Articles

Stereocontrolled Construction of Condensed γ-Lactam Ring Systems by Cationic Cyclizations. Rearrangement of a γ-Lactam to a δ-Lactam

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A new condensation of 3-alkenamides with benzaldehyde in acidic media, notably polyphosphoric acid, leads to γ-lactam rings with high regio- and stereocontrol. One such γ-lactam was shown to undergo a novel and stereocontrolled ring-expansion to a δ-lactam.

The importance of stereocontrol in the synthesis of substituted pyrrolidines is exemplified in the acromelic acids, potent neuroexcitatory agents, and in the related kainic acid **1**.[1] Since the pyrrolidinone ring is also found in natural products and a variety of pharmacologically active compounds, a means of assembly of functionalized five-membered *N*-heterocycles with stereocontrol, from acyclic precursors, is of considerable interest. Examples of such systems include the hypolipidemics **2**, appropriate for the treatment of arteriosclerosis,[2a] the alkaloid cotinine **3**, lactams such as **4** which act on the nervous system,[2b] and nootropic drugs such as **5**.[2c]

We recently reported the first condensations under acidic conditions of acyclic β,γ-unsaturated amides with carbonyl compounds to give one or more new rings.[3,4] In principle, either terminus of the alkenyl moiety could participate, and we have shown that appropriate conditions and reagents will favor one terminus over the other in the same alkenamide.[3,4] Thus, both regio- and stereoselective syntheses of both γ- and δ-lactams are possible starting from the same 3-alkenamide and the same carbonyl compound. In the related processes of the condensation of 3-alkenamines (with[5] or without[6] silicon termini) with formaldehyde equivalents, only the C-4 terminus becomes bonded to the carbonyl carbon atom, thereby leading to a six-membered *N*-heterocycle. In contrast, examples of bond formation between the carbon atom of an aldehyde and the N and C-3 termini of 3-alkenamides are herein described. The processes occur at around 35 °C, are stereoselective, three contiguous stereogenic centers being formed in one pot from achiral precursors, and require no Lewis acid catalysts or stabilizing or activating groups.

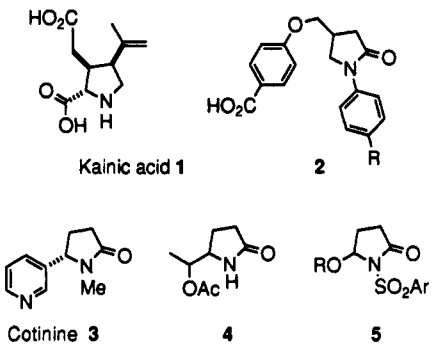

Figure 1.

In any condensation of 3-butenamide with carbonyl compounds the C-4 terminus would be expected to become bonded to the carbonyl component, since the resulting carbocation would be secondary, in contrast to a primary one which would be generated were the C-3 terminus to participate. Consistent with this, we have shown[4] that 3-butenamide condenses with benzaldehyde in polyphosphate ester (PPE) at 60 °C to give 6-phenyl-5,6-dihydro-2(1*H*)-pyridinone (51%) as the only product that was isolated.[4] 3-Pentenamides were next investigated, since secondary carbocations could equally be formed by participation of either the C-3 or the C-4 terminus of the alkenamide with the carbonyl compound. (*E*)-3-Pente-

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(1) Konno, K.; Hashimoto, K.; Ohfune, Y.; Shirahama, H.; Matsumoto, T. *J. Am. Chem. Soc.* **1988**, *110*, 4807.

(2) (a) Diaz, R. S.; Monreal, J.; Lucas, M. *J. Neurochem.* **1990**, *55*, 134. European Patent 393,607. *Chem. Abstr.* **1991**, *114*, 22874a. (b) Woo, E. P.; Mullins, M. J. U.S. Patent US 4,943,640. *Chem. Abstr.* **1991**, *114*, 23798c. (c) Toja, E.; Gorini, C.; Zirotti, C.; Barzaghi, F.; Galliani, G. European Patent, 229, 566, 1987.

(3) Marson, C. M.; Grabowska, U.; Walsgrove, T.; Eggleston, D. S.; Baures, P. W., *J. Org. Chem.* **1991**, *56*, 2603.

(4) Marson, C. M.; Grabowska, U.; Walsgrove, T. *J. Org. Chem.* **1992**, *57*, 5045.

(5) (a) Overman, L. E.; Malone, T. C.; Meier, G. P. *J. Am. Chem. Soc.* **1983**, *105*, 6993. (b) Flann, C.; Malone, T. C.; Overman, L. E. *J. Am. Chem. Soc.* **1987**, *109*, 6097. (c) Blumenkopf, T. A.; Overman, L. E. *Chem. Rev.*, **1986**, *86*, 857.

(6) (a) Grewe, R.; Hamann, R.; Jacobsen, G.; Nolte, E.; Riecke, K. *Ann.* **1953**, *581*, 85. (b) Grob, C. A.; Wohl, R. A. *Helv. Chim. Acta* **1966**, *49*, 2175.

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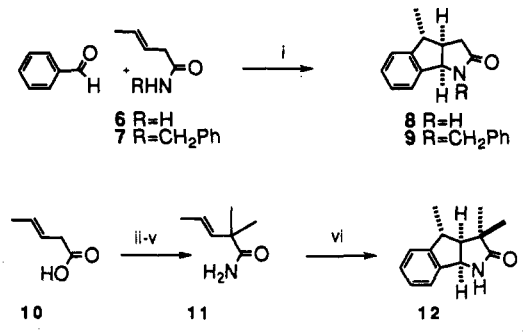
Scheme 1



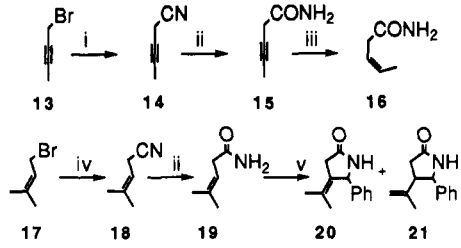
[a] Reagents: (i) PPA (for **6**) or PPE (for **7**), 35 °C; (ii) LDA, THF, HMPA; (iii) MeI; (iv) $SOCl_2$; (v) NH_3; (vi) PhCHO, PPA.

namide **6** was prepared in 85% yield by treatment of (*E*)-3-pentenenitrile with alkaline H_2O_2 and tetra-*n*-butylammonium hydrogen sulfate.[7] Condensation of (*E*)-3-pentenamide (1 equiv) with benzaldehyde (2 equiv) was effected in polyphosphoric acid (PPA) at 35 °C for 72 h. Chromatography on silica gel afforded the tricyclic lactam **8**, mp 175–176 °C, in 74% yield (Scheme 1).

The high yield of a single diastereoisomer is notable, and its relative configuration **8** was established by single-crystal X-ray analysis.[8] In view of conversions of nitriles into amides by PPA,[9] and of many α-amidoalkylations which proceed either using nitriles or amides,[10] (*E*)-3-pentenenitrile was substituted for (*E*)-3-pentenamide, whereupon lactam **8** was obtained in 67% yield. The tolerance of this condensation toward an *N*-substituent was probed by reacting (*E*)-*N*-benzyl-3-pentenamide **7** (1 equiv) with benzaldehyde (2 equiv) in PPE at 35 °C for 24 h; the tricyclic lactam **9** was obtained (52%) as the sole isolated product. From the same reaction conducted in PPA at 45 °C for 24 h, only starting materials were recovered; when the reaction was carried out at 60 °C, polymerization occurred. Interestingly, the significant steric crowding created by the proximity of carbonyl, benzyl, and aryl groups does not retard the formation of a γ-lactam. Additionally, only the C-3 terminus acts as the nucleophilic site; no δ-lactam was detected.

The tolerance of this unprecedented condensation toward substituents of the 3-alkenamide was examined using pent-3-enamides **11** and **16**. Addition of (*E*)-3-pentenoic acid **10**[11] to a solution of LDA in THF and HMPA, followed by addition of MeI afforded (*E*)-2,2-dimethyl-3-pentenoic acid.[11] Thionyl chloride converted the acid into (*E*)-2,2-dimethyl-3-pentenoyl chloride[12] which was reacted with aqueous ammonia to give the amide **11** (Scheme 1). Reaction of **11** (1 equiv) with benzaldehyde (2 equiv) in PPA at 35 °C for 48 h and subsequent chromatography afforded the indano[1,2-*b*]-pyrrol-2-(1*H*)-one **12** (32%) as the only product that was isolated. This reaction established that enolization of the amidic carbonyl group in PPA is either not necessary or, more likely, is not occurring prior to the ring-closure to give a γ-lactam. The reaction is presumed to proceed through an *N*-acyliminium species.

Scheme 2



[a] Reagents: (i) CuCN, LiBr; (ii) NaOH, H_2O_2, $(n\text{-Bu})_4NHSO_4$; (iii) H_2, Lindlar's catalyst, quinoline; (iv) CuCN, KI; (v) PhCHO, PPE.

The preparation of (*Z*)-3-pentenamide **16** was necessary for the comparison of its reactivity in acidic media with (*E*)-3-pentenamide **6**. 1-Bromo-2-butyne (**13**) was prepared by reacting but-2-yn-1-ol with PBr_3 using a modification of the method of Brandsma.[13] The reaction was carried out at high dilution in order to avoid the otherwise considerable amounts of HBr adducts; low temperatures were used to avoid rearrangement.[13] The alkynic nitrile **14** was also prepared by a modified method of Brandsma[13] which involved heating the bromide **13** with the copper(I) cyanide and lithium bromide. A catalytic quantity of the copper salt was effective, since it formed a soluble complex with the lithium halide. Hydrolysis of the nitrile **14** using the method of Cacchi[14] afforded 3-pentynamide **15**; under those conditions the alkynic moiety did not react. Hydrogenation of **15** in the presence of Lindlar's catalyst afforded a mixture of (*Z*)-3-pentenamide (**16**) and pentanamide in a ratio of 10:1. On poisoning the catalyst with quinoline the desired (*Z*)-3-pentenamide (**16**) was obtained exclusively in 95% yield. Reaction of (*Z*)-3-pentenamide **16** (1 equiv) with benzaldehyde (2 equiv) in PPA or PPE at 40 °C did not lead to the isolation of any lactams. It is tentatively concluded that the *cis*-disposed methyl group is sufficient to create nonbonding interactions that prevent the attainment of a cationic species of sufficiently low energy and of the appropriate geometry for subsequent cyclization.

Despite the failure of amide **16** to react, it was considered that a *gem*-dimethyl terminus, as present in 4-methylpent-3-enamide (**19**) might suffice to induce cyclization, presumably *via* a tertiary carbocation formed as a result of cyclization at the C-3 terminus of the 3-alkenamide. Reaction of 4-bromo-2-methyl-2-butene (**17**) with CuCN and KI afforded 4-methyl-3-pentenenitrile **18** (68%)[15] which was treated with alkaline aqueous H_2O_2 and tetra-*n*-butylammonium hydrogen sulfate to give 4-methyl-3-pentenamide (**19**) (80%) (Scheme 2).[16] Reaction of amide **19** with benzaldehyde (2 equiv) in PPE at 35 °C for 24 h afforded the γ-lactams **20** (32%) and **21** (28%) which, though possessing closely similar retention times on silica gel, could be separated by column chromatography. The 12-Hz vicinal coupling of H-5 in **21** is consistent with a

(7) For related preparations see: Cacchi, S.; Misiti, D.; La Torre, F. *Synthesis* **1980**, 243.

(8) Eggleston, D. S.; Baures, P. W.; Grabowska, U.; Marson, C. M.; Walsgrove, T. *Acta Crystallogr.* **1992**, *C48*, 2177.

(9) (a) Snyder, H. R.; Elston, C. T. *J. Am. Chem. Soc.* **1954**, *76*, 3039 (b) Rowlands, D. A. In *Synthetic Methods*; Pizey, J. S., Ed.; Wiley: New York, **1985**, Vol. 6, p 367.

(10) The synthesis of a pyridin-2-one, which lacks ring-fusion, by an intramolecular α-amidoalkylation involving an amide or nitrile has not been previously reported. For reviews on α-amidoalkylation see: (a) Zaugg, H. E.; *Synthesis* **1984**, 181. (b) Zaugg, H. E. *Synthesis* **1970**, 49.

(11) Van der Veen, R. H.; Cerfontain, H. *J. Org. Chem.* **1985**, *50*, 342.

(12) Schiess, P.; Radimerski, P. *Helv. Chim. Acta* **1974**, *57*, 2583.

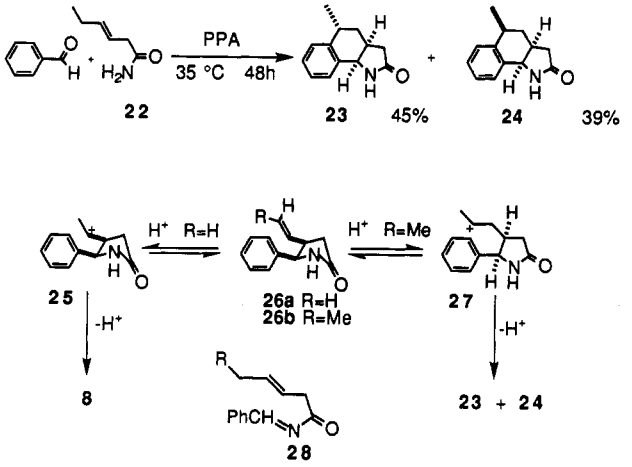
(13) Brandsma, L.; Verkruijsse, H. D. *Synthesis of Acetylenes, Allenes, and Cumulenes*; Elseveier, Amsterdam, **1981**, Vol. 8, p 225.

(14) Cacchi, S.; Misiti, D.; La Torre, F. *Synthesis*, **1980**, 243.

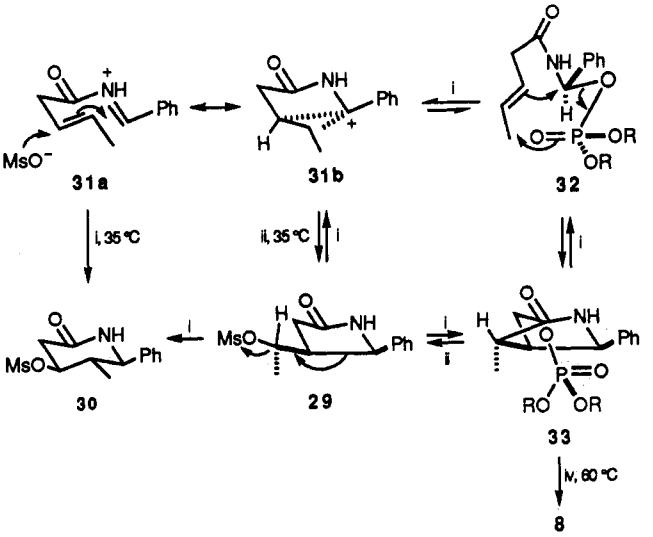
(15) Katagiri, T.; Agata, A.; Takabe, K.; Tanaka, J. *Bull. Chem. Soc. Jpn.* **1976**, *49*, 3715.

(16) Letch, R. A.; Linstead, R. P. *J. Chem. Soc.* **1932**, 443.

Scheme 3



Scheme 4



[a] Reagents: (i) PPA; (ii) P_2O_5–$MeSO_3H$, 35 °C.

trans-disubstitution of the γ-lactam ring. The formation of both lactams **20** and **21** is consistent with a cationic cyclization[17] involving the C-3 terminus and leading to a tertiary carbocation which is subsequently deprotonated.

The constitution of **8** and **9**, and the conversion of **29** into **8** (Scheme 4) under acidic conditions (*vide infra*) strongly suggest that the latter part of the overall process involves an intramolecular Friedel–Crafts alkylation.[18] Accordingly, reaction of (*E*)-3-hexenamide with benzaldehyde was examined in an attempt to obtain products unlike **8**, but whose formation is consistent with carbocationic mechanisms. Reaction of (*E*)-3-hexenamide (1 equiv) with benzaldehyde (2 equiv) in PPA at 35 °C for 72 h afforded a mixture of isomeric lactams (Scheme 3), one of which, **23**, was isolated in 45% yield by recrystallizing from benzene the crude reaction mixture obtained from the usual workup.[19] The relative configuration of the methyl group was established by single-crystal X-ray analysis.[8] The other lactam, assigned as the epimer **24** on the basis of ^1H and ^{13}C NMR data, was obtained in 39% yield. The high overall yield of two lactams differing only by *epimeric methyl* groups can be rationalized by the unified pathway of Scheme 3; product formation would be controlled by the relative stability of secondary over primary carbocations (for **8**) and by the greater thermodynamic stability of lactams **23** and **24** containing central six-membered (as opposed to five-membered) rings. However, the formation of cation **27** *via* a hydride shift cannot be excluded.

The reactions were probed by using $MeSO_3H$–P_2O_5 (10:1), a medium which has been used as an alternative to PPA.[20] The pyrrolidinone **29** (Scheme 4)[19,21] was isolated in 63% when (*E*)-3-pentenamide (1 equiv) and benzaldehyde (2 equiv) were heated in that medium at 35 °C for 18 h, none of **8** being detected. Pyrrolidinone **29** underwent clean conversion into the isomeric piperidinone **30**,[19] in PPA at 35 °C in 96% yield (Scheme 4). That the phenyl, methyl, and mesylate groups all occupy the equatorial positions is confirmed by the transdiaxial coupling constants, $J_{4,5}$ and $J_{5,6}$, found to be 9 and 10 Hz, respectively. Perhaps surprisingly, no monocyclic pyrrolidinone was isolated when (*E*)-3-hexenamide and benzaldehyde were condensed in $MeSO_3H$–P_2O_5; **23** and **24** (7:6) were formed in 60% yield. The mesylate **29** was converted into the lactam **8** in 80% yield by heating in PPA at 60 °C for 25 h. In a separate experiment, after 18 h at 60 °C, only a small quantity of unreacted **29** and the lactam **8** could be identified. Moreover, since piperidinone **30** was not converted into **8** by PPA at 60 °C for 72 h, but was recovered quantitatively, piperidinone **30** is unlikely to be an intermediate in the formation of **8** from **29**. Additionally, the tricyclic lactam **8** was recovered (>90%) after treatment with methanesulfonic acid–phosphorus pentoxide (10:1) at 60 °C for 16 h.

Reaction Pathways. The present evidence strongly suggests there are species common to the pathways which lead to the pyrrolidinones[21] *and* to the tricyclic lactams. Formation of the lactams **8**, **9**, **23**, and **24** could proceed *via* the *cis*-4,5-disubstituted pyrrolidinones **26** which are topologically related to the acylimines **28** (Scheme 3) by the *formalism* of an imino ene process.[23,24] The lack of formation of a monocyclic pyrrolidinone from (*E*)-3-hexenamide may indicate the importance of **26b** and its protonation to give **27** whose ring closure is more rapid in comparison with the five-membered ring closure of **25**.

The origins of the high diastereoselectivities leading to **29** and **30** can be tentatively interpreted in terms of a

(17) For a related but less-efficient 5-*endo-trig* process involving 4-methylpent-3- enamine see: (a) Cope, A. C.; Burrows, W. D. *J. Org. Chem.* **1965**, *30*, 2163. (b) Cope, A. C.; Burrows, W. D. *J. Org. Chem.* **1966**, *31*, 3099.

(18) Barclay, L. R. C. In *Friedel-Crafts and Related Reactions*; Olah, G. A., Ed.; Wiley: New York, **1964**, Vol. 2, p 785.

(19) The constitution and relative configuration of lactams **8**, **23**, **29**, and **30** were established by single-crystal X-ray analysis (see ref 8). All the depicted configurations refer to racemic materials.

(20) Eaton, P. E.; Carlson, G. R.; Lee, J. T. *J. Org. Chem.* **1973**, *38*, 4071.

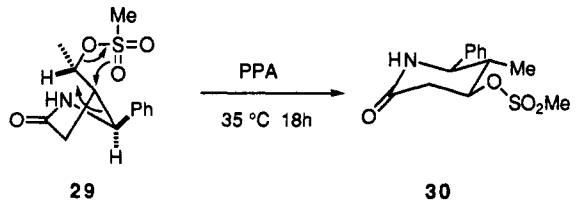
(21) For other acid-catalyzed cyclizations to give pyrrolidinones, see (a) Ben-Ishai, D. *J. Chem. Soc., Chem. Commun.* **1980**, 687, in which the alkylamide of a bis(alkoxycarbonyl)aminoacetic acid was converted by methanesulfonic acid into a putative cationic intermediate which was trapped by mesylate to give the pyrrolidinone, and (b) Tamura, Y.; Maeda, H.; Akai, S.; Ishiyama, K.; Ishibashi, H. *Tetrahedron Lett.* **1981**, *22*, 4301.

(22) The ring expansion of **29** into **30** is unprecedented. For a ring expansion of a 2- substituted pyrrolidine into a 3-substituted piperidine see: Biel, J. H.; Aboad, L. G.; Hoya, W. K.; Leiser, H. A.; Nuhfer, P. A.; Kluchesky, E. F. *J. Org. Chem.* **1961**, *26*, 4046, and Brain, E. G.; Doyle, F. P.; Mehta, M. D. *J. Chem. Soc.* **1961**, 633.

(23) Imino ene reactions have been effected at around 0 °C by using Lewis acids or *N*-tosylimines: (a) Tschaen, D. M.; Tsuros, E.; Weinreb, S. M. *J. Org. Chem.* **1984**, *49*, 5058, (b) Achmatowicz, O.; Pietraszkiewicz, M. *J. Chem. Soc., Perkin Trans. 1* **1981**, 2680, and (c) Melnick, M.; Freyer, A. J.; Weinreb, S. M. *Tetrahedron Lett.* **1988**, *29*, 3891.

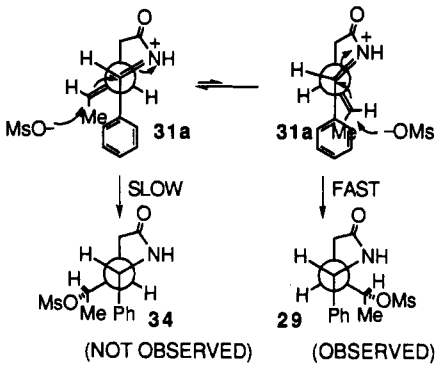
(24) Several processes considered to be imino ene reactions involve high temperatures, *e.g.* (a) Koch, K.; Lin, J.-M.; Fowler, F. W. *Tetrahedron Lett.* **1983**, *24*, 1581. (b) Tschaen, D. M.; Turos, E.; Weinreb, S. M. *J. Org. Chem.*, **1984**, *49*, 5058. (c) Lin, J.-M.; Koch, K.; Fowler, F. W. *J. Org. Chem.* **1986**, *51*, 167. (d) Braxmeier, H.; Kresze, G. *Synthesis* **1985**, 683.

Scheme 5



29 30

Scheme 6



cationic alkene cyclization involving a two-electron three-center bonded π-complex[25] for which only the product arising by *trans*-addition across the 3,4-double bond of the 3-alkenamide would be expected owing to the inhibition of rotation about the C=C double bond.[25] Pyrrolidinone **29** would then be converted by PPA into **30**, presumably *via* the cationic π-complex **31** formed by ring opening (Scheme 4). However, a concerted migration of the C-4,C-5 σ-bond and the mesylate group in a dyotropic rearrangement[26] would also be predicted to give **30** (Scheme 5).

The cyclization of **29** to give **8** [at a higher temperature (60 °C) than the isomerization of **29** into **30**] may be consistent with the need for the formation of a secondary carbocation. The relative configuration of the methyl group in **8** would be expected whether a free carbocation was formed (developing nonbonding interactions in the transition state favor a convex orientation of the methyl group) or whether **29** cyclized to **8** simply by inversion of configuration at the carbon atom bearing the departing mesylate group. An additional possibility that cannot currently be excluded is the involvement of intermediates such as **32** and **33** which could be interconvertible by disrotatory electrocyclic processes. The relative configuration of the three stereogenic centers of **33** could then be rationalized by assuming (i) that the phenyl group in **32** occupies the position which minimizes the development of nonbonding interactions (involving the axial hydrogen atom NC*H*Ph), and (ii) that there is a subsequent inversion of configuration (a mesylate intermediate, analogous to **32**, could also be involved).

The simplest explanation for the formation of **29**, however, involves the direct attack of mesylate anion on the nonclassical cation **31b**;[27] this would be predicted to lead to **29** (Scheme 6) on the assumption that the π-bonds of the alkene and iminium moieties participate only in an anticlinal arrangement, a requirement that has been invoked in order to rationalize the formation of spirocycles *via* *N*-acyliminium species.[28] A synchronous transcoplanar attack of cation **31a** (anticlinal conformation; Scheme 6) would lead to **29**, the only stereoisomer detected. An alternative formation of **29** involving initial attack of C-3 of the alkenamide on the carbonyl group of benzaldehyde in a Prins-type process can be excluded because *trans*-4,5-disubstitution of the resulting pyrrolidinone ring (*i.e.* **34**) would be predicted; additionally, the observed stereocontrolled attack of mesylate anion at C-4 would not be expected.

The reaction pathways can be markedly subject to changes in the nature of the phosphate medium, and to small changes in temperature (which may be important in changing the constitution of the phosphate medium). Consequently, the involvement of imino ene reactions[23,24] of *N*-acylimines such as **28** appears unlikely in view of the usual requirement for imino ene reactions of either a Lewis acid catalyst[23] or relatively high temperatures.[24] However, the present investigation does not definitely exclude either imino ene processes or cationic cyclizations[29] other than those detailed herein.

The condensation of 3-alkenamides with benzaldehyde in acidic media affords one-pot stereocontrolled routes to substituted lactams. Activating or stabilizing groups are not required, and condensations proceed under mild conditions and can be effected in multigram quantities.

Experimental Section

Materials and Methods. All melting points are uncorrected. NMR spectra were run in $CDCl_3$ unless otherwise stated; chemical shifts are quoted in ppm downfield from internal tetramethylsilane, and the line separations (J) are expressed in hertz. ^1H and ^{13}C NMR spectra were recorded at 220 and 68.8 MHz, respectively. Mass spectra were obtained operating in chemical ionization (CI) or electron impact (EI) mode, as specified. Infrared spectra were obtained as a thin film or KBr disc. TLC was performed on aluminum-backed silica plates and visualized using ultraviolet light or developed using ceric sulfate spray or iodine. Column chromatography was performed using Merck silica gel 60 (230–400 mesh) as the stationary phase under gravity. Petroleum ether (40–60 °C fraction) and ethyl acetate were distilled prior to use. PPA was purchased from BDH Chemicals Ltd., Poole, England. Evaporation refers to the removal of solvent under reduced pressure, unless otherwise stated.

The folowing were prepared according to literature procedures: (*E*)-3-pentenoic acid;[11] (*E*)-pent-3-enoyl chloride;[30] (*E*)-hex-3-enoyl chloride;[31] 4-methylpent-3-enenitrile;[15] (*E*)-2,2-dimethylpent-3-enoic acid.[32]

(*E*)-3-Pentenamide (6). To a solution of (*E*)-3-pentenenitrile (10.0 g, 0.12 mol) in dichloromethane (45 mL) cooled in an ice–salt bath were added hydrogen peroxide (27.5%, 58 mL), tetra-*n*-butylammonium hydrogen sulfate (8.3 g, 0.02 mol), and an aqueous solution of sodium hydroxide (46 mL, 20%). The

(25) Dewar, M. J. S.; Reynolds, C. H. *J. Am. Chem. Soc.* **1984**, *106*, 1744.
(26) (a) Reetz, M. T. *Adv. Organomet. Chem.* **1977**, *16*, 33. (b) Reetz, M. T. *Angew. Chem. Int. Ed. Engl.* **1972**, *11*, 129.
(27) Dijkink, J.; Schoemaker, H. E.; Speckamp, W. N. *Tetrahedron Lett.* **1975**, *46*, 4043.
(28) (a) Schoemaker, H. E.; Kruk, C.; Speckamp, W. N. *Tetrahedron Lett.* **1979**, *26*, 2437. (b) Deslongchamps, P. *Stereoelectronic Effects in Organic Chemistry*; Pergamon Press: New York, 1983; p 1.
(29) (a) For 5-*exo*-*trig* cyclizations proceeding with stereocontrol at three contiguous stereogenic centers, and believed to proceed by a synchronous transcoplanar attack of an acyliminium ion and formic acid on a double bond, see: ref 26a. (b) For Lewis acid-induced π-cyclizations affording substituted 3-vinylprolines see: Mooiweer, H. H.; Hiemstra, H.; Fortgens, H. P.; Speckamp, W. N. *Tetrahedron Lett.* **1987**, *28*, 3285. (c) For an extraordinary tetracyclization involving stereoselective π-cyclization onto an iminium ion in the synthesis of methyl homosecodaphniphyllate, see: Ruggeri, R. B.; Hansen, M. M.; Heathcock, C. H. *J. Am. Chem. Soc.* **1988**, *110*, 8734. (d) For the formation of a five-membered heterocycle involving a stabilized benzylic cation see: Baldwin, J. E.; Cutting, J.; Dupont, W.; Kruse, L.; Silberman, L.; Thomas, R. C. *J. Chem. Soc., Chem. Commun.* **1976**, 736.
(30) Goldberg, A. A.; Linstead, R. P. *J. Chem. Soc.* **1928**, 2351.
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progress of the reaction was monitored by TLC; the disappearance of the nitrile usually occurred within 45 min. Dichloromethane (50 mL) was then added and the organic layer separated. The aqueous layer was extracted with dichloromethane (2 × 30 mL). The combined organic extracts were dried (Na_2SO_4), and evaporated *in vacuo* to give **6** (9.9 g, 81%) as plates, mp 69.5 °C (from ethyl acetate) (lit.[33] mp 70–71 °C) by chromatography on a short silica column, employing as eluant ethyl acetate:δ_H ($CDCl_3$) 1.73 (3H, dd, J = 6, and 1), 2.95 (2H, dd, J = 7, and 1,), 5.52 (1H, m), 5.66 (1H, m), 5.90 (1H, br s), and 6.50 (1H, br s); δ_C 174.5, 130.2, 123.6, 39.7, and 17.7; m/z (%) +EI 99 (43), 71 (41), 55 (77), and 44 (100) . Anal. Calcd for C_5H_9NO: C, 60.58; H, 9.15; N, 14.13. Found: C, 60.82; H, 9.26; N, 13.89.

(*E*)-*N*-Benzyl-3-pentenamide (7). (*E*)-3-Pentenoyl chloride (3.2 g, 24 mmol) was added dropwise to a solution of benzylamine (2.59 g, 24 mmol) in aqueous NaOH (1.9 g, 48 mmol), with efficient stirring. Vigorous shaking resulted in a white precipitate, which was extracted with dichloromethane (40 mL). The extract was washed consecutively with aqueous NaOH (20 mL, 1 M), aqueous HCl (20 mL, 1 M), and water until neutral, dried ($MgSO_4$), and evaporated *in vacuo*. Recrystallization afforded **7** (3.44 g, 70%) as prisms: mp 66 °C (from ethyl acetate); δ_H ($CDCl_3$) 1.70 (3H, dd, J = 7 and 1), 2.99 (2H, dd, J = 6 and 1), 4.43 (2H, d, J = 5), 5.60 (2H, m), 5.95 (1H, br s), and 7.30 (5H, m); δ_C 171.2, 138.3, 130.8, 128.6, 127.6, 127.3, 123.6, 43.45, 40.4, and 17.9; m/z (%) +EI 189 (10), 131 (9), 104 (11), and 91 (100). Anal. Calcd for $C_{12}H_{15}NO$: C, 76.15; H, 7.99; N, 7.40%. Found: C, 76.04; H, 7.88; N, 7.40.

(3aα,4α,8bα)-(±)-3,3a,4,8b-Tetrahydro-4-methylindeno-[1,2-*b*]pyrrol-2-(1*H*)-one (8). (a) From (*E*)-3-pentenamide (6). Polyphosphoric acid (10 g) was weighed into a two-necked flask, and to it were added successively (*E*)-3-pentenamide (**6**) (0.50 g, 5.05 mmol) and benzaldehyde (1.07 g, 10 mmol). The reaction was maintained at 35 °C for 48 h under a nitrogen atmosphere. After this time the reaction mixture was cooled, added to water (30 mL), neutralized with solid sodium carbonate, and extracted with chloroform (3 × 20 mL). The combined organic extracts were dried (Na_2SO_4) and evaporated *in vacuo*, and the residue was chromatographed on silica gel employing as eluant 3:1 ethyl acetate:petroleum ether, to give **8** (0.70 g, 74%) as needles: mp 175–176 °C (from ethyl acetate); ν_{max} 3220 (NH) and 1680 cm^{-1} (γ-lactam); δ_H ($CDCl_3$) 1.33 (3H, d, J = 7), 2.27 (1H, dd, J = 7 and 3), 2.71 (1H, dd, J = 17 and 6.5), 2.78 (1H, m, J = 6.5, 6, and 3), 3.07 (1H, m, J = 6), 4.99 (1H, d, J = 6.5), and 7.27 (6H, m); δ_C 177.6, 147.8, 140.9, 128.8, 127.3, 124.8, 124.1, 62.3, 47.0, 45.6, 36.7, and 20.0; m/z (%) +EI 187 (70), 143 (100), and 129 (72). Anal. Calcd for $C_{12}H_{13}NO$: C, 77.0; H, 7.0; N, 7.5. Found: C, 76.7; H, 7.0; N, 7.35.

(b) From (*E*)-3-Pentenenitrile. Polyphosphoric acid (10 g) was weighed into a two-necked flask, and to it were added successively (*E*)-3-pentenenitrile (0.50 g, 6.2 mmol) and benzaldehyde (1.31 g, 12 mmol). The reaction was maintained at 35 °C for 48 h under a nitrogen atmosphere. After this time the reaction mixture was cooled, added to water (30 mL), neutralized with solid sodium carbonate, and extracted with chloroform (3 × 20 mL). The combined organic extracts were dried (Na_2SO_4) and evaporated *in vacuo*, and the residue was chromatographed on silica gel employing as eluant 3:1 ethyl acetate:petroleum ether, to give **8** (0.77 g, 67%) as needles, mp 175–176 °C (from ethyl acetate). Spectral data as in a above.

(3aα,4α,8bα)-(±)-1-Benzyl-3,3a,4,8b-tetrahydro-4-methyl-indeno[1,2-*b*]pyrrol-2-(1*H*)-one (9). Polyphosphate ester (10 g) was weighed into a two-necked flask, and to it were added successively (*E*)-*N*-benzyl-3-pentenamide (**7**) (0.50 g, 2.65 mmol) and benzaldehyde (0.56 g, 5.29 mmol). The reaction was maintained at 30–40 °C for 24 h under a nitrogen atmosphere. After this time the reaction mixture was cooled and, with caution, was rendered basic employing an aqueous solution of sodium hydroxide. After stirring for another 2 h, the reaction was extracted with chloroform (3 × 20 mL). The combined organic extracts were dried (Na_2SO_4) and evaporated *in vacuo*, and the residue was chromatographed on silica gel employing as eluant 3:2 ethyl acetate:petroleum ether, to give **9** (0.38 g, 52%) as needles: mp 108–109 °C (from ethyl acetate:petroleum ether 60–80 °C); δ_H ($CDCl_3$) 1.36 (3H, d, J = 7), 2.51 (1H, dt, J = 17, 1.5), 2.65 (1H, ddt, J = 7, 5, and 1.5), 2.81 (1H, dd, J = 17 and 7), 3.08 (1H, quintet, J = 7), 3.85 (1H, d, J = 10.5), 4.73 (1H, d, J = 5), 5.11 (1H, d, J = 10.5), 7.30 (9H, m); δ_C 173.8, 148.8, 138.9, 136.4, 128.9, 128.6, 127.8, 127.3, 126.6, 125.6, 123.95, 64.9, 45.5, 45.15, 43.7, 36.35, and 18.7; m/z (%) +EI 277 (30), 146 (43), 130 (46), and 91 (100). Anal. Calcd for $C_{19}H_{19}NO$: C, 82.28; H, 6.90; N, 5.05. Found: C, 82.34; H, 6.81; N, 4.96.

(*E*)-2,2-Dimethyl-3-pentenamide (11). To a solution of ammonium hydroxide solution (5 mL, 14 M, 0.06 mol) in diethyl ether (100 mL) cooled in an ice-bath was added (*E*)-2,2-dimethyl-3-pentenoyl chloride (4.0 g) dropwise. After the reaction had been left to stir overnight, the diethyl ether was separated from the solid by gravity filtration. The solid was washed with further portions of diethyl ether (3 × 20 mL), and the combined organic extracts were dried (Na_2SO_4), the solvent was removed *in vacuo*, and the residue was chromatographed on silica gel employing as eluant ethyl acetate:petroleum ether (1:1), to give **11** (0.5 g, 17%) as plates: mp 155 °C (from ethyl acetate); R_f = 0.35 (I_2/UV-active). δ_H ($CDCl_3$) 1.24 (6H, s), 1.71 (3H, d, J = 3), 5.61 (2H, m), and 5.90 (2H, br d); δ_C 180.0, 136.3, 124.6, 44.2, 25.2, and 17.9; m/z (%) +CI 128 (53) and 94 (58). Anal. Calcd for $C_7H_{13}NO$: C, 66.10; H, 10.30; N, 11.01. Found: C, 65.9; H, 10.09; N, 11.16.

(3aα,4α,8bα)-(+)-3,3,4-Trimethyl-3,3a,4,8b-tetrahydro-4-methylindeno[1,2-*b*]pyrrol-2-(1*H*)-one (12). Polyphosphoric acid (10 g) was weighed into a two-necked flask, and to it were added successively (*E*)-2,2-dimethyl-3-pentenamide (**11**) (0.20 g, 1.6 mmol) and benzaldehyde (0.33 g, 3.1 mmol). The reaction was maintained at 30–40 °C for 48 h under a nitrogen atmosphere. After this time the reaction mixture was cooled, neutralized with solid sodium carbonate, and extracted with chloroform (3 × 10 mL). The combined organic extracts were dried (Na_2SO_4) and evaporated *in vacuo*, and the residue was chromatographed on silica gel employing as eluant 3:1 ethyl acetate:petroleum ether, to give **12** as needles (0.11 g, 32%): mp 181–183 °C (from ethyl acetate); HRMS, EI calcd for $C_{14}H_{17}NO$ 215.1310, found 215.1299; δ_H ($CDCl_3$) 1.26 (3H, s), 1.32 (3H, s), 1.37 (3H, d, J = 7), 2.44 (1H, dd, J = 8 and 6), 3.30 (1H, dq, J = 8 and 7), 4.91 (1H, d, J = 6), and 7.26 (4H, m); m/z (%) +EI 215 (30).

1-Bromo-2-butyne (13). To a mixture of 2-butyn-1-ol (5 g, 0.07 mol), diethyl ether (20 mL), and pyridine (0.4 mL) was added with cooling to −40 °C phosphorus tribromide (2.37 mL, 0.025 mol) over a period of 45 min. The temperature was maintained for 2 h at −40 °C during which time a slow nitrogen flow was introduced. Subsequently the temperature was allowed to rise to 20 °C over 3 h. A heavy lower layer was formed. The reaction was then heated to and kept at 40 °C for 30 min. The reaction mixture was poured onto a saturated solution of NaCl (40 mL). After shaking, the upper layer was separated. The aqueous layer was extracted with diethyl ether (10 mL). The combined organic extracts were dried ($MgSO_4$), the ether was removed at atmospheric pressure, and the residue was distilled at reduced pressure to give **13** (7.6 g, 80%) as a colorless oil: bp 60–65 °C/80 mmHg (lit.[13] bp 60 °C/80 mmHg); δ_H (80 MHz; $CDCl_3$) 3.90 (2H, q, J = 3) and 1.86 (3H, t, J = 3 Hz).

3-Pentynenitrile (14). To a solution of anhydrous lithium bromide (1.28 g, 0.015 mol) in dry tetrahydrofuran (15 mL) were added successively copper cyanide (5.92 g, 0.066 mol) and 1-bromo-2-butyne **13** (7.5 g, 0.056 mol). The mixture was warmed to 40 °C. The suspension dissolved and a brown solution was formed. After heating at 75 °C for an additional 30 min, the mixture was poured into a vigorously stirred solution of sodium cyanide (7.1 g, 0.145 mol) and ammonium chloride (7.1 g, 0.133 mol) in water (42 mL). The temperature was kept below 20 °C by efficient cooling in an ice–salt bath. The product was isolated by extraction with diethyl ether (5 × 20 mL). The combined organic extracts were dried ($MgSO_4$), and the ether removed by distillation at atmospheric pressure. The residue was distilled at reduced pressure to give **14** (3.1 g, 70%) as a colorless oil, bp 60 °C/20 mmHg (lit.[13] bp 47 °C/15 mmHg), which was used immediately in the next step of the synthesis: δ_H ($CDCl_3$) 3.22 (2H, q, J = 2) and 1.75 (3H, t, J = 2).

3-Pentynamide (15). To a solution of 3-pentynenitrile **14** (3.0 g, 0.04 mol) in dichloromethane (25 mL) were added successively hydrogen peroxide (27.5%, 18.8 mL, 0.58 mol), tetra-

(33) Chiusoli, G. P. *Chim. Ind. (Milan)* **1959**, *41*, 503.

n-butylammonium hydrogen sulfate (2.55 g, 0.008 mol), and an aqueous solution of sodium hydroxide (14.2 mL, 20%). The progress of the reaction was monitored by TLC; the disappearance of the nitrile occurred in about 60 min. Dichloromethane (20 mL) was then added and the organic layer was separated. The aqueous layer was extracted with dichloromethane (2 × 20 mL). The combined organic extracts were dried (Na_2SO_4), and concentrated *in vacuo*. Purification of the residue by column chromatography on silica gel, employing as eluant ethyl acetate:petroleum ether (3:2), gave **15** (1.6 g, 43%), as needles: mp 117.5–119 °C (from ethyl acetate), R_f (ethyl acetate:petroleum ether (3:2)) 0.3; δ_H (220 MHz; $CDCl_3$) 1.80 (3H, t, J = 2), 3.06 (2H, q, J = 2), and 6.50 (2H, br s). Anal. Calcd for C_5H_7NO: C, 61.83; H, 7.27; N, 14.42. Found: C, 61.58; H, 7.30; N, 14.39.

(*Z*)-3-Pentenamide (16). To a solution of 3-pentynamide (**15**) (1.6 g, 0.016 mol) in ethyl acetate (50 mL) was added Lindlar's catalyst (0.84 g) and quinoline (0.84 g, 0.007 mol). The reaction was then allowed to take up hydrogen. After the calculated amount of hydrogen was taken up, the hydrogenation did not proceed further. At this point the reaction was stopped, the catalyst filtered off, and the ethyl acetate removed *in vacuo*. The residue was chromatographed on silica, employing as eluant ethyl acetate, to give **16** (1.55 g, 95%) as colorless plates: mp 64–65 °C (from ethyl acetate/petroleum ether; R_f (ethyl acetate) 0.25; δ_H ($CDCl_3$) 1.67 (3H, dd, J = 7 and 2), 3.04 (2H, dd, J = 7.5 and 2), 5.59 (1H, ddq, J = 11, 7, and 2), 5.78 (1H, ddt, J = 11, 7.5, and 2), 5.80 (1H, br s), and 6.25 (1H, br s); δ_C 173.85, 128.9, 122.7, 34.3, and 12.7. Anal. Calcd for C_5H_9NO: C, 60.58; H, 9.15; N, 14.13. Found: C, 60.49; H, 9.24; N, 14.13.

4-Methyl-3-pentenamide (19). To a solution of 4-methyl-3-pentenenitrile[15] (**18**) (0.55 g, 0.0058 mol) in dichloromethane (5 mL) cooled in an ice–salt bath were added hydrogen peroxide (27.5%, 3 mL), tetra-*n*-butylammonium hydrogen sulfate (0.39 g, 0.001 mol), and an aqueous solution of sodium hydroxide (2.2 mL, 20%). The progress of the reaction was monitored by TLC; the disappearance of the nitrile usually occurred in 50 min. Dichloromethane (20 mL) was then added and the organic layer separated. The aqueous layer was extracted with dichloromethane (2 × 20 mL). The combined organic extracts were dried (Na_2SO_4), evaporated *in vacuo* to give **19** (0.53 g, 80%) as plates, mp 63 °C (from ethyl acetate) (lit.[16] mp 81–82 °C), by chromatography on a short silica column, employing as eluant ethyl acetate; δ_H ($CDCl_3$) 1.67 (3H, J = 1), 1.79 (3H, q, J = 1), 2.96 (1H, d septet, J = 8 and 1), 5.32 (1H, t septet, J = 8 and 1), and 5.90 (2H, br d); δ_C 174.5, 137.1 , 116.8, 35.5, 25.6, and 17.7; m/z (%) +EI 113 (100), 95 (40), 69 (71), and 55 (42). Anal. Calcd for $C_6H_{11}NO$: C, 63.68; H, 9.80; N, 12.38. Found: C, 63.83; H, 9.68; N, 12.31.

5-Phenyl-4-(2-isopropylidene)-2-pyrrolidinone (20) and -4-(2-propenyl)-5-phenyl-2-pyrrolidinone (21). Polyphosphate ester (10 g) was weighed into a two-necked flask, and to it were added successively 4-methyl-3-pentenamide (**19**) (0.60 g, 5.31 mmol) and benzaldehyde (1.20 g, 11.3 mmol). The reaction was maintained at 30–40 °C for 24 h under a nitrogen atmosphere. After this time the reaction mixture was cooled and, with caution, was rendered basic employing an aqueous solution of sodium hydroxide. After stirring for another 3 h, the reaction was extracted with chloroform (3 × 20 mL). The combined organic extracts were dried (Na_2SO_4) and evaporated *in vacuo*, and the residue was chromatographed on silica gel employing as eluant 1:1 ethyl acetate:petroleum ether, to yield **20** (0.34 g, 32%) as needles, R_f = 0.29 (ethyl acetate), mp 127–128 °C (from ethyl acetate); MS, HR, EI; M^+ calcd for $C_{13}H_{15}NO$ 201.1154, found 201.1142; δ_H ($CDCl_3$) 1.45 (3H, s), 1.68 (3H, s), 3.15 (2H, dd), 5.20 (1H, br s), 6.25 (1H, br s), and 7.30 (5H, m); δ_C 175.5, 142.1, 128.9, 128.4, 127.9, 127.35, 127.15, 61.8, 35.3, 21.6, and 19.9; m/z (%) +EI 201 (37), 186 (100), 143 (27), and 124 (40); and **21** (0.30 g, 28%) as needles: R_f = 0.28 (ethyl acetate), mp 125 °C (from ethyl acetate); δ_H ($CDCl_3$) 1.24 (3H, s), 2.30 (1H, dd, J = 17 and 10), 2.53 (1H, dd, J = 17 and 12), 3.35 (1H, q, J = 10), 4.67 (2H, d), 4.83 (1H, d, J = 7), and 7.30 (5H, m).

(*E*)-3-Hexenamide (22). To a solution of ammonium hydroxide (8.8 mL, 14 M) in diethyl ether (100 mL), cooled in an ice bath, was added dropwise (*E*)-3-hexenoyl chloride (8.1 g, 0.06 mol). After the reaction had been stirred for 3 h, the diethyl ether was separated from the solid by gravity filtration. The solid residue was washed with further portions of diethyl ether (3 × 20 mL), and the combined organic extracts were dried (Na_2SO_4). The solvent was removed *in vacuo* and recrystallization of the residue afforded **22** (4.35 g, 63%) as needles: mp 87.5–88.5 °C (from water) (lit.[16] mp 86 °C); δ_H 1.01 (3H, t, J = 7.5), 2.09 (2H, m), 2.96 (2H, dm, J = 7), 5.62 (2H, m), and 6.01 (2H, br s); δ_C 174.5, 137.4, 121.5, 39.75, 25.3, and 13.25; m/z (%) +EI 113 (51), 98 (60), 70 (73), and 55 (100). Anal. Calcd for $C_6H_{11}NO$: C, 63.69; H, 9.80; N, 12.38. Found: C, 63.89; H, 9.94; N, 12.39.

(3aα,5α,9bα)-(±)-1,3,3a,4,5,9b-Hexahydro-5-methyl-2*H*-benz[*g*]indol-2-one (23) and (3aα,5β,9bα)-(±)-1,3,3a,4,5,9b-Hexahydro-5-methyl-2*H*-benz[*g*]indol-2-one (24). (a) Condensation in Polyphosphoric Acid. Polyphosphoric acid (10 g) was weighed into a two-necked flask, and to it were added successively (*E*)-3-hexenamide **22** (0.50 g, 4.4 mmol) and benzaldehyde (1.07 g, 10 mmol). The reaction was maintained at 30–40 °C for 72 h under a nitrogen atmosphere. After this time the reaction mixture was cooled, neutralized with solid sodium carbonate, and extracted with chloroform (3 × 20 mL). The combined organic extracts were dried (Na_2SO_4) and evaporated *in vacuo*, and the residue was chromatographed on silica gel employing as eluant 3:1 ethyl acetate:petroleum ether, to give **23** and **24**. The lactam **23** (0.40 g, 45%) was obtained by fractional recrystallization as needles: mp 174–176 °C (from benzene); ν_{max} 3220 (NH) and 1690 cm^{-1} (γ-lactam); δ_H ($CDCl_3$) 1.25 (3H, d, J = 7), 1.63 (1H, m) 1.82 (1H, m), 2.15 (1H, dd, J 17 and 3), 2.78 (3H, m), 4.76 (1H, d, J = 7), 7.20 (5H, m), and 7.53 (1H, br s); δ_C 177.1, 142.3, 133.4, 129.0, 128.1, 127.9, 126.6, 54.7, 38.0, 33.4, 31.3, 29.6, and 22.0; m/z (%) +EI 201 (23), 159 (76), and 142 (100). Anal. Calcd for $C_{13}H_{15}NO$: C, 77.6; H, 7.5; N, 7.0. Found: C, 77.4; H, 7.4; N, 6.8. Lactam **24** (0.35 g, 39%) obtained as needles (from ethyl acetate): δ_H ($CDCl_3$) 1.36 (3H, d, J = 7), 1.63 (1H, m) 1.82 (1H, m), 2.13 (1H, dd, J = 17 and 3), 2.80 (3H, m), 4.72 (1H, d, J = 7), 7.20 (5H, m), and 7.53 (1H, br s); δ_C 176.6, 141.9, 133.8, 128.4, 128.0, 126.5, 126.0, 55.0, 38.7, 35.6, 34.2, 31.8, and 19.7.

(b) Condensation in Methanesulfonic Acid–Phosphorus Pentoxide. Methanesulfonic acid–phosphorus pentoxide (1:10) (10 g) was weighed into a two-necked flask, and to it were added successively (*E*)-3-hexenamide **22** (0.5 g, 4.4 mmol) and benzaldehyde (1.07 g, 10 mmol). The reaction was maintained at 35 °C for 18 h under a nitrogen atmosphere. After this time the reaction mixture was cooled and added dropwise to water (40 mL), with efficient stirring, over 1 h. After addition was complete, stirring was continued for another 30 min. The reaction mixture was then rendered basic (Na_2CO_3) and extracted with chloroform (3 × 30 mL). The combined organic extracts were dried (Na_2SO_4) and evaporated *in vacuo*, and the residue was chromatographed on silica gel employing as eluant 3:1 ethyl acetate:petroleum ether, to give **23** (0.29 g, 33%) as needles: mp 174–176 °C (from benzene) and **24** (0.25 g, 28%) as needles (from ethyl acetate). See above for spectral data.

[4α(*R*),5α]-(±)-4-[1*R*-[(Methylsulfonyl)oxy]ethyl]-5-phenyl-2-pyrrolidinone (29). A mixture of methanesulfonic acid–phosphorus pentoxide (1:10) (5 g) was weighed into a two-necked flask, and to it were added successively (*E*)-3-pentenamide (**6**) (0.40 g, 0.004 mol) and benzaldehyde (0.86 g, 0.008 mol). The reaction was maintained at 35 °C for 18 h under a nitrogen atmosphere. After this time the reaction mixture was cooled and added dropwise to water (20 mL), with efficient stirring, over a period of 1 h. After addition was complete, stirring was continued for another 30 min. The reaction mixture was then rendered basic (Na_2CO_3), and extracted with chloroform (3 × 20 mL). The combined organic extracts were dried (Na_2SO_4) and evaporated *in vacuo*, and the residue was chromatographed on silica gel employing as eluant 2:1 ethyl acetate:petroleum ether, to give **29** (0.72 g, 63%) as needles: mp 159 °C (from ethyl acetate); ν_{max} 3220 (NH), 1700 (γ-lactam), 1350 (asymmetric RSO_3R), and 1170 cm^{-1} (symmetric RSO_3R); δ_H ($CDCl_3$) 1.33 (3H, d, J = 6), 2.50 (1H, dd, J = 17 and 9), 2.66 (1H, dd, J = 17 and 11), 2.82 (3H, s), 2.99 (1H, m), 4.33 (1H, dq, J = 8.5 and 6), 4.72 (1H, d, J = 8), 6.61 (1H, br s), and 7.3 (5H, m); δ_C 176.3, 137.6, 129.2, 128.9, 127.4, 78.5, 59.3, 45.9, 38.7, 32.6, and 20.3; m/z (%) +EI 283 (40), 187 (96), and 106 (177). Anal. Calcd for $C_{13}H_{17}NO_4S$: C, 55.1; H, 6.05; N, 4.9; S, 11.3. Found: C, 55.05; H, 5.9; N, 4.7; S, 11.1.

(4α,5β,6α)-(±)-5-Methyl-4-[(methylsulfonyl)oxy]-6-phenyl-2-piperidinone (30). PPA (5 g) was weighed into a two-necked flask, and to it was added pyrrolidinone **29** (0.20 g, 0.7 mmol). The reaction was maintained at 35 °C for 18 h under a nitrogen atmosphere. After this time the reaction mixture was cooled, added to water (20 mL), neutralized with solid sodium carbonate, and extracted with chloroform (3 × 20 mL). The combined organic extracts were dried (Na_2SO_4) and evaporated *in vacuo*, and the residue was recrystallized to give **30** (0.192 g, 96%) as needles: mp 162–163 °C (from ethyl acetate). ν_{max} 3220 (NH), 1680 (δ-lactam), 1350 (asymmetric RSO_3R), and 1175 cm^{-1} (symmetric RSO_3R); δ_H ($CDCl_3$) 0.98 (3H, d, J = 6), 2.10 (1H, m), 2.78 (1H, dd, J = 17 and 9), 3.11 (1H, dd, J = 17 and 5), 3.10 (3H, s), 4.10 (1H, d, J = 10), 4.80 (1 H, dt, J = 10 and 6), and 7.37 (5H, m); δ_C 169.4, 140.0, 128.8, 128.6, 127.2, 78.3, 60.7, 40.9, 38.4, 38.1, and 13.3; *m/z* (%) +EI 283 (5), 187 (96), and 106 (77). Anal. Calcd for $C_{13}H_{17}NO_4S$: C, 55.1; H, 6.05; N, 4.9; S, 11.3. Found C, 55.0; H, 5.9; N, 4.9; S, 11.25.

Reaction of Pyrrolidinone 29 with Polyphosphoric Acid at 60 °C. Polyphosphoric acid (3 g) was weighed into a two-necked flask, and to it was added pyrrolidinone **29** (0.10 g, 0.35 mmol). The reaction was maintained at 60 °C for 25 h under a nitrogen atmosphere. After this time the reaction mixture was cooled, added to water (10 mL), neutralized with solid sodium carbonate, and extracted with chloroform (3 × 10 mL). The combined organic extracts were dried (Na_2SO_4), evaporated *in vacuo*, and recrystallized to give **8** (0.053 g, 80%) as needles, mp 175–176 °C (from ethyl acetate). See above for spectral data.

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