axanes, see: Fattoruso, E.; Magno, S.; Mayol, L.; Santacroce, C.; Sica, D. *Tetrahedron* **1975**, *31*, 269. Iengo, A.; Mayol, L.; Santacroce, C. *Experientia* **1977**, *33*, 11. Iengo, A.; Santacroce, C.; Sodano, G. *Experientia* **1979**, *35*, 10.

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(6) Cimino, G.; De Rosa, S.; De Stefano, S.; Sodano, G. *Comp. Biochem. Physiol.* **1982**, *73B*, 471.

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(8) For a communication that describes a portion of this research, see: Guevel, A.-C.; Hart, D. J. *Synlett* **1994**, 169.

(9) For another synthesis of these natural products, see: Piers, E.; Yeung, B. W. A. *Can. J. Chem.* **1986**, *64*, 2475. Piers, E.; Yeung, B. W. A.; Rettig, S. J. *Tetrahedron* **1987**, *43*, 5521.

(10) For syntheses of the stereochemically less complex axane-4 family of sesquiterpenoids, see: Hart, D. J.; Lai, C.-S. *Synlett* **1989**, 49. Chenera, B.; Chuang, C.-P.; Hart, D. J.; Lai, C.-S. *J. Org. Chem.* **1992**, *57*, 2018. Ohkubo, T.; Akino, H.; Asaoka, M.; Takei, H. *Tetrahedron Lett.* **1995**, *36*, 3365.

(11) Guevel, A.-C.; Hart, D. J. *J. Org. Chem.* **1996**, *61*, 465−472.

(12) Prepared from the bromide: Biernacki, W.; Gdula, A. *Synthesis* **1979**, 37.

(13) Posner, G. H. In *Organic Reactions*; Dauben, W. G., Ed.; Wiley: New York, 1972; Vol. 19, pp 1−113.

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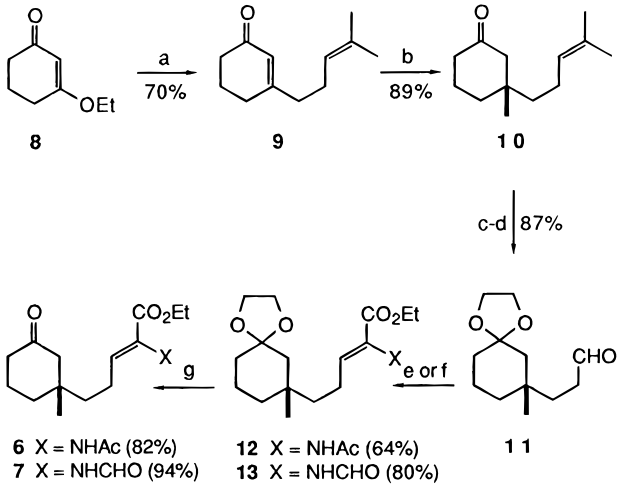
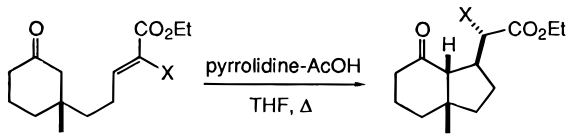
Scheme 2



(a) $BrMg(CH_2)_2CH{=}C(Me)_2$, Et_2O; H_2SO_4, H_2O (b) Me_2CuLi, Et_2O (c) $HOCH_2CH_2OH$, *p*-TsOH, $(MeO)_3CH$, PhH (d) O_3, MeOH-CH_2Cl_2; Me_2S (e) $EtO_2CCH(NHAc)CO_2H$, Ac_2O, pyridine (f) EtO_2CCH-$(NHCHO)PO(OEt)_2$, DBU, CH_2Cl_2 (g) HCl, H_2O, THF

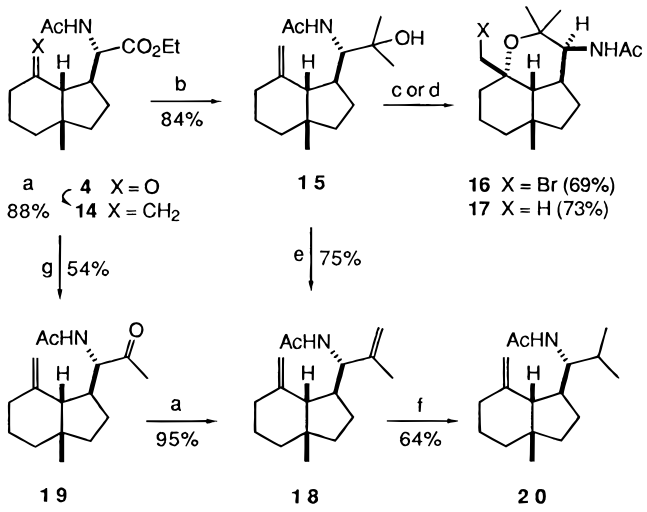
Scheme 3



On the basis of results obtained with related substrates, cyclization of **6** and **7** was expected to provide **4** and **5**, respectively, with excellent stereoselectivity at each stereogenic center.[11] This proved to be the case (Scheme 3). Treatment of **6** and **7** with pyrrolidine and acetic acid in tetrahydrofuran afforded **4** and **5** in 85% and 86% yields, respectively. The structure of **5** was determined by X-ray crystallographic analysis while the structure of **4** was assigned by analogy.[17]

As will be seen, converting perhydroindans **4** and **5** to the target sesquiterpenoids was challenging. Our efforts began with **4** as this was the first perhydroindan we had prepared (Scheme 4). Wittig olefination of **4** gave **14** (88%), which reacted with methylmagnesium bromide to afford tertiary alcohol **15** (84%). Attempts to convert the tertiary alcohol to a halide for subsequent reduction, not surprisingly, met with failure. For example, treatment of **15** with conditions known to accomplish such transformations gave electrophile-initiated cyclization products such as **16** and **17**.[18,19] It was possible to dehydrate **15** to diene **18** in 75% yield using Martin's sulfurane.[20] An alternate route from **14** to **18** was also developed. Thus, treatment of **14** with methylmagnesium bromide

Scheme 4



(a) $Ph_3P{=}CH_2$, PhMe, KO-*t*-Bu (b) MeMgBr (c) $(Me_3Si)_2$, pyridinium•Br_3, $CHCl_3$ (d) Me_3SiCl, NaI, MeCN (e) $Ph_2S[OC(CF_3)_2Ph]_2$, CH_2Cl_2 (f) Ir(cod)py$(PCy_3)PF_6$, H_2, CH_2Cl_2 (g) MeMgBr, Et_3N, PhMe

in the presence of triethylamine gave ketone **19** (54%),[21] and subsequent Wittig olefination gave **18** in 95% yield. Finally, selective hydrogenation of **18** using Crabtree's catalyst gave **20** (64%) along with 5% of its $\Delta^{1,2}$-isomer.[22] Unfortunately, numerous attempts to hydrolyze acetamide **20** met with failure and we eventually prepared perhydroindan **5** (*vide supra*) and examined its conversion to the target structures.[23] As will be seen, this was also not without problems.

The first problem was encountered during the Wittig olefination of **5**. Although this could be accomplished in 83% yield, the product was a 2:1 mixture of **21** and its C_{10} isomer. Thus, the α-formamido ester was more susceptible to base-promoted isomerization than the α-acetamido ester. It was eventually found that **5** reacted with the reagent prepared from [(trimethylsilyl)methyl]-magnesium chloride and cerium trichloride to afford olefinic acid **22** (71%) (Scheme 5).[24] The acid could then be converted to ester **21** (85%) using iodoethane and cesium fluoride.[25] The production of acid **22** was actually a surprise as we had anticipated that the reaction of **5** would give an allylsilane which, upon protonolysis, would give diene **24**. Apparently the intermediate ketone addition product reacts with the neighboring ester, ultimately leading to the carboxylic acid. We next hoped to convert **21** to diene **24** using a Peterson olefination procedure.[24,26] Again we were surprised to find that the reaction of [(trimethylsilyl)methyl]magnesium chloride–

(15) Zoller, U.; Ben-Ishai, D. *Tetrahedron* **1975**, *31*, 863. Schmidt, U.; Lieberknecht, A.; Schanbacher, U.; Beuttler, T.; Wild, J. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 776. Schmidt, U.; Lieberknecht, A.; Wild, J. *Synthesis* **1984**, 53. Schmidt, U.; Griesser, H.; Leitenberger, A.; Lieberknecht, A.; Mangold, R.; Meyer, R.; Riedl, B. *Synthesis* **1992**, 487.

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(17) We thank Dr. Judith C. Gallucci for performing the X-ray crystallographic analysis of **5** at The Ohio State University Crystallography Facility.

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(19) Olah, G. A.; Narang, S. C.; Balaram Gupta, B. G.; Malhotra, R. *J. Org. Chem.* **1979**, *44*, 1247.

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(21) Kikkawa, I.; Yorifugi, T. *Synthesis* **1980**, 877.

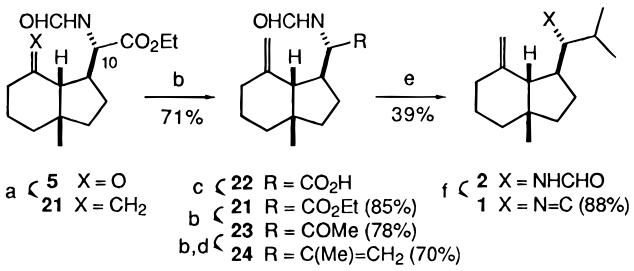
(22) Crabtree, R. H.; Felkin, H.; Fillebeen-Kahn, T.; Morris, G. E. *J. Organomet. Chem.* **1979**, *168*, 183. For amide-directed hydrogenations using this catalyst, see: Schultz, A. G.; McCloskey, P. J. *J. Org. Chem.* **1985**, *50*, 5905.

(23) Acidic conditions were not investigated due to the known acid sensitivity of the exocyclic methylene. Conditions that failed included hydrolysis with potassium hydroxide (Pearson, A. J.; Rees, D. C. *J. Am. Chem. Soc.* **1982**, *104*, 1118), hydrazinolysis (Fujinaga, M.; Matsuhima, Y. *Bull. Chem. Soc. Jpn.* **1964**, *37*, 468), an amide exchange procedure (Flynn, D. L.; Zelle, R. E.; Grieco, P. A. *J. Org. Chem.* **1983**, *48*, 2424), and activation with Meerwein's reagent followed by hydrolysis with dilute acid or base (Muxfeldt, H.; Rogalski, W. *J. Am. Chem. Soc.* **1965**, *87*, 933). The last procedure gave the desired imidate, but attempts to hydrolyze this material failed.

(24) Narayanan, B. A.; Bunnelle, W. H. *Tetrahedron Lett.* **1987**, *28*, 6261.

(25) Sato, T.; Otera, J.; Nozaki, H. *J. Org. Chem.* **1992**, *57*, 2166.

Scheme 5



(a) $Ph_3P=CH_2$, PhMe, KO-*t*-Bu (b) $TMSCH_2MgCl$, $CeCl_3$, THF-Et_2O (c) EtI, CsF, DMF (d) KH, THF (e) Ir(cod)py(PCy_3)PF_6, H_2, CH_2Cl_2 (f) *p*-TsCl, pyridine

cerium trichloride with **21** stopped at the stage of methyl ketone **23** (78%). Apparently enolization of the presumed intermediate α-trimethylsilyl ketone, or desilylation of that intermediate, prevents addition of the second mole of organometallic.[27] Fortunately, treatment of **23** with the same Peterson olefination reagent finally delivered diene **24** in 70% yield.[24,26]

All that remained was to selectively hydrogenate the isopropenyl group of **24** using Crabtree's catalyst.[22] Once again the formamide behaved differently from the acetamide as the isolated yield of axamide-1 (**2**) was only 39%. Other products that could be detected in the ^{1}H-NMR spectrum of the crude reaction mixture included (±)-axamide-4[10] and perhydroindans in which the exocyclic olefin had isomerized into the ring. One clear difference between acetamide **18** and formamide **24** is amide geometrical isomerism. Whereas **18** appears to exist as a single geometrical isomer, **24** is clearly a 2.5:1 mixture of isomers at room temperature in chloroform by NMR. This geometrical difference may translate into the observed difference in behavior because acetamide **18** should populate a conformation that can undergo a directed hydrogenation of the isopropenyl group, while the *E*-isomer of formamide **24** cannot.[28] Whatever the reason for the disappointing yield in the hydrogenation, we subjected (±)-axamide-1 (**2**) to *p*-toluenesulfonyl chloride to obtain (±)-axisonitrile-1 (**1**) in 87% yield.[29] Since **1** has previously been converted to axisothiocyanate-1 (**3**),[9] this also constitutes a formal total synthesis of the third member of this triad of sesquiterpenoids.

In summary, syntheses of racemic **1**−**3** have been achieved. The route to **1** requires 13 steps from vinylogous ester **8** and proceeds in 4% overall yield. Key steps involve a highly diastereoselective intramolecular Michael addition and a series of cerium-mediated olefinations.

Experimental Section[30]

3-(4-Methyl-3-pentenyl)-2-cyclohexen-1-one (9). To 1.03 g (42.3 mmol) of magnesium turnings were added with stirring a few drops of a solution of 6.16 g (37.8 mmol) of 1-bromo-4-methyl-3-pentene[12] in 25 mL of dry Et_2O. After the onset of Grignard formation, the remaining ethereal solution of bromide was added over a 20 min period, at a rate such that the mixture maintained a gentle reflux. After the addition was complete, the dark grey reaction mixture was heated under reflux for 50 min and then cooled to rt. A solution of 3.5 g (25 mmol) of 3-ethoxycyclohex-2-en-1-one[31] in 15 mL of dry Et_2O was then added dropwise over a 15 min period, at a rate such that the mixture maintained a gentle reflux. The resulting olive green mixture was heated under reflux for another 1.3 h and then cooled to rt. A 10% aqueous H_2SO_4 solution (30 mL) was added to 0 °C with stirring, and the mixture turned deep red, then orange, and then dark yellow. The organic phase was separated, and the aqueous layer was extracted with three 30 mL portions of ether. The organic layers were combined, washed with four 15 mL portions of brine and 25 mL of saturated aqueous $NaHCO_3$, dried ($MgSO_4$), and concentrated in vacuo to afford 4.2 g of **9** as a pale yellow oil, a 4 g portion of which was distilled to give 3.0 g (70%) of enone **9** as a clear colorlesss liquid: bp 80 °C at 0.3 mmHg; IR (neat) 1671, 1625 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.59 (s, 3H, CH_3), 1.67 (s, 3H, CH_3), 1.89−2.02 (m, 2H), 2.12−2.37 (m, 8H), 5.05 (m, 1H, =CH), 5.86 (t, J = 1.1 Hz, 1H, =CH); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 17.6 (q), 22.7 (t), 25.5 (t), 25.6 (q), 29.7 (t), 37.3 (t), 38.0 (t), 122.7 (d), 125.8 (d), 132.7 (s), 166.0 (s), 199.8 (s); exact mass calcd for $C_{12}H_{18}O$ *m/e* 178.1357, found *m/e* 178.1374.

(±)-3-Methyl-3-(4-methyl-3-pentenyl)cyclohexanone (10). To a suspension of 21.5 g (113 mmol) of CuI in 150 mL of dry Et_2O at 0 °C was slowly added 125 mL (175 mmol) of 1.4 M ethereal methyllithium. The resulting straw yellow mixture was cooled to −78 °C and allowed to stir at that temperature for 35 min. To this mixture was added dropwise via syringe pump 11.0 g (61.8 mmol) of enone **9** in 35 mL of dry Et_2O over a 15 min period. The resulting mixture was allowed to warm to −30 °C and stir for 2.6 h between −30 and −10 °C. The reaction mixture was then poured into 500 mL of chilled 10% aqueous NH_4Cl. The resulting mixture was stirred for 2.8 h, and the organic layer was separated and washed with two 120 mL portions of saturated aqueous NH_4Cl. The combined dark blue aqueous phases were extracted with two 250 mL portions of ether. The combined organic phases were washed with two 200 mL portions of brine, dried ($MgSO_4$), and concentrated in vacuo to afford 10.6 g (88%) of ketone **10** as a pale yellow oil: IR (neat) 3071, 1714, 1640 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.91 (s, 3H, CH_3), 1.26 (bt, J = 8.6 Hz, 2H, CH_2), 1.48−1.67 (m, 2H), 1.57 (s, 3H, =CCH_3), 1.65 (d, J = 1.0 Hz, 3H, =CCH_3), 1.80−1.95 (m, 4H), 2.08 (d, J = 12.9 Hz, 1H, CHC(O)), 2.18 (d, J = 13.4 Hz, 1H, CHC(O)), 2.25 (t, J = 6.8 Hz, 2H, CH_2), 5.05 (bt, J = 7.1 Hz, 1H, =CH); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 17.5 (q), 22.1 (t, two carbons), 24.9 (q), 25.6 (q), 35.8 (t), 38.5 (s), 41.0 (t), 41.6 (t), 53.6 (t), 124.3 (d), 131.5 (s), 212.1 (s); exact mass calcd for $C_{13}H_{22}O$ *m/e* 194.1670, found *m/e* 194.1718.

7-Methyl-1,4-dioxaspiro[4.5]decane-7-propionaldehyde (11). A solution of 10.6 g (54.7 mmol) of ketone **10**, 16 mL (287 mmol) of ethylene glycol, 27 mL of dry benzene, 16 mL (146 mmol) of trimethyl orthoformate, and 133 mg (699 mmol) of *p*-toluenesulfonic acid monohydrate was stirred at rt for 3.25 h, and the reaction was quenched by addition of 25 mL of saturated aqueous $NaHCO_3$. The organic phase was separated and concentrated in vacuo, and the residue was diluted with 200 mL of ether. The solution was washed with two 50 mL portions of brine, dried (Na_2SO_4), and concentrated in vacuo. The residual liquid (13.0 g) was chromatographed over 200 g of silica gel (eluted with petroleum ether−EtOAc, 24:1) to give 12.4 g (95%) of (±)-7-methyl-7-(4-methyl-3-pentenyl)-1,4-dioxaspiro[4.5]decane as a clear colorless liquid; IR (neat) 1673 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.96 (s, 3H, CH_3), 1.18−1.40 (m, 4H), 1.46 (d, J = 7.0 Hz, 1H, CH), 1.49−1.64 (m, 5H), 1.59 (s, 3H, =CCH_3), 1.67 (s, 3H, =CCH_3), 1.90 (m, 2H), 3.90 (m, 4H, $(OCH_2)_2$), 5.10 (tt, J = 7.1, 1.4 Hz, 1H, =CH); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 17.5 (q), 19.7 (t), 22.3 (t), 25.4 (q), 25.7 (q), 34.5 (s), 35.1 (t), 37.2 (t), 42.8 (t), 44.7 (t), 63.9 (t), 64.1 (t), 109.5 (s), 125.2 (d), 130.8 (s); exact mass calcd for $C_{15}H_{26}O_2$ *m/e* 238.1934, found *m/e* 238.1941.

Through a stirred solution of 7.02 g (29.5 mmol) of the ketal and a spatula tipful of $NaHCO_3$ in 60 mL of CH_2Cl_2 and 15 mL of methanol at −78 °C was passed a stream of ozone

(26) Hudrlik, P. F.; Peterson, D. *J. Am. Chem. Soc.* **1975**, *97*, 1464. Johnson, C. R.; Tait, B. D. *J. Org. Chem.* **1987**, *52*, 281. For overviews of the Peterson olefination, see: Kelly, S. E. In *Comprehensive Organic Synthesis*, Trost, B. M., Ed.; Pergamon Press: New York, 1991; Vol. 1, p 729. Chan, T.-H. *Acc. Chem. Res.* **1977**, *10*, 442.

(27) Demuth, M. *Helv. Chim. Acta* **1978**, *61*, 3136.

(28) Brown, J. M.; Cutting, I.; James, A. P. *Bull. Soc. Chim. Fr.* **1988**, 211.

(29) This transformation has also been reported by Piers.[9] Spectral data for **1** and **2** were in accord with those reported by Piers.

(30) General experimental considerations were the same as those presented in the preceding article (ref 11).

(31) Gannon, W. F.; House, H. O. *Org. Synth.* **1973**, *5*, 539.

(Welsbach ozone generator) at a flow rate of 1.0 mmol min^{-1}. When the reaction mixture maintained a blue color for 1 min, the stream of ozone was replaced by argon and the solution was stirred until the color dissipated (1.5 h). To the resulting clear reaction mixture was added 22 mL of dimethyl sulfide. The reaction mixture was stirred at −78 °C for 45 min, then the dry ice−acetone bath was removed, and the mixture was stirred overnight for another 12.7 h. The solvent was removed in vacuo, and the residual crude liquid (9.55 g) was chromatographed over 100 g of silica gel (eluted with hexane−EtOAc, 5:1) to give 5.77 g (92%) of aldehyde **11** as a clear colorless oil. Spectral data of **11** were consistent with data published in the literature:[10] ^{1}H NMR ($CDCl_3$, 250 MHz) δ 0.94 (s, 3H, CH_3), 1.23−1.30 (m, 2H, CH_2), 1.45 (d, J = 3.8 Hz, 2H, CH_2), 1.51−1.78 (m, 6H), 2.36 (m, 2H, CH_2CHO), 3.89 (bs, 4H, $(OCH_2)_2$), 9.76 (t, J 2.0 Hz, 1H, CHO).

Ethyl (±)-(Z)-2-Acetamido-5-(7-methyl-1,4-dioxaspiro-[4.5]dec-7-yl)-2-pentenoate (12). To 380 mg (2.01 mmol) of neat ethyl 2-acetamidomalonate at rt was added a solution of 421 mg (1.99 mmol) of aldehyde **11** in 1.6 mL (19.6 mmol) of pyridine. The resulting mixture was cooled to about 13 °C using an ice bath, and 0.58 mL (6.40 mmol) of acetic anhydride was added dropwise over a 2 min period. The resulting yellow-orange solution was stirred at rt for 3.8 h, and another 112 mg (0.592 mmol) portion of ethyl 2-acetamidomalonate was added. The resulting mixture was stirred at rt for 1.8 h, the reaction was quenched by addition of 2.3 g of crushed ice, and the solution was stirred for another 1.5 h. The mixture was then diluted with 26 mL of water and extracted with two 50 mL portions of ether. The combined organic phases were dried (Na_2SO_4) and concentrated in vacuo to afford 1.13 g of an orange oil. The residue was chromatographed over 45 g of silica gel (eluted with EtOAc−hexane, 2:1) to afford 389 mg (64%) of **12** as a heavy oil: IR ($CDCl_3$) 3416, 1691, 1096 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.95 (s, 3H, CH_3), 1.30 (t, J = 7.1 Hz, 3H, OCH_2CH_3), 1.21−1.59 (m, 10H), 2.12 (s, 3H, CH_3-CO), 2.01−2.21 (m, 2H, CH_2C=), 3.91 (s, 4H, $(OCH_2)_2$), 4.21 (q, J = 7.1 Hz, 2H, OCH_2CH_3), 6.69 (t, J = 7.2 Hz, 1H, =CH), 6.80 (bs, 1H, NH); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 14.2 (q), 19.6 (t), 23.4 (q), 23.7 (t), 25.7 (q), 34.6 (s), 34.9 (t), 37.1 (t), 40.4 (t), 44.6 (t), 61.4 (t), 64.0 (t, 2 carbons), 109.4 (s), 124.7 (s), 139.4 (d), 164.8 (s), 168.2 (s); exact mass calcd for $C_{18}H_{29}NO_5$ *m/e* 339.2046, found *m/e* 339.2044.

Ethyl (±)-(Z)-2-Formamido-5-(7-methyl-1,4-dioxaspiro-[4.5]dec-7-yl)-2-pentenoate (13). To a solution of 9.77 g (36.6 mmol) of ethyl formamido(diethylphosphono)acetate in 40 mL of dry CH_2Cl_2 at −30 °C was added dropwise 4.5 mL (30.1 mmol) of DBU. The resulting solution was stirred for 1.2 h between −30 and −13 °C and then cooled to −30 °C. A solution of 5.08 g (23.9 mmol) of aldehyde **11** in 35 mL of dry CH_2Cl_2 was added dropwise over a 20 min period. The resulting mixture was stirred for 1.7 h at −30 °C and for an additional 2.5 h at rt and diluted with 300 mL of EtOAc. The resulting solution was washed with 100 mL of saturated aqueous NH_4Cl. The organic layer was separated, and the aqueous phase was extracted with two 100 mL portions of EtOAc. The combined organic phases was dried (Na_2SO_4) and concentrated in vacuo. The residual yellow oil (11 g) was chromatographed over 200 g of silica gel (eluted with hexane−EtOAc, 1:1) to give 6.2 g (80%) of **13** as a pale yellow oil. This material was a 1:1 mixture of geometrical isomers by integration of selected peaks in the ^{1}H NMR spectrum of the mixture. The ^{13}C NMR of this mixture also showed two geometrical isomers: IR ($CDCl_3$) 3400, 1698, 1654, 1489 cm^{-1}; ^{1}H NMR ($CDCl_3$, 250 MHz) δ 0.95 (s, 3H, CH_3), 1.25−1.68 (m, 13H), 2.08−2.22 (m, 2H), 3.91 (s, 4H, $(OCH_2)_2$), 4.25 (m, 2H, OCH_2-CH_3), 6.61 (t, J = 7.84 Hz, 0.5H, =CH), 6.73 (t, J = 7.24 Hz, 0.5H, =CH), 6.97 (bs, 1H, NH), 8.22−8.26 (m, 1H, CHO); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 14.2 (q), 18.2 (s), 19.5 (t) and 19.6 (t), 22.7 (t) and 24.0 (t), 25.8 (q) and 26.9 (q), 34.5 (t) and 34.9 (t), 37.1 (t) and 37.8 (t), 39.3 (t) and 40.1 (t), 44.1 (t) and 44.5 (t), 61.5 (t) and 61.7 (t), 63.8 (t) and 63.9 (t), 64.0 (t) and 64.2 (t), 109.2 (s) and 109.4 (s), 123.2 (s) and 125.5 (s), 134.9 (d) and 139.7 (d), 158.8 (d) and 163.9 (d), 164.3 (s); exact mass calcd for $C_{17}H_{27}NO_5$ *m/e* 325.1889, found *m/e* 325.1893.

Ethyl (±)-(Z)-2-Acetamido-5-(1-methyl-3-oxocyclohexyl)-2-pentenoate (6). To a solution of 9.55 g (28.2 mmol) of ketal **12** in 165 mL of THF was added 225 mL of 0.3 N aqueous HCl. The reaction mixture was stirred for rt for 11 h, diluted with 500 mL of Et_2O, and neutralized with two 250 mL portions of saturated aqueous $NaHCO_3$. The combined washes were extracted with 300 mL of Et_2O, and the combined organic phases were washed with two 250 mL portions of saturated brine, dried (Na_2SO_4), and concentrated to afford 6.74 g (82% crude) of **6** as a pale yellow heavy oil: IR ($CDCl_3$) 3412, 1701, 1492 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.92 (s, 3H, CH_3), 1.28 (t, J = 7.1 Hz, 3H, OCH_2CH_3), 1.23−1.32 (m, 1H), 1.36−1.47 (m, 2H, CH_2), 1.52−1.67 (m, 2H, CH_2), 1.85 (td, J = 13, 6.5 Hz, 2H, CH_2CH_2C=O), 2.05−2.17 (m, 3H), 2.12 (s, 3H, CH_3C=O), 2.22−2.28 (m, 2H, CH_2C=O), 4.20 (q, J = 7.1 Hz, 2H, OCH_2CH_3), 6.61 (t, J = 7.3 Hz, 1H, =CH), 6.96 (s, 1H, NH); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 14.1 (q), 22.1 (t), 23.4 (t), 23.4 (q), 24.8 (q), 35.8 (t), 38.6 (s), 39.6 (t), 40.9 (t), 53.3 (t), 61.5 (t), 125.0 (s), 137.7 (d), 164.6 (s), 168.3 (s), 212.0 (s); exact mass calcd for $C_{16}H_{25}NO_4$ *m/e* 295.1783, found *m/e* 295.1787.

Ethyl (±)-(Z)-2-Formamido-5-(1-methyl-3-oxocyclohexyl)-2-pentenoate (7). To a solution of 6.20 g (19.0 mmol) of ketal **13** in 120 mL of THF was added 150 mL of 0.3 N aqueous HCl. The reaction mixture was stirred at rt for 2.5 h, diluted with 225 mL of Et_2O, and neutralized with 110 mL of saturated aqueous $NaHCO_3$. The organic layer was separated, and the aqueous phase was extracted with 120 mL of Et_2O. The combined organic phases were washed with 100 mL brine, dried (Na_2SO_4), and concentrated in vacuo to afford 6.74 g (95%) of crude **7** as a pale yellow heavy oil. This material was a 1.5:1 mixture of geometrical isomers by integration of selected peaks in the ^{1}H NMR spectrum of the mixture. The ^{13}C NMR of this mixture also showed two isomers: IR ($CDCl_3$) 3400, 1701, 1655, 1489 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.94 (bs, 3H, CH_3), 1.31 (t, J = 7.1 Hz, 3H, OCH_2CH_3), 1.40−1.49 (m, 2H), 1.52−1.65 (m, 2H), 1.86 (m, 2H), 2.10−2.30 (m, 6H), 4.23 (q, J = 7.0 Hz, 2H, $(OCH_2)_2$), 6.56 (t, J = 7.6 Hz, 0.4H, =CH), 6.67 (t, J = 7.3 Hz, 0.6H, =CH), 7.00 (bs, 0.4H, NH), 7.01 (bs, 0.6H, NH), 8.18 (d, J = 11.4 Hz, 0.4H, CHO), 8.25 (s, 0.6H, CHO); ^{13}C NMR ($CDCl_3$, 62.9 MHz, for major isomer) δ 14.1 (q), 22.0 (t), 23.8 (t), 24.8 (q), 35.6 (t), 38.5 (s), 39.6 (t), 40.9 (t), 53.4 (t), 61.6 (t), 123.4 (s), 138.2 (d), 158.8 (d), 163.7 (s), 211.9 (s); exact mass calcd for $C_{15}H_{23}NO_4$ *m/e* 281.1627, found *m/e* 281.1621.

Ethyl (±)-(α*R,1*R**,3a*R**,7a*S**)-α-αcetamidohexahydro-3a-methyl-7-oxo-1-indanacetate (4).** To a solution of 6.73 g (22.8 mmol) of **6** in 100 mL of THF was added 2.10 mL (25.2 mmol) of pyrrolidine followed by 3.2 mL (55.8 mmol) of glacial acetic acid. The resulting mixture was heated under reflux for 3 h, diluted with 250 mL of Et_2O, and washed with a solution of 50 mL of saturated aqueous $NaHCO_3$ in 50 mL of water. The aqueous phase was extracted with two 100 mL portions of Et_2O, and the combined organic phases were washed with two 100 mL portions of saturated brine, dried (Na_2SO_4), and concentrated in vacuo to afford 6.16 g (91%) of perhydroindan **4** as a pale yellow solid. This material was used directly in subsequent reactions without further purification. Recrystallization of a sample from hexane−carbon tetrachloride, however, gave pure **4** as a white solid (snow flakes): mp 123−125 °C; IR ($CDCl_3$) 3426, 1736, 1677, 1514 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.12 (s, 3H, CH_3), 1.26 (t, J = 7.1 Hz, 3H, OCH_2CH_3), 1.44−1.90 (m, 8H), 1.99 (s, 3H, CH_3CO), 2.02 (bd, J = 7.8 Hz, 1H, CHCO), 2.23−2.47 (m, 2H), 2.71 (p, J = 8.5 Hz, 1H, CH), 4.16 (q, J = 7.1 Hz, 2H, OCH_2-CH_3), 4.29 (dd, J = 8.7, 6.7 Hz, 1H, CHNHAc), 6.68 (bd, J = 6.5 Hz, 1H, NH); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 14.1 (q), 20.8 (t), 23.0 (q), 27.1 (t), 27.8 (q), 35.0 (t), 39.0 (t), 39.7 (t), 43.8 (d), 46.1 (s), 56.8 (d), 61.2 (t), 62.0 (d), 170.3 (s), 171.7 (s), 215.2 (s); exact mass calcd for $C_{16}H_{25}NO_4$ *m/e* 295.1783, found *m/e* 295.1787.

Anal. Calcd for $C_{16}H_{25}NO_4$: C, 65.06; H, 8.53. Found: C, 64.90; H, 8.55.

Ethyl (±)-(α*R,1*R**,3a*R**,7a*S**)-α-Formamidohexahydro-3a-methyl-7-oxo-1-indanacetate (5).** To a solution of 5.00 g (17.8 mmol) of **7** in 80 mL of dry THF was added 1.65 mL (19.8 mmol) of pyrrolidine followed by 2.6 mL (45 mmol) of glacial acetic acid. The resulting mixture was heated under reflux for 1.7 h, diluted with 200 mL of ether, and washed with a solution of 40 mL of saturated aqueous $NaHCO_3$ in 40

mL of water. The organic layer was separated, and the aqueous phase was extracted with two 75 mL portions of ether. The combined organic phases were washed with 100 mL of brine, dried (Na_2SO_4), and concentrated in vacuo to afford 4.53 g (91%) of perhydroindan **5** as a pale yellow solid. Recrystallization of a sample from hexane−carbon tetrachloride gave pure **5** (86% recovery) as colorless crystals. This material was a 14:1 mixture of geometrical isomers by integration of selected peaks in the ^{1}H NMR spectrum of the mixture. The ^{13}C NMR of this mixture also showed one major isomer and one minor isomer: mp 82−84 °C; IR ($CDCl_3$) 3416, 3352, 1737, 1690, 1506 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.13 (s, 3H, CH_3), 1.27 (t, J = 7.1 Hz, 3H, OCH_2CH_3), 1.47−1.92 (m, 8H), 2.03 (d, J = 7.9 Hz, 1H, CHC=O), 2.23−2.46 (m, 2H, CH_2C=O), 2.78 (p, J = 8.5 Hz, 1H, CH), 4.18 (q, J = 7.1 Hz, 2H, OCH_2CH_3), 4.42 (t, J = 8.0 Hz, 1H, $CHCO_2Et$), 6.75 (bs, 1H, NH), 8.18 (s, 1H, CHO); ^{13}C NMR ($CDCl_3$, 62.9 MHz, for major isomer) δ 14.1 (q), 20.8 (t), 27.1 (t), 27.8 (q), 35.1 (t), 39.0 (t), 39.7 (t), 43.6 (d), 46.1 (s), 55.2 (d), 61.5 (t), 61.7 (d), 161.1 (d), 171.1 (s), 215.2 (s); exact mass calcd for $C_{15}H_{23}NO_4$ *m/e* 281.1627, found *m/e* 281.1636. The structure of **5** was confirmed by X-ray crystallography.

Anal. Calcd for $C_{15}H_{23}NO_4$: C, 64.03; H, 8.24. Found: C, 63.94; H, 8.27.

Ethyl (±)-(α*R*,1R*,3aR*,7aR)-α-Acetamidohexahydro-3a-methyl-7-methylene-1-indanacetate (14).** A mixture of 1.88 g (5.26 mmol) of methyltriphenylphosphonium bromide and 393 mg (3.51 mmol) of potassium *tert*-butoxide in 8 mL of toluene was stirred at rt for 3.7 h followed by the addition of a solution of 689 mg (2.34 mmol) of **4** in 20 mL of toluene dropwise over a 15 min period. The reaction mixture was stirred at rt for 1.8 h, neutralized with 15 mL of saturated aqueous NH_4Cl in 60 mL of water, and diluted with 100 mL of ether. The organic phase was separated, and the aqueous layer was extracted with three 50 mL portions of ether. The combined organic phases were washed with 100 mL of brine, dried (Na_2SO_4), and concentrated in vacuo. The residue was chromatographed over 80 g of silica gel (eluted with hexane−EtOAc, 1:2) to give 601 mg (88%) of olefin **14** as a white solid: mp 122−125 °C; IR ($CDCl_3$) 3434, 1731, 1673, 1510 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.94 (s, 3H, CH_3), 1.26 (t, J = 7.1 Hz, 3H, OCH_2CH_3), 0.97−1.66 (m, 8H), 1.99 (s, 3H, CH_3CO), 1.87−2.14 (m, 3H), 2.64 (m, 1H, CH), 4.12 (q, J = 7.1 Hz, 2H, OCH_2CH_3), 4.54 (dd, J = 7.9, 6.5 Hz, 1H, CHNHAc), 4.66 (d, J = 2.5 Hz, 1H, =CH), 4.79 (d, J = 2.5 Hz, 1H, =CH), 6.00 (bd, J = 7.6 Hz, 1H, NH); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 14.1 (q), 23.1 (q), 24.0 (t), 24.5 (q), 25.3 (t), 30.7 (t), 32.8 (t), 40.0 (t), 42.3 (d), 44.5 (s), 55.5 (d), 57.3 (d), 61.0 (t), 111.3 (t), 148.3 (s), 170.0 (s), 171.9 (s); exact mass calcd for $C_{17}H_{27}NO_3$ *m/e* 293.1991, found *m/e* 293.1985.

Anal. Calcd for $C_{17}H_{27}NO_3$: C, 69.59; H, 9.28. Found: C, 69.47; H, 9.35.

(±)-*N*-[(1*R)-1-[(1*R**,3a*R**,7a*R*)-Hexahydro-3a-methyl-7-methylene-1-indanyl]-2-hydroxy-2-methylpropyl]-acetamide (15).** To an ice-cooled solution of 174 mg (0.59 mmol) of **14** in 5.4 mL of dry THF was added dropwise with stirring 1.20 mL (2.04 mmol) of 1.7 M ethereal methylmagnesium bromide. The resulting mixture was stirred at 5 °C for 1.5 h, the reaction was quenched with 7 mL of saturated aqueous NH_4Cl in 30 mL of water, and the solution was diluted with 100 mL of ether. The organic layer was separated, and the aqueous phase was extracted with three 50 mL portions of ether. The combined organic phases were washed with 130 mL brine, dried (Na_2SO_4), and concentrated in vacuo to afford the crude alcohol as a pale yellow solid. Recrystallization from hexane−CH_2Cl_2 afforded 140 mg (84%) of **15** as a white solid: mp 142−145 °C; IR ($CDCl_3$) 3500, 3433, 1662, 1506 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.93 (s, 3H, CH_3), 1.16 (d, J = 6.9 Hz, 6H, $(CH_3)_2$), 1.00−1.80 (m, 8H), 2.04 (s, 3H, CH_3CO), 1.90−2.20 (m, 4H), 2.59 (tt, J = 10.4, 5.2 Hz, 1H, CH), 3.97 (dd, J = 9.9, 5.2 Hz, 1H, CH), 4.74 (d, J = 2.5 Hz, 1H, =CH), 4.94 (bd, J = 2.1 Hz, 1H, =CH), 6.01 (bd, J = 9.6 Hz, 1H, NH); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 23.3 (q), 24.2 (q), 24.8 (t), 27.3 (q), 27.9 (q), 30.1 (t), 31.2 (t), 32.2 (t), 40.2 (t), 40.3 (d), 45.8 (s), 56.9 (d), 60.9 (d), 73.3 (s), 111.3 (t), 152.4 (s), 170.6 (s); exact mass calcd for $C_{17}H_{29}NO_2$ *m/e* 280.2276, found *m/e* 280.2276.

(±)-*N*-[(3*R,3a*R**,5a*R**,8a*R**,8b*S**)-8a-(Bromomethyl)-decahydro-2,2,5a-trimethyl-2*H*-cyclopenta[*de*]-1-benzopyran-3-yl]acetamide (16).** To a suspension of 50 mg (0.16 mmol) of pyridinium bromide perbromide in 0.4 mL of chloroform was added under argon 33.8 mg (0.121 mmol) of alcohol **15**, followed by 31 μL (0.15 mmol) of hexamethyldisilane. The resulting pale orange solution was stirred at rt for 50 min, dissolved in 20 mL of ether, washed with three 15 mL portions of water, dried (Na_2SO_4), and concentrated in vacuo to afford 47 mg of a pale yellow solid. Purification by column chromatography (eluted with EtOAc−hexane, 2:1) yielded 30 mg (69%) of **16** as a white solid: mp 188−189 °C dec; IR ($CDCl_3$) 3417, 1665, 1514 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.14 (s, 3H, CH_3), 1.22−1.83 (m, 16H), 2.06 (s, 3H, CH_3C=O), 1.97−2.14 (m, 1H, CH), 2.49 (m, 1H, CH), 3.47 (d, J = 10.6 Hz, 1H, CH(H)Br), 3.79 (d, J = 10.6 Hz, 1H, C(H)HBr), 4.04 (dd, J = 10.1, 2.4 Hz, 1H, CHNH), 5.91 (bd, J = 10.3 Hz, 1H, NH); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 21.6 (t), 23.4 (q), 25.1 (t), 26.8 (q), 28.3 (q), 28.5 (q), 33.1 (t), 36.0 (t), 36.9 (d), 39.9 (t), 40.2 (s), 45.0 (d), 46.3 (t), 52.8 (d), 75.4 (s), 76.4 (s), 170.1 (s); exact mass calcd for $C_{17}H_{29}NO_2Br$ + H *m/e* 358.1382, found *m/e* 358.1380.

(±)-*N*-[(3*R,3a*R**,5a*R**,8a*R**,8b*S**)-Decahydro-2,2,5a,-8a-tetramethyl-2*H*-cyclopenta[*de*]-1-benzopyran-3-yl]-acetamide (17).** To a solution of 30 mg (0.11 mmol) of alcohol **15** and 16.1 mg (0.107 mmol) of sodium iodide in 0.4 mL of acetonitrile was added dropwise under argon 15 μL (0.12 mmol) of trimethylsilyl chloride. The resulting solution was stirred for 55 min, and 20 mL of ether was added, which resulted in darkening of the solution. After successively washing with 15 mL of water, 15 mL of 10% aqueous sodium thiosulfate, and 15 mL of brine, the organic layer was dried (Na_2SO_4) and concentrated in vacuo to afford 48 mg of crude product. This material was purified by column chromatography to yield 22 mg (73%) of **17** as a whilte solid: mp 209−211 °C dec; IR ($CDCl_3$) 3446, 1665, 1509 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.12 (s, 6H, CH_3), 1.15−1.99 (m, 11H), 1.30 (s, 3H, CH_3), 1.40 (s, 3H, CH_3), 2.05 (s, 3H, CH_3C=O), 2.51 (m, 1H, CH), 4.03 (bd, J = 10.2, 3.1 Hz, 1H, CHN), 5.55 (bd, J = 9.1 Hz, 1H, NH); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 21.9 (t), 23.4 (q), 24.7 (t), 28.0 (q), 29.0 (q), 29.4 (q), 30.2 (q), 34.1 (t), 35.8 (t), 37.1 (d), 39.9 (t), 41.0 (s), 51.7 (d), 52.9 (d), 74.6 (s), 77.1 (s), 170.0 (s); exact mass calcd for $C_{17}H_{29}NO_2$ + H *m/e* 280.2276, found *m/e* 280.2254.

(±)-*N*-[(1*R)-1-[(1*R**,3a*R**,7a*R**)-Hexahydro-3a-methyl-7-methylene-1-indanyl]-2-methylallyl]acetamide (18). A. Preparation by Dehydration of Alcohol 15.** To a solution of 175 mg (0.63 mmol) of alcohol **15** in 5 mL of CH_2Cl_2 was added a solution of 687 mg (1.02 mmol) of Martin's sulfurane $[Ph_2S(OC(CF_3)_2Ph)_2]$ in 5 mL of CH_2Cl_2 in one portion. The mixture was stirred at rt for 25 min and concentrated in vacuo. The residue was chromatographed over 50 g of silica gel (eluted with hexane−EtOAc, 2:1) to give 124 mg (75%) of diene **18** as a pale yellow oil. **B. Preparation by Olefination of Ketone 19.** A mixture of 1.32 g (3.70 mmol) of methyltriphenylphosphonium bromide and 282 mg (2.52 mmol) of potassium *tert*-butoxide in 4 mL of toluene was stirred at rt for 3.2 h followed by the addition via cannula of a solution of 251 mg (0.95 mmol) of **19** in 10 mL of toluene over a 5 min period. The reaction mixture was stirred at rt for 2 h, neutralized with 20 mL of saturated aqueous NH_4Cl in 40 mL of water, and diluted with 100 mL of ether. The organic phase was separated, and the aqueous layer was extracted with two 50 mL portions of ether. The combined organic phases were washed with 100 mL of brine, dried (Na_2SO_4), and concentrated in vacuo. The residue was chromatographed over 75 g of silica gel (eluted with hexane−EtOAc, 1:2) to give 235 mg (95%) of olefin **18** as a pale yellow solid. The material was used directly in subsequent reactions without further purification. Recrystallization of a sample from hexane, however, afforded **18** as a white solid: mp 98−100 °C; IR ($CDCl_3$) 1665, 1509 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.93 (s, 3H, CH_3) 1.20 (bd, J = 10 Hz, 1H, CH), 1.35−1.70 (m, 6H), 1.65 (bs, 3H, $=CCH_3$), 1.87 (s, 3H, CH_3CO), 1.81−2.29 (m, 5H), 4.22 (dd, J = 10.7, 8.0 Hz, 1H, CHNHAc), 4.69 (bd, J = 2.0 Hz, 1H, =CH), 4.80 (bd, J = 2.0 Hz, 1H, =CH), 4.85 (bs, 1H, =CH), 4.95 (bs, 1H, =CH), 5.47 (bs, 1H, NH); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 18.5 (q), 23.3 (q), 24.3 (q), 24.4 (t), 27.1 (t), 31.3 (t), 32.7 (t), 39.9 (t), 41.5 (d),

45.5 (s), 59.7 (d), 61.7 (d), 110.6 (t), 113.5 (t), 144.3 (s), 150.6 (s), 169.3 (s); exact mass calcd for $C_{17}H_{27}NO$ *m/e* 261.2094, found *m/e* 261.2080.

Anal. Calcd for $C_{17}H_{27}NO$: C, 78.11; H, 10.41. Found: C, 78.02; H, 10.32.

(±)-*N*-[(1*R)-1-[(1*R**,3a*R**,7a*R**)-Hexahydro-3a-methyl-7-methylene-1-indanyl]-2-methylpropyl]acetamide (20) and (±)-*N*-[(1*R**)-2-Methyl-1-[(1*S**,3a*S**,7a*R**)-3a,4,5,7a-tetrahydro-3a,7-dimethyl-1-indanyl]propyl]acetamide.** A solution of 130 mg (0.5 mmol) of **18** in 15 mL of CH_2Cl_2 was purged with argon for 10 min. To this solution was added in one portion under argon 19 mg (0.024 mmol) of Crabtree's catalyst $[Ir(COD)P(Cy)_3(py)]PF_6$. The resulting bright orange solution was placed under 1 atm of hydrogen and stirred until about 12 mL (0.5 mmol) of hydrogen had been absorbed (the color became faint as soon as stirring began). The solution was filtered through Celite, and the filter cake was washed with CH_2Cl_2. The combined layers were dried (Na_2SO_4) and concentrated in vacuo. The residue was chromatographed over silica gel (eluted with hexane−EtOAc, 2:1) to afford 84 mg (64%) of **20** (which was further recrystallized from CH_2Cl_2−hexane to afford **20** as a clear solid (cubes)) and 55 mg of a mixed fraction which was purified by MPLC to give a product, which after recrystallization afforded 7 mg (5%) of (±)-*N*-[(1*R**)-2-methyl-1-[1*S**,3a*S**,7a*R**)-3a,4,5,7a-tetrahydro-3a,7-dimethyl-1-indanyl]propyl]acetamide as white needles. Amide **20**: mp 124−125 °C; IR (CCl_4) 3450, 3070, 1682, 1386, 1368 cm^{-1}; ^1H NMR ($CDCl_3$, 250 MHz) δ 0.77 (d, J = 6.8 Hz, 3H, CH(C*H*$_3$)CH$_3$), 0.88 (d, J = 6.8 Hz, 3H, CH(CH$_3$)C*H*$_3$), 0.92 (s, 3H, CH$_3$), 1.17 (bd, J = 12.2 Hz, 1H, CH), 1.35−1.69 (m, 6H), 1.80−2.11 (m, 5H), 1.91 (s, 3H, CH$_3$CO), 2.24 (qd, J = 9.9, 5.2 Hz, 1H, CH), 3.84 (td, J = 10.0, 3.6 Hz, 1H, C*H*NHAc), 4.63 (d, J = 2.8 Hz, 1H, =CH), 4.75 (bs, 1H, =CH), 5.02 (bd, J = 9.0 Hz, 1H, NH); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 15.9 (q), 20.5 (q), 23.5 (q), 24.3 (q), 24.6 (t), 27.8 (t), 30.6 (d), 31.1 (t), 32.9 (t), 39.8 (t), 42.0 (d), 45.1 (s), 59.3 (d), 59.3 (d), 109.9 (t), 150.2 (s), 170.0 (s); exact mass calcd for $C_{17}H_{29}NO$ *m/e* 263.2249, found *m/e* 263.2243. Anal. Calcd for $C_{17}H_{29}NO$: C, 77.51; H, 11.10. Found: C, 77.62; H, 11.15. (±)-*N*-[(1*R**)-2-Methyl-1-[1*S**,3a*S**,7a*R**)-3a,4,5,7a-tetrahydro-3a,7-dimethyl-1-indanyl]-propyl]acetamide: mp 198−200 °C; IR ($CDCl_3$) 3446, 1664, 1511, 1371 cm^{-1}; ^1H NMR ($CDCl_3$, 250 MHz) δ 0.81 (d, J = 6.9 Hz, 3H, CH(C*H*$_3$)CH$_3$), 0.92 (d, J = 6.8 Hz, 3H, CH(CH$_3$)-C*H*$_3$), 1.03 (s, 3H, CH$_3$), 1.23−1.37 (m, 2H), 1.41−1.60 (m, 3H), 1.65 (d, J = 1.4 Hz, 3H, =CCH$_3$), 1.72−2.04 (m, 6H), 2.02 (s, 3H, CH$_3$CO), 3.89 (dt, J = 10.5, 2.8 Hz, 1H, CHN), 5.15 (bd, J = 11.0 Hz, 1H, NH), 5.39 (bs, 1H, =CH); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 14.9 (q), 21.0 (q), 22.1 (t), 23.1 (q), 23.8 (q), 28.0 (t), 28.1 (q), 29.2 (d), 32.2 (t), 36.2 (t), 41.2 (s), 46.6 (d), 51.8 (d), 58.7 (d), 122.0 (d), 135.8 (s), 169.1 (s); exact mass calcd for $C_{17}H_{29}NO$ *m/e* 263.2249, found *m/e* 263.2245.

(±)-*N*-[(1*R)-1-[(1*R**,3a*R**,7a*R*)-Hexahydro-3a-methyl-7-methylene-1-indanyl]acetonyl]acetamide (19).** To an ice-cooled mixture of 1.55 mL (2.63 mmol) of 1.7 M ethereal methylmagnesium bromide and 0.72 mL (5.16 mmol) of triethylamine in 5 mL of toluene was added dropwise via syringe pump a solution of 238 mg (0.81 mmol) of **14** in 8 mL of THF over a 45 min period. The resulting mixture was stirred at a temperature ranging from 5 to 10 °C for 4 h, acidified with 10 mL of 5% aqueous HCl in 60 mL of water (pH 3), and diluted with 100 mL of ether. The organic layer was separated, and the aqueous phase was extracted with two 50 mL portions of ether. The combined organic phases were dried (Na_2SO_4) and concentrated in vacuo. The residue was chromatographed over 50 g of silica gel (eluted with EtOAc−hexane, 2:1) to afford 81 mg (34%) of recovered ester **14**, along with 22 mg (9%) of alcohol **15** and 115 mg (54%) of **19**. Recrystallization of a 45 mg sample from CH_2Cl_2−hexane afforded 43 mg of pure **19**: mp 116−117 °C; IR ($CDCl_3$) 3420, 1716, 1671, 1505 cm^{-1}; ^1H NMR ($CDCl_3$, 250 MHz) δ 0.94 (s, 3H, CH$_3$), 1.18−1.74 (m, 7H), 1.88−2.22 (m, 4H), 1.99 (s, 3H, CH$_3$C=O), 2.17 (s, 3H, CH$_3$C=O), 2.60 (m, 1H, CH), 4.56 (t, J = 7.1 Hz, 1H, CHAc), 4.62 (d, J = 2.4 Hz, 1H, =CH), 4.81 (s, 1H, =CH), 6.14 (bs, 1H, NH); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 23.0 (q), 24.1 (t), 24.4 (q), 26.4 (t), 28.4 (q), 30.8 (t), 32.7 (t), 40.1 (t), 40.7 (d), 44.8 (s), 57.5 (d), 62.6 (d), 112.0 (t), 148.7 (s), 170.3 (s), 206.7 (s); exact mass calcd for $C_{16}H_{25}NO_2$ *m/e* 263.1885, found *m/e* 263.1873. Anal. Calcd for $C_{16}H_{25}NO_2$: C, 72.96; H, 9.57. Found: C, 73.08; H, 9.55.

(±)-(α*R,1*R**,3a*R**,7a*R**)-α-Formamidohexahydro-3a-methyl-7-methylene-1-indanacetic Acid (22).** Cerium trichloride (3.61 g, 14.6 mmol) was dried at 145 °C and 0.1 mmHg for 6 h. The flask was cooled to rt and vented to a dry-argon atmosphere. Dry THF was added (35 mL), and the suspension was stirred at rt under argon for 14 h. The light grey slurry was then cooled to −78 °C, and a solution of *t*-BuLi (3.0 M in hexanes) was added until an orange color was obtained. A 12 mL solution (12 mmol) of (trimethylsilyl)-methylmagnesium chloride (1.0 M in Et_2O) was added dropwise, and the resulting suspension was stirred at −78 °C for 3.5 h, at which time 564 mg (2.00 mmol) of ester **5** in 7 mL of dry THF was added dropwise. The resulting mixture was allowed to stir overnight (21 h) and warm to rt. The reaction was quenched by addition of 70 mL of 1 N aqueous HCl solution. The organic layer was separated, and the aqueous phase was extracted with three 50 mL portions of CH_2Cl_2. The combined organic phases were dried ($MgSO_4$) and concentrated in vacuo to afford 533 mg of a beige solid. Trituration with CH_2Cl_2−hexane afforded several crops which overall accounted for 358 mg (71%) of acid **22** as a white solid: mp 178−180 °C dec; IR (KBr pellet) 3327, 3300−2500, 3070, 1726, 1617 cm^{-1}; ^1H NMR (DMSO-d_6, 300 MHz) δ 0.89 (s, 3H, CH$_3$), 1.10−1.19 (m, 1H, CH), 1.24−1.50 (m, 5H), 1.54−1.60 (m, 1H, CH), 1.82−2.11 (m, 4H), 2.57−2.64 (m, 1H, CH), 4.38 (dd, J = 9.1, 4.3 Hz, 1H, CHN), 4.65−4.70 (m, 2H, =CH$_2$), 8.03 (d, J = 1.0 Hz, 1H, CHO), 8.29 (bd, J = 9.2 Hz, 1H, NH), 12.5 (bs, 1H, CO_2H); ^{13}C NMR (DMSO-d_6, 75.5 MHz) δ 23.6 (t), 24.6 (q), 25.1 (t), 30.2 (t), 32.6 (t), 39.6 (t), 41.8 (d), 43.8 (s), 52.0 (d), 55.3 (d), 111.3 (t), 147.2 (s), 161.3 (d), 172.0 (s); exact mass calcd for $C_{14}H_{21}NO_3$ *m/e* 251.1521, found *m/e* 251.1522.

Anal. Calcd for $C_{14}H_{21}NO_3$: C, 66.90; H, 8.42. Found: C, 66.26; H, 8.44.

Ethyl (±)-(α*R,1*R**,3a*R**,7a*R**)-α-Formamidohexahydro-3a-methyl-7-methylene-1-indanacetate (21).** A mixture of 237 mg (0.94 mmol) of acid **22**, 0.16 mL (2.0 mmol) of iodoethane, and 287 mg (1.89 mmol) of cesium fluoride in 5 mL of dry *N,N*-dimethylformamide was stirred at 13 °C under argon for 24 h. The reaction mixture was combined with 35 mL of saturated aqueous $NaHCO_3$ and extracted with two 50 mL portions of EtOAc. The combined organic phases were dried (Na_2SO_4) and concentrated in vacuo. The residual oil (271 mg) was purified by flash chromatography over 25 g of silica gel (eluted with hexane−EtOAc, 2:1) to afford 223 mg (85%) of ester **21** as a clear colorless oil. This material was a 3.5:1 mixture of geometrical isomers by integration of selected peaks in the ^1H NMR spectrum of the mixture. The ^{13}C NMR of this mixture also showed one major isomer and one minor isomer: IR ($CDCl_3$) 3424, 3072, 1733, 1690, 1645 cm^{-1}; ^1H NMR ($CDCl_3$, 250 MHz) δ 0.95 (s, 3H, CH$_3$), 1.26 (t, J = 7.16 Hz, 3H, CH$_2$C*H*$_3$), 1.23−1.68 (m, 7H), 1.89−2.16 (m, 4H), 2.67−2.80 (m, 1H, CHCN), 4.12 (q, J = 7.15 Hz, 2H, OC*H*$_2$CH$_3$), 4.62−4.65 (m, 1H, =CH), 4.70 (dd, J = 8.4, 5.4 Hz, 1H, CHCO$_2$-Et), 4.78−4.80 (m, 1H, =CH), 6.15 (bd, J = 6.0 Hz, 1H, NH), 8.00 (d, J = 11.7 Hz, 0.23 H, CHO), 8.22 (s, 0.77 H, CHO); ^{13}C NMR ($CDCl_3$, 75.5 MHz, for major isomer) δ 14.3 (q), 24.2 (t), 24.8 (q), 25.5 (t), 30.8 (t), 33.0 (t), 40.1 (t), 42.5 (d), 44.6 (s), 53.5 (d), 56.8 (d), 61.4 (t), 111.8 (t), 147.8 (s), 161.3 (d), 171.4 (s); exact mass calcd for $C_{16}H_{25}NO_3$ *m/e* 279.1834, found *m/e* 279.1837.

(±)-*N*-[(1*R)-1-[(1*R**,3a*R**,7a*R**)-Hexahydro-3a-methyl-7-methylene-1-indanyl]acetonyl]formamide (23).** Cerium trichloride (1.12 g, 4.54 mmol) was dried at 145 °C and 0.1 mmHg for 8 h. The flask was cooled to rt and vented to a dry-argon atmosphere. Dry THF was added (20 mL), and the suspension was stirred at rt under argon for 12 h. The light grey slurry was then cooled to −78 °C, and a solution of *t*-BuLi (3.0 M in hexanes) was added until an orange color was obtained. A 3.8 mL solution (3.8 mmol) of (trimethylsilyl)-methylmagnesium chloride (1.0 M in Et_2O) was added dropwise, and the resulting suspension was stirred at −78 °C for 5 h, at which time 223 mg (0.80 mmol) of ester **21** in 3 mL of dry THF was added dropwise. The resulting mixture was allowed to stir overnight (19 h) and warm to rt. The reaction was quenched by addition of 15 mL of a 1 N aqueous HCl

solution. The organic layer was separated, and the aqueous phase was extracted with three 25 mL portions of CH_2Cl_2. The combined organic phases were dried ($MgSO_4$) and concentrated in vacuo. The residual yellow oil (218 mg) was purified by flash chromatography over 25 g of silica gel (eluted with hexane−EtOAc, 5:1, then 2:1) to afford 155 mg (78%) of ketone **23** as a white solid. The material was used directly in subsequent reactions without further purification. Recrystallization of a sample from CH_2Cl_2−hexane, however, afforded **23** as white needles. This material was a 9:1 mixture of geometrical isomers by integration of selected peaks in the ^{1}H NMR spectrum of the mixture. The ^{13}C NMR of this mixture also showed one major isomer and one minor isomer: mp 75−77 °C; IR ($CDCl_3$) 3409, 1716, 1675, 1644 cm^{-1}; ^{1}H NMR ($CDCl_3$, 250 MHz) δ 0.94 (s, 3H, CH_3), 1.21 (bd, J = 10.3 Hz, 1H, CH), 1.32−1.54 (m, 4H), 1.57−1.70 (m, 2H, CH), 1.88 (d, J = 10.3 Hz, 1H, CH), 1.95−2.13 (m, 3H), 2.17 (s, 3H, $COCH_3$), 2.70 (m, 1H, CH), 4.60 (bs, 1H, =CH), 4.70 (dd, J = 7.9, 5.9 Hz, 1H, C*H*NCHO), 4.80 (t, J = 1.8 Hz 1H, =CH), 6.33 (bs, 1H, NH), 8.2 (s, 1H, CHO); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 24.0 (t), 24.4 (q), 26.4 (t), 28.1 (q), 30.8 (t), 32.7 (t), 40.0 (t), 40.6 (d), 44.7 (s), 56.7 (d), 60.7 (d), 112.6 (t), 147.8 (s), 161.3 (d), 205.6 (s); exact mass calcd for $C_{15}H_{23}NO_2$ *m/e* 249.1728, found *m/e* 249.1743.

Anal. Calcd for $C_{15}H_{23}NO_2$: C, 72.25; H, 9.30. Found: C, 72.25; H, 9.32.

(±)-*N*-[(1*R)-1-[(1*R**,3a*R**,7a*R**)-Hexahydro-3a-methyl-7-methylene-1-indanyl]-2-methylallyl]formamide (24).** Cerium trichloride (877 mg, 3.56 mmol) was dried at 145 °C and 0.1 mmHg for 8 h. The flask was cooled to rt and vented to a dry-argon atmosphere. Dry THF was added (18 mL), and the suspension was stirred at rt under argon for 11 h. The light grey slurry was then cooled to −78 °C, and a solution of *t*-BuLi (3.0 M in hexane) was added until an orange color was obtained. A 2.8 mL solution (2.8 mmol) of (trimethylsilyl)-methylmagnesium chloride (1.0 M in Et_2O) was added dropwise, and the resultng suspension was stirred at −78 °C for 4 h, at which time 146 mg (0.58 mmol) of ketone **23** in 7 mL of dry THF was added dropwise. The resulting mixture was allowed to stir overnight (20 h) and warm up to rt. The reaction was quenched by addition of 25 mL of a 1 N aqueous HCl solution. The organic layer was separated, and the aqueous phase was extracted with three 35 mL portions of CH_2Cl_2. The combined organic phases were dried ($MgSO_4$) and concentrated in vacuo to afford 164 mg of hydroxysilane as an off-white solid. Potassium hydride (35% oil dispersion, 5.23 mmol) was washed with three 2 mL portions of hexane, and 5 mL of dry THF was added by syringe. A solution of 163 mg (0.48 mmol) of the hydroxysilane in 5 mL of dry THF was added dropwise. The mixture was stirred for 2.5 h at rt and neutralized with 25 mL of saturated aqueous NH_4Cl. The organic layer was separated, and the aqueous phase was extracted with three 30 mL portions of pentane−ether (1:2). The combined organic phases were washed with 20 mL brine, dried (Na_2SO_4), and concentrated in vacuo. The residual oil was chromatographed over 25 g of silica gel (eluted with hexane−EtOAc, 2:1) to give 93 mg (69% from ketone) of diene **24**. This material was a 2.5:1 mixture of geometrical isomers by integration of selected peaks in the ^{1}H NMR spectrum of the mixture. The ^{13}C NMR of this mixture also showed one major isomer and one minor isomer: IR ($CDCl_3$) 3427, 3155, 3073, 1672 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.91 (s, 2.1H, CH_3), 0.92 (s, 0.9H, CH_3), 1.15−1.46 (m, 6H), 1.50−1.85 (m, 1H), 1.63 (bs, 3H, =CCH_3), 1.87−2.30 (m, 5H), 3.68 (dd, J = 9.6, 6.8 Hz, 0.28H, C*H*NHCHO), 4.29 (t, J = 9.2 Hz, 0.72 H, C*H*NHCHO), 4.68−4.94 (m, 4H, =CH), 5.80 (bs, 0.71H, NH), 6.10 (bs, 0.28H, NH), 7.95 (d, J = 12 Hz, 0.28H, CHO), 8.02 (bs, 0.72H, CHO); ^{13}C NMR ($CDCl_3$, 75.5 MHz, major isomer) δ 18.7 (q), 24.6 (q), 24.5 (t), 27.2 (t), 31.5 (t), 32.9 (t), 40.0 (t), 41.0 (d), 45.7 (s), 59.7 (d), 60.6 (d), 111.6 (t), 114.1 (t), 144.0 (s), 150.3 (s), 161.0 (d); ^{13}C NMR ($CDCl_3$, 75.5 MHz, minor isomer) δ 17.7 (q), 24.4 (t), 24.7 (q), 26.7 (t), 31.3 (t), 33.1 (t), 39.9 (t), 41.9 (d), 45.6 (s), 60.5 (d), 65.5 (d), 112.7 (t), 114.9 (t), 144.6 (s), 149.1 (s), 164.4 (d); exact mass calcd for $C_{16}H_{25}NO$ *m/e* 247.1936, found *m/e* 247.1934.

(±)-*N*-[(1*R)-1-[(1*S**,3a*S**,7a*S**)-Hexahydro-3a-methyl-7-methylene-1-indanyl]-2-methylpropyl]formamide (2).** A solution of 62.6 mg (0.25 mmol) of diene **24** in 5 mL of CH_2Cl_2 was purged with argon for 10 min. To this solution was added in one portion under argon 6 mg (7 μmol) of [Ir(COD)P(Cy)$_3$(py)]PF_6. The resulting bright orange solution was hydrogenated at 1 atm for 2 h (although no clear sign of hydrogen uptake was detected). The solution was filtered through Celite, and the filter cake was washed with CH_2Cl_2. The combined layers were dried (Na_2SO_4) and concentrated in vacuo. The residue was chromatographed over silica gel (eluted with hexane−EtOAc, 2:1) to afford 76 mg of material which, after chromatography over silica gel (eluted with petroleum ether−Et_2O, 2:1), afforded 24 mg (39%) of axamide-1 (**2**) along with 23 mg of a mixture of products containing material with the endocyclic methylene and 16 mg of a mixture containing the epimer of axamide-1 at the position α to the formamide group. Spectral data of amide **2** were consistent with data published in the literature for (±)-axamide-1.[9] After a few weeks on the bench top and/or in the freezer, amide **2** crystallized as a white solid without any change in the spectral data. This material was a 1.8:1 mixture of geometrical isomers by integration of selected peaks in the ^{1}H NMR spectrum of the mixture. The ^{13}C NMR of this mixture also showed one major isomer and one minor isomer: mp 71−74 °C; IR (neat) 3278, 1660, 890 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.79 (d, J = 6.8 Hz, 1.92H, CH(C*H*$_3$)(CH_3)), 0.80 (d, J = 6.8 Hz, 1.08H, CH(CH_3)(C*H*$_3$)), 0.89 (d, J = 6.8 Hz, 1.92H, CH(C*H*$_3$)(CH_3)), 0.90 (d, J = 6.8 Hz, 1.08H, CH(CH_3)(C*H*$_3$)), 0.92 (s, 1.92H, CH_3), 0.95 (s, 1.08H, CH_3), 1.19−1.53 (m, 6H), 1.60−1.71 (m, 1H), 1.84−2.42 (m, 5H), 2.95 (ddd, J = 12.5, 8.4, 4.2 Hz, 0.36H, CH), 3.91 (td, J = 9.9, 4.1 Hz, 0.64 H, CH), 4.65 (bs, 0.36H, =CH), 4.68 (d, J = 2.6 Hz, 0.64H, =CH), 4.75 (t, J = 1.8 Hz, 0.64H, =CH), 4.82 (t, J = 2.0Hz, 0.36H, =CH), 5.12 (bs, 0.64H, NH), 5.28 (bs, 0.36H, NH), 7.90 (d, J = 11.8 Hz, 0.36H, CHO), 8.15 (d, J = 2.1 Hz, 0.64H, CHO); ^{13}C NMR ($CDCl_3$, 75.5 MHz, major isomer) δ 16.2 (q), 20.5 (q), 24.3 (q), 24.5 (t), 27.8 (t), 30.4 (d), 31.1 (t), 32.8 (t), 39.7 (t), 40.8 (d), 45.1 (s), 58.9 (d), 63.9 (d), 110.7 (t), 149.9 (s), 161.7 (d); ^{13}C NMR ($CDCl_3$, 75.5 MHz, minor isomer) δ 16.3 (q), 20.5 (q), 24.3 (q), 24.4 (t), 27.7 (t), 29.7 (d), 31.1 (t), 32.1 (t), 39.7 (t), 42.2 (d), 44.8 (s), 58.1 (d), 59.4 (d), 111.7 (t), 148.2 (s), 164.2 (d); exact mass calcd for $C_{16}H_{27}NO$ *m/e* 249.2092, found *m/e* 249.2091.

(±)-(1*R)-1-[(1*S**,3a*S**,7a*S**)-Hexahydro-3a-methyl-7-methylene-1-indanyl]-2-methylpropyl Isocyanide (1).** To a stirred solution of 17.1 mg (0.068 mmol) of (±)-axamide-1 (**2**) in 1 mL of pyridine was added under an argon atmosphere 46 mg (0.24 mmol) of *p*-toluenesulfonyl chloride, and the mixture was stirred at rt for 2.5 h. A few chips of ice were added, and the mixture was poured into 10 mL of ice-cooled water and then extracted with two 10 mL portions of pentane. The combined extracts were washed with two 5 mL portions of water, dried ($MgSO_4$), and concentrated in vacuo to afford 13.7 mg (87%) of (±)-axisonitrile-1 (**1**) as a white solid. Spectral data of isonitrile **1** were consistent with data published in the literature for (±)-axisonitrile-1: mp 45−46 °C; IR (CCl_4) 3072, 2135, 1637, 1390, 1375, 898 cm^{-1}; ^{1}H NMR ($CDCl_3$, 250 MHz) δ 0.88 (d, J = 6.7 Hz, 3H, CH(C*H*$_3$)(CH_3)), 0.99 (s, 3H, CH_3), 1.01 (d, J = 6.6 Hz, 3H, CH(CH_3)(C*H*$_3$)), 1.20−1.26 (m, 1H), 1.43−1.66 (m, 6H), 1.98−2.19 (m, 5H), 2.48 (m, 1H, CH), 3.23 (tt, J = 5.6, 1.8 Hz, 1H, CHN=C), 4.82 (bs, 2H, =CH_2); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 18.9 (q), 19.7 (q), 24.2 (q), 24.2 (t), 27.6 (t), 29.6 (d), 31.2 (t), 33.2 (t), 39.5 (t), 40.1 (d), 45.0 (s), 57.1 (d), 67.6 (td, J_{CNC} = 5.3 Hz), 111.5 (t), 148.5 (s), the isonitrile carbon singlet was not detected; exact mass calcd for $C_{16}H_{25}N$ *m/e* 231.1987, found *m/e* 231.1988.

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Supporting Information Available: ^{1}H and ^{13}C NMR spectra for compounds prepared (50 pages). This material is contained in 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.

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