($CDCl_3$) δ 19.3, 25.1, 125.8, 126.7, 127.7, 129.7, 130.4, 130.6, 130.8, 131.2, 132.5, 132.7, 133.2, 137.4, 143.4, 157.9, 183.8; IR (CCl_4) 1669.5 (C=O) cm^{-1}; MS (70 eV), *m/e* (relative abundance) 138 (100), 193 (100), 199 (100); molecular ion calcd for $C_{17}H_{14}N_2O$ *m/e* 262.1106, found 262.1105.

Isopropyl ether: ^1H NMR ($CDCl_3$) δ 1.07 (d, *J* = 6.0 Hz, 6 H, methyl), 3.76 (m, *J* = 6.0 Hz, 1 H, methine), 5.74 (s, 1 H, CHOR).

(b) In *tert*-Butyl Alcohol. DAAN (55 mg, 0.25 mmol) was dissolved in 50 mL of *tert*-butyl alcohol; two 25-mL aliquots were treated as described above. Photolysis to 83% completion afforded bianthronyl (39%), anthrone (<1%), unsymmetrical azine (7%), and the expected *tert*-butyl ether (33%) as determined by ^1H NMR spectroscopy.

tert-Butyl ether: ^1H NMR ($CDCl_3$) δ 1.46 (s, 9 H, methyl), 5.73 (s, 1 H, CHOR).

Photolysis of DAAN in Hydrocarbons. (a) In Cyclohexane. DAAN (16 mg, 0.075 mmol) was dissolved in 25 mL of cyclohexane. Photolysis to 98% completion afforded bianthronyl (61%), anthrone (1%), and 10-cyclohexylanthrone (12%) as determined by ^1H NMR spectroscopy.

10-Cyclohexanthrone: ^1H NMR ($CDCl_3$) δ 0.6-2.0 (m, 11 H, cyclohexyl), 4.10 (d, *J* = 4 Hz, 1 H, anthronyl), 7.48 (m, 6 H, Ar), 8.22 (dd, 2 H, Ar); [lit.[9] δ ($CDCl_3$) 4.05 (d)]; MS (10 eV), *m/e* (relative abundance) 276 (2.51), 195 (15.11), 194 (100); molecular ion calcd for $C_{20}H_{20}O$ *m/e* 276.1514, found 276.1511.

Irradiation of DAAN in a 6.5:1 Mixture of Cyclohexane-d_{12} and Cyclohexane. A stock solution of DAAN (8.9×10^{-3} M) in benzene was prepared. A mixture containing 1.0 mL of the stock solution, 1.3 mL of C_6D_{12}, and 0.20 mL of C_6H_{12} was placed in a 1.0-cm quartz fluorescence cell, equipped with a stir bar; the mixture was purged with dry nitrogen for 7 min. A second solution, 1.0 mL of stock and 1.5 mL of C_6H_{12}, was similarly prepared. The two solutions were irradiated (Rayonet) for 45 min and then concentrated. Appropriate analysis by mass spectrometry (CI) of the 10-cyclohexylanthrone and the deuteriated sample revealed that crossover product (30%) was formed.

(b) In Benzene. DAAN (29 mg, 0.13 mmol) was dissolved in 25 mL of benzene and two 10-mL aliquots were treated as previously described. Photolysis to 98% completion afforded bianthronyl (42, 45%) and anthrone (5, 6%), determined via ^1H NMR, and biphenyl (27, 25%), determined by GLPC using dodecane as an internal standard (6 ft × 0.125 in. glass column containing 10% OV-101 on Chrom W-H.P., 100/120 mesh).

Irradiation of DAAN in Benzene at >385 nm in the Presence of α-Methylstyrene and/or Pyridine *N*-Oxide; Run I. Four samples were prepared in Pyrex cells, each containing DAAN (4.8×10^{-3} M). Each sample was purged with dry nitrogen for 10 min and irradiated for 45 min at >385 nm (450-W mercury lamp with ferric chloride filter). Sample 2 also contained α-methylstyrene (0.25 M), while sample 3 contained pyridine *N*-oxide (0.88 M). Sample 4 contained both α-methylstyrene (0.25 M) and pyridine N-oxide (0.91 M). The conversion (100% for each run) was determined by monitoring the diazo absorption at 2056 cm^{-1}. The volatiles were removed from the samples by rotary evaporation at reduced pressure and the products analyzed by ^1H NMR (200 MHz) spectroscopy and GLPC (undecane internal standard).

Run II. Six samples were prepared in quartz cells, each containing DAAN (2.0×10^{-3} M); samples 1-5 also contained pyridine *N*-oxide (0.931 M). Each sample contained α-methylstyrene (1, 0.094 M; 2, 0.075 M; 3, 0.066 M; 4, 0.038 M; 5-6, 0.019 M). The samples were purged with dry nitrogen (10 min) and irradiated to completion (15 min) as described in run I. The anthraquinone yields were determined by analytical HPLC, anthracene internal standard, (sample no., yield: 1, 48; 2, 49; 3, 58; 4, 63; 5, 80; 6, 14).

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Synthesis and Reactions of Iodo Lactams†

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The synthesis of a series of iodo lactams has been achieved by a new cyclization method that depends on generating *N,O*-bis(trimethylsilyl)imidate derivatives as intermediates. Treatment of an unsaturated amide with trimethylsilyl triflate in pentane and then iodine in tetrahydrofuran gives the iodo lactam. Some reactions of this new difunctional group with bases, nucleophiles, and Michael acceptors leading to functionalized or elaborated lactams are presented. In general, iodo lactams undergo direct S_N2 reactions with reactive (but weakly basic) nucleophiles like azide and triphenylphosphine and elimination or decomposition in the presence of bases or basic nucleophiles. Sodium hydride may be used to generate an *N*-acylaziridine intermediate, which can be opened with azide to deliver an azido lactam with overall retention of stereochemistry. Silver-assisted solvolysis of iodo lactams gives the hydroxy lactams with retention of configuration, probably also because of participation by the lactam nitrogen. The sodium salt of 5-(iodomethyl)-2-pyrrolidinone (3), generated at −20 °C, undergoes an annulation reaction with unsaturated esters (but not sulfones), leading to pyrrolizidine derivatives.

We recently reported a method for the synthesis of iodo lactams from the corresponding unsaturated amides, illustrated below by the conversion of 4-pentenamide (1) to 5-(iodomethyl)-2-pyrrolidinone (3).[1] Whereas 1 cannot be cyclized to 3 directly,[2-5] prior conversion of 1 to its *N,O*-bis(trimethylsilyl) derivative 2 allows a cyclization process analogous to the familiar and useful iodolactonization reaction.[6,7] The resulting iodo lactams constitute a new class of difunctional compounds, one whose chemistry is expected to reflect the close interaction of the two groups. In this paper, we describe the exper-

† This paper is dedicated to Prof. Jerrold Meinwald on the occasion of his 60th birthday.

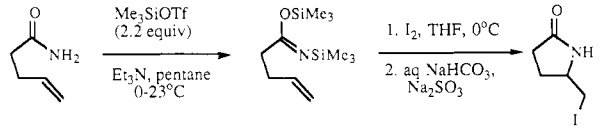
(1) Knapp, S.; Rodriques, K. E.; Levorse, A. T.; Ornaf, R. M. *Tetrahedron Lett.* **1985**, *26*, 1803.

(2) Treatment of 1 with a solution of iodine in THF gave the iodo lactone 6 as the only cyclization product after aqueous workup. A similar result was observed by Ganem, who attempted to reproduce a literature report of the synthesis of 3. Biloski, A. J.; Wood, R. D.; Ganem, B. *J. Am. Chem. Soc.* **1982**, *104*, 3233 (see footnote 8 therein).

(3) Intentional O-iodocyclization of unsaturated amides to give lactones: (a) Corey, E. J.; Shibasaki, M.; Knolle, J. *Tetrahedron Lett.* **1977**, 1625. (b) Tamaru, Y.; Mizutani, M.; Furukawa, Y.; Kawamura, S.; Yoshida, Z.; Yanagi, K.; Minobe, M. *J. Am. Chem. Soc.* **1984**, *106*, 1079.

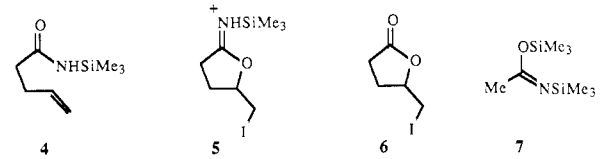
0022-3263/88/1953-4006$01.50/0

imental details for the "iodolactamization" procedure, its application to the synthesis of a series of iodo lactams, and the results of our studies on the reactions of these compounds with various bases, nucleophiles, and electrophiles.



1 2 3 86%

"Iodolactamization" Procedure. Primary amides such as **1** undergo a double silylation[8] when treated with 2.2 equiv of trimethylsilyl trifluoromethanesulfonate[9] in pentane or dichloromethane solution in the presence of triethylamine. The extent of conversion may be monitored conveniently by IR spectroscopic analysis of aliquots taken directly from the reaction mixture. After the addition of 1.1 equiv of silylating reagent, the two N–H absorbances of **1** at 3410 and 3320 cm^{-1} were replaced by an N–H absorbance at 3370, attributable to the N-silylated intermediate **4**. That initial silylation of **1** took place on nitrogen was confirmed by treatment of the silylation reaction mixture at this point with a tetrahydrofuran (THF) solution of iodine, resulting in the formation of 5-(iodomethyl)butyrolactone (**6**).[10] This product probably arose from hydrolysis upon workup of the presumed primary cyclization intermediate **5**.



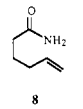
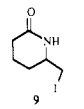
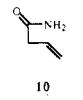
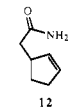
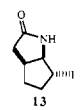
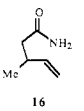
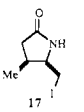
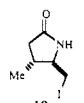
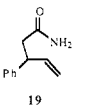
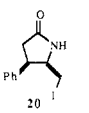
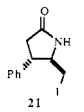
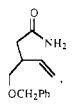
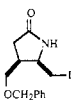
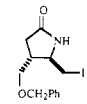
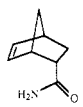
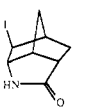
4 5 6 7

Further treatment of **4** with silylating reagent resulted in the disappearance of the 3370 absorbance, indicative of its conversion to the *N,O*-bis(silyl)imidate **2**. This derivative may be successfully prepared only if reagents and glassware are scrupulously dried, and care is taken in all transfers not to introduce traces of moisture. Otherwise, some **2** reverts to **4**, and the cyclization reaction gives the lactone **6** to the same extent. Compound **2** has the same functionality as the commercially available silylating agent *N,O*-bis(trimethylsilyl)acetimidate (**7**),[7] and having to generate this group in the presence of a solvent or another group in the same molecule that may also silylate should be considered as a factor that may complicate its cyclization chemistry.

For successful iodocyclization it was necessary to separate the *N,O*-bis(silyl) derivative **2** from the oily triethylammonium trifluoromethanesulfonate that accompanies its formation. When the silylation was carried out in dichloromethane, some of the salt was carried over into the iodocyclization step, and the yield was reduced. Removal of the dichloromethane and transfer of **2** using pentane improved the yield,[1] but some **2** was lost amid the salt nevertheless. Better results were obtained by conducting the silylation in pentane directly, whereupon the salt separated as it formed, and a more efficient transfer of **2** could be achieved. This last modification improved the yield of **3** from 64% to 86% and was beneficial in all cases but one (**25**) where the starting amide has very low solubility in pentane.

A number of solvents were examined for the iodocyclization reaction of **2**, and both pentane and dichloromethane proved less than satisfactory, as did toluene, acetonitrile, carbon tetrachloride, ether, and dioxane. The best results were obtained by using THF with no other solvent present, that is, the pentane used for the transfer of **2** was removed before the iodine and THF were added. The efficacy of THF may be due in part to its Lewis basicity and ability to dissolve iodine.[12] However, it also

Table I. Preparation of Iodo Lactams

unsaturated amide	iodo lactam(s)	% yield (cis/trans)
 8	 9	35[a]
 10	 11	35[b]
 12	 13	86
 14	 15	88
 16	 17 +  18	84 (3:1)
 19	 20 +  21	88 (2:1)
 22	 23 +  24	86 (1:1)
 25	 26	80[c]

[a] 10–20% of starting amide was also recovered. [b] 54% of crotonamide was also isolated. [c] Overall yield after separate desilylation.

(4) Other O-cyclizations of unsaturated amides: (a) Corey, E. J.; Fleet, G. W. J.; Kato, M. *Tetrahedron Lett.* **1973**, 3963. (b) Clive, D. L. J.; Wong, C. K.; Kiel, W. A.; Menchen, S. M. *J. Chem. Soc., Chem. Commun.* **1978**, 379. (c) Kozikowski, A. P.; Scripko, J. *Tetrahedron Lett.* **1983**, *24*, 2051 (compound **17** therein). (d) Toshimitsu, A.; Terao, K.; Uemura, S. *J. Chem. Soc., Chem. Commun.* **1986**, 530.

(5) N-Cyclizations of unsaturated *amides* using various electophiles: (a) Wilson, S. R.; Sawicki, R. A. *J. Org. Chem.* **1979**, *44*, 330. (b) Aida, T.; Legault, R.; Dugat, D.; Durst, T. *Tetrahedron Lett.* **1979**, 4993. (c) Harding, K. E.; Burks, S. R. *J. Org. Chem.* **1981**, *46*, 3920. (d) Hegedus, L. S.; McKearin, J. M. *J. Am. Chem. Soc.* **1982**, *104*, 2444. (e) Danishefsky, S.; Taniyama, E. *Tetrahedron Lett.* **1983**, *24*, 15. (f) Toshimitsu, A.; Terao, K.; Uemura, S. *J. Org. Chem.* **1986**, *51*, 1724. (g) Rajendra, G.; Miller, M. J. *J. Org. Chem.* **1987**, *52*, 4471. (h) Rajendra, G.; Miller, M. J. *Tetrahedron Lett.* **1987**, *28*, 6257.

(6) References for and discussion of the iodolactonization reaction: Chamberlin, A. R.; Mulholland, R. L.; Kahn, S. D.; Hehre, W. J. *J. Am. Chem. Soc.* **1987**, *109*, 672.

(7) Other unsaturated imidate halocyclizations giving lactams: (a) Kano, S.; Yokomatsu, T.; Iwasawa, H.; Shibuya, S. *Heterocycles* **1987**, *26*, 359. (b) Takahata, H.; Takamatsu, T.; Mozumi, M.; Chen, Y.; Yamazaki, T.; Aoe, K. *J. Chem. Soc., Chem. Commun.* **1987**, 1627.

(8) Yoder, C. H.; Copenhafer, W. C.; DuBeshter, B. *J. Am. Chem. Soc.* **1974**, *96*, 4283.

(9) Emde, H.; Domsch, D.; Feger, H.; Frick, U.; Gotz, A.; Hergott, H. H.; Hofmann, K.; Kober, W.; Krageloh, K.; Oesterle, T.; Steppan, W.; West, W.; Simchen, G. *Synthesis* **1982**, 1.

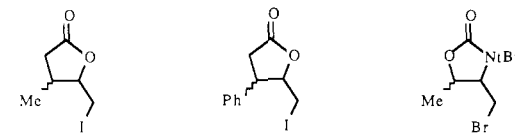
(10) Dowle, M. D.; Davies, D. I. *Chem. Soc. Rev.* **1979**, *8*, 171.

(11) Klebe, J. F.; Finkbeiner, H.; White, D. M. *J. Am. Chem. Soc.* **1966**, *88*, 3390.

plays a direct chemical role, as described below. In any case, this combination of reaction conditions allowed the synthesis of a number of iodo lactams from the corresponding unsaturated amides, as listed in Table I. In general the unsaturated amides were prepared from the carboxylic acids, many of which are commercially available or makable by Claisen rearrangement, malonate alkylation, or Diels–Alder reaction.

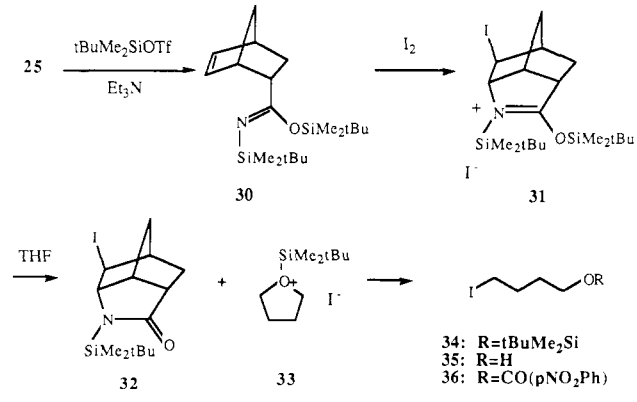
Structures were initially assigned to the cyclization products in Table I by analogy to the corresponding iodolactonization reaction products.[6,10] The γ-lactams **13**, **15**, **17**, **18**, **20**, **21**, **23**, and **24** showed the characteristic IR carbonyl absorbance at 1680–1700 cm^{-1}, whereas 6-(iodomethyl)-2-piperidone (**9**) and 4-(iodomethyl)-2-azetidinone (**11**, a known compound[13,14]) showed the expected absorbances at 1660 and 1740 cm^{-1}, respectively. The structures of **9**, **11**, **13**, and **15** were also confirmed by further transformations, as described below. The cis/trans pairs **17**/**18** and **20**/**21** were originally misassigned on the basis of the ^1H NMR spectra of the mixtures.[1] The revised structures shown here result from comparison of their ^{13}C NMR spectra with those of the corresponding *lactones* **27** and **28**.[15] In particular, the signals for carbons 4 and 5 in all four cis compounds (lactams and lactones) are upfield from the corresponding signals of the trans isomers. Likewise, all the methyl and iodomethyl carbons are upfield in the cis isomers, relative to the trans. In the 400-MHz ^1H NMR spectrum of the cis isomer **20**, the signal for the iodomethyl group is strongly shielded by the nearby phenyl ring, a characteristic also observed for cis-4,5-disubstituted oxazolidinones where one substituent is a phenyl.[16] The structures of **23** and **24** follow from the similarity of their ^{13}C NMR spectra to those of **17** and **18**. We were unable to separate the cis/trans isomers **17**/**18** or **23**/**24** by chromatography or crystallization, but **20** could be obtained free of the trans isomer **21** by crystallization from ether/hexane.

The improved silylation conditions allowed the isolation of the sensitive azetidinone **11**, a compound of some interest as a precursor to β-lactam antibiotics.[13,14,17] Previously[1] only crotonamide could be isolated from this reaction, and it continues to be the major product. TLC analysis or quenching of the crude silylation product from **10** suggests that the conjugated product arises later, during or after the iodocyclization step. The slight predominance of the cis isomer from cyclization of the 3-substituted pentenamides **16** and **19** is reminiscent of the "kinetic" ratios observed for the corresponding iodolactonization reactions to give **27** and **28**,[6,15] the bromocyclization reaction of a carbonimidothioate derived from 1-buten-3-ol to give **29**,[18] and several other related N-cyclizations.[5g,6,7b] Contrary to our earlier indication[1] the cyclization reaction as currently constituted appears to be an irreversible, "kinetic" process. A particular disappointment was the lack of stereocontrol in the cyclization of **22**, since either product (**23** or **24**) might serve as a useful precursor to pyrrolizidine alkaloids. This example does show, however, that the *O*-benzyl group survives the silylation and cyclization steps.



27 (c:t = 3.8:1) **28** (c:t = 2.4:1) **29** (c:t = 1.5:1)

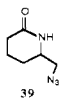
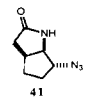
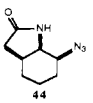
Accompanying the iodo lactam product, 4-iodobutanol (**35**) is also formed during the iodocyclization step and can be isolated in varying amounts by column chromatography (R_f 0.68, ether). This suggests that THF becomes silylated during the course of the reaction. Some insight into how this might occur was provided by a cyclization sequence applied to *endo*-5-norbornene-2-carboxamide (**25**) using *tert*-butyldimethylsilyl trifluoromethanesulfonate[19] as the silylating agent. The resulting *N*,*O*-bis(silyl) derivative **30** was treated with iodine in THF solution in the usual way, but the reaction was quenched with aqueous sodium sulfite alone (omitting the sodium bicarbonate). This allowed the isolation of the *N*-*tert*-butyldimethylsilyl lactam **32** in 88% yield and the *tert*-butyldimethylsilyl ether of 4-iodobutanol (**34**) in 61% yield. Using aqueous hydrogen fluoride in acetonitrile solution,[20] lactam **32** was desilylated to give **26**, and **34** was desilylated to give **35**. Further, **35** was converted to its known[21] *p*-nitrobenzoate derivative **36**. A logical sequence of events consistent with these observations is that cyclization of **30** occurs initially to give the iminium species **31**, which is analogous to the intermediates isolated from other halocyclizations.[18,22] The *O*-silyl group of **31** is then transferred to the oxygen of THF, either directly or by way of *tert*-butyldimethylsilyl iodide,[23] giving the siloxonium species **33**, which in turn is opened by iodide (or triiodide[10]), leading to **34**. The ability of THF to "trap"the iminium salt **31** may help account for the fact that this cyclization reaction appears to work best in this particular solvent.



Reactions of Iodo Lactams. Since the iodo lactams in Table I could now be prepared in quantities sufficient

(12) For a compilation of solubilities of iodine in various media, see: Seidell, A. *Solubilities of Inorganic and Metal Organic Compounds*; D. Van Nostrand Co.: New York, 1964; Vol. 1, p 672.
(13) Tanaka, T.; Miyadera, T. *Heterocycles* **1982**, *19*, 1497.
(14) Salzmann, T. N.; Ratcliffe, R. W.; Christensen, B. G.; Bouffard, F. A. *J. Am. Chem. Soc.* **1980**, *102*, 6161.
(15) Gunther, H. J.; Guntrum, E.; Jager, V. *Liebigs Ann. Chem.* **1984**, 15.
(16) Knapp, S.; Kukkola, P. J.; Sharma, S.; Pietranico, S. *Tetrahedron Lett.* **1987**, *28*, 5399.
(17) Fujimoto, K.; Iwano, Y.; Hirai, K. *Tetrahedron Lett.* **1984**, *25*, 1151.
(18) Knapp, S.; Patel, D. V. *J. Am. Chem. Soc.* **1983**, *105*, 6985.
(19) Corey, E. J.; Cho, H.; Rucker, C.; Hua, D. H. *Tetrahedron Lett.* **1981**, *22*, 3455.
(20) Newton, R. F.; Reynolds, D. P. *Tetrahedron Lett.* **1979**, *20*, 3981.
(21) Long, L. H.; Freeguard, G. F. *Nature (London)* **1965**, *207*, 403.
(22) Winstein, S.; Goodman, L.; Boschan, R. *J. Am. Chem. Soc.* **1950**, *72*, 2311.
(23) *Iodotrimethylsilane* opened THF at 60 °C to give the trimethylsilyl ether of **35**: Olah, G. A.; Narang, S. C. *Tetrahedron* **1982**, *38*, 2225 (see ref 92 therein). A solution of *tert*-butyldimethylsilyl chloride and sodium iodide in acetonitrile at 55 °C converted THF to **34**: Nystrom, J.-E.; McCanna, T. D.; Helquist, P.; Amouroux, R. *Synthesis* **1988**, 56.

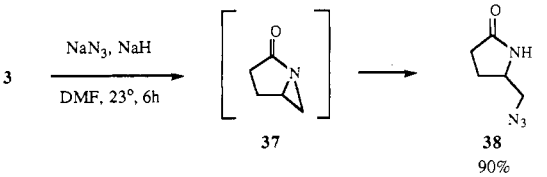
Table II. Synthesis of Azido Lactams from Iodo Lactams

iodo lactam	azido lactam	conditions[a]	% yield[b]	% alkene
9	 39	A, 60 °C, 15 h	50	50
		B	20	80
11	 40	A, 60 °C, 24 h	98	
13	 41	B	90	
13	 42	A, 75 °C, 30 h	36	54
15	 43	B	93	
15	 44	A, 110 °C, 12 h	80	20

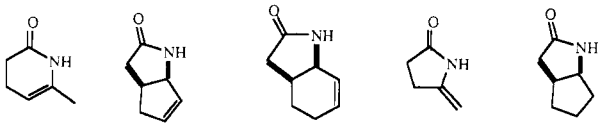
[a] "A" = 10 equiv of NaN_3 in DMF, "B" = 10 equiv of NaN_3, 0.1 equiv of NaH in DMF, 23 °C, 6 h. [b] Isolated yields except for **42**.

for further transformations, we turned our attention to the question of how this difunctional group would behave chemically. It was of particular interest whether and how the two groups, lactam and iodo, could be made to interact with each other. Only a smattering of examples of reactions of halo lactams with nucleophiles, all of the direct S_N2 type, is found in the literature.[13,14,17,24]

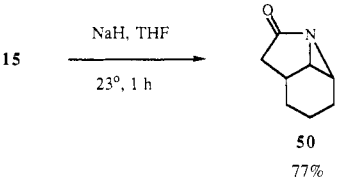
We first investigated[25] the reaction of iodo lactams with sodium azide, a strong nucleophile yet weak base. The resulting azido lactams could serve as precursors to vicinal diamines, which are of general interest as components of biologically active compounds and as ligands. Reaction of 5-(iodomethyl)-2-pyrrolidinone (**3**) with sodium azide under conventional conditions, 60 °C in dimethylformamide (DMF) solution, gave the expected azido lactam **38**, but the conversion was slow, about 40% after 24 h. Addition of a catalytic amount (0.1 equiv) of sodium hydride greatly accelerated the reaction, leading to **38** after only several hours at room temperature. We infer that sodium hydride promoted the ring closure of **3** to the *N*-acylaziridine **37**, which in turn suffered nucleophilic attack by azide at the methylene carbon to give **38**.



Four of the other iodo lactams were also treated with sodium azide, either under the conventional conditions (designated A) or with added catalytic sodium hydride (B), as shown in Table II. Whereas 4-(iodomethy)-2-azetidinone (**11**), which is relatively unhindered, reacted by substitution only under A, the corresponding piperidone **9** gave, in addition to the azido lactam **39**, a large amount of the product of elimination, **45**. Switching to B accelerated the reaction, but the percentage of elimination increased. The problem of competing elimination was not seen in the case of the bicyclic iodo lactams (**13** and **15**) under B. In fact, each of these substrates reacted to give a single azido lactam in high yield (**41** and **43**, respectively). That these were products of substitution with retention was demonstrated by subjecting **13** and **15** to A, which gave, after prolonged heating, the products of substitution with inversion, **42** and **44**, respectively. Some elimination occurred here also, giving **46** and **47** as byproducts. The three unsaturated lactams **45**, **46**, and **47** were independently synthesized from the appropriate iodo lactams in the yields shown by treatment with 1,6-diazabicyclo[5.4.0]-undec-6-ene (DBU) in refluxing toluene. Curiously, we were unable to isolate the unsaturated lactam **48** or an endocyclic isomer from the reaction of **3** with DBU. Instead, only very polar material that resisted analysis was formed, implying that **48** formed but polymerized or that the lactam ring was cleaved. The tendency of **3** to give this material under basic conditions places limits on its reaction with nucleophiles, as described below.



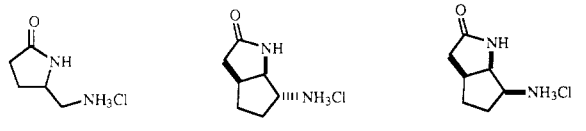
The interesting displacements by azide with retention of configuration (**41** and **43**) reflect the nucleophilic participation of the lactam nitrogen, leading to an *N*-acylaziridine intermediate. Direct evidence for this intermediate in the reaction of **15** with sodium hydride in DMF was obtained by omitting the sodium azide. After 2 h at 23 °C, a new product was observed by TLC at higher R_f than the starting material. Infrared analysis of the crude reaction mixture revealed a carbonyl absorption at 1750 cm^{-1}, indicating the presence of the *N*-acylaziridine **50**.[26] The same product formed when **15** was treated with a full 1.1 equiv of sodium hydride in THF solution, and in this case pure **50**, the putative intermediate, was isolated by column chromatography.



The catalytic hydrogenation of three of the azido lactams (**38**, **41**, and **42**) was carried out, leading to amino lactams which were isolated as their hydrochloride salts (**51**, **52**, and **53**, respectively) in the yields shown. Compound **51** was needed for another project involving the synthesis of inhibitors of polyamine metabolism,[25] whereas the reduction of **42** served to separate it from the alkene **46** (which was itself reduced to **49** in the process) and thus allowed a comparison of the pure cis and trans amino lactams **52** and **53** by high-field ^1H NMR.

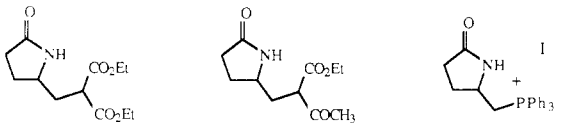
A few examples of reactions of iodo lactam **3** with carbon nucleophiles were examined beginning with the sodium salt of diethylmalonate. A slight excess of sodium hydride was

(24) Confalone, P. N.; Pizzolato, G.; Bassiolini, E. J.; Lollar, D.; Uskokovic, M. R. *J. Am. Chem. Soc.* **1975**, *97*, 5936; **1978**, *99*, 7020.
(25) Knapp, S.; Levorse, A. T. *Tetrahedron Lett.* **1987**, *28*, 3213.
(26) Brown, I.; Edwards, E. O.; McIntosh, J. M.; Vocelle, D. *Can. J. Chem.* **1969**, *47*, 2751.



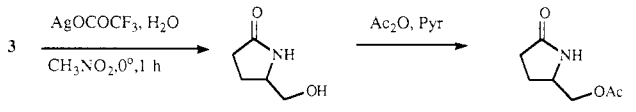
51 84% 52 86% 53 78%

used to form the malonate anion in DMF solution. Addition of **3** followed by 12 h of stirring at room temperature led to the product of substitution, **54**, in high yield. Similarly, ethyl acetoacetate gave **55**, but the yield dropped significantly. Use of 1,3-cyclohexanedione as the nucleophile gave no comparable substitution product at all under these conditions. Finally, treatment of **3** with sodium hydride in DMF solution at room temperature in the absence of a nucleophile led to rapid destruction of the starting material, but there was no evidence for the formation of either the *N*-acylaziridine **37** or the unsaturated lactam **48**. Thus while the intervention of **37** improves the substitution reaction of **3** with reactive nucleophiles such as azide, there is no benefit with weaker nucleophiles. Triphenylphosphine, which formed phosphonium salt **56** when heated with **3** at 100 °C in DMF solution, did not intercept **37** under the conditions for making azido lactams (sodium hydride, 23 °C, 6 h). Clearly more study is required to discover conditions under which a wider range of carbon nucleophiles will displace the iodide of iodo lactams.[27,28]



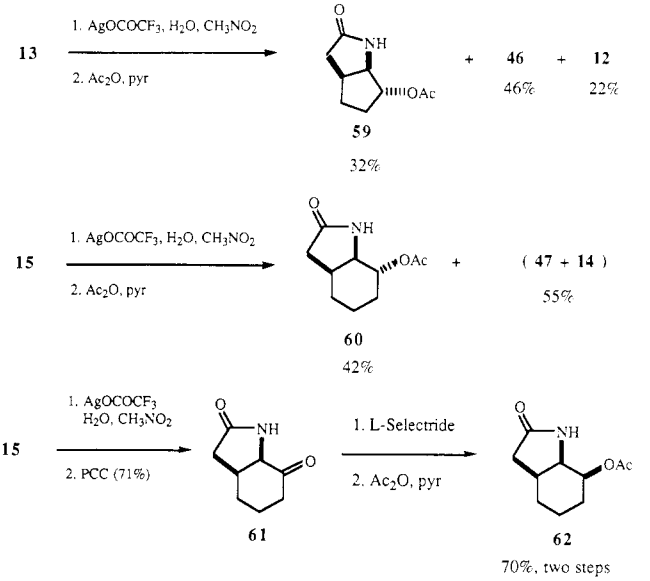
54 92% 55 52% 56 73%

Displacement of the iodide of iodo lactams by oxygen nucleophiles under solvolysis conditions was examined, since this is potentially a stereocontrolled route to amino alcohols. The best conditions for converting **3** to the corresponding hydroxy lactam **57** among several examined were those we had worked out earlier for the synthesis of hydroxyoxazolidinones from iodooxazolidinones.[29] Treatment of **3** with silver(I) trifluoroacetate and 1 equiv of water in nitromethane solution converted it rapidly to the alcohol **57**, which was isolated as its acetate derivative, **58**. The polar byproducts that plague reactions of **3** under basic conditions were not a problem in this acidic medium.



57 58 80% overall

The same conditions converted the bicyclic iodo lactams **13** and **15** to the corresponding acetoxy lactams **59** and **60**, accompanied by substantial amounts of the elimination products **46** and **47**, as expected for secondary iodides. An unexpected side product in both cases was the unsaturated amide (**12** and **14**), the (possibly acid catalyzed) result of a formal reductive ring opening. In both cases the substitutions proceeded with complete retention of configuration, indicating that the solvolysis probably occurred with participation of the nearby lactam nitrogen.[29] The assignment of stereochemistry of **59** and **60** rests on the similar coupling constants in their high-field NMR spectra to those of the starting iodo lactams and the corresponding azido lactams (**41** and **43**, respectively). In addition, the alcohol derived from **15** was taken through an oxidation–reduction sequence designed[29] to produce the endo acetoxy lactam **62**, which proved different from **60**. The routes from **15** to either acetoxy lactam isomer and to the keto lactam **61** may serve as prototypes for functionalization of more complex iodo lactams.

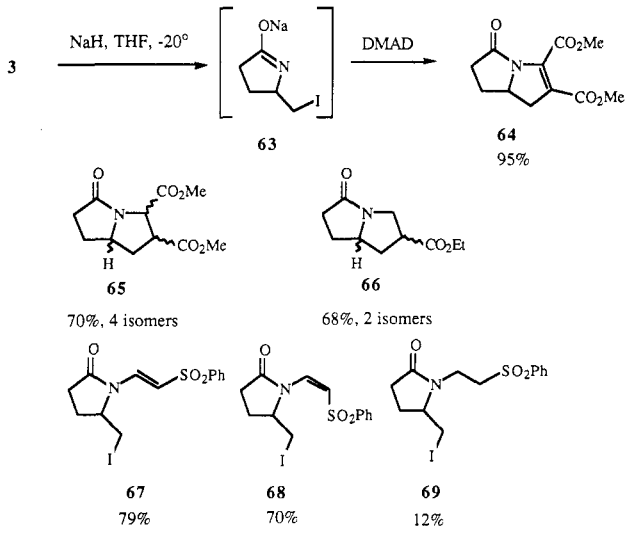


59 32% 46 46% 12 22% 60 42% 47 + 14 55% 61 62 70%, two steps

During our attempts to isolate the *N*-acylaziridine **37** derived from iodo lactam **3**, we treated **3** with sodium hydride in THF solution at −20 °C and observed hydrogen gas evolution, even though TLC analysis showed that **3** had not been consumed. This suggests that the derived sodium salt (**63**) is stable under these conditions, although it self-destructs above 0 °C. The presence of a nucleophilic center and an electrophilic center in the same species is a situation that can sometimes be exploited for an annulation process, so **63** was treated with a variety of Michael acceptors in the hope that ring formation would occur.[17] Indeed, with dimethyl acetylenedicarboxylate, dimethyl fumarate, and ethyl acrylate, **63** gave the desired products (**64**, **65**, and **66**, respectively) in yields that indicate that this may be a useful transformation. With *trans*-bis(phenylsulfonyl)ethylene, however, an addition–elimination process[30] occurred instead, leading to **67**. Similarly, **63** gave **68** with *cis*-bis(phenylsulfonyl)ethylene, but no ring closure. The alkene configuration of **67** and **68** was assigned on the basis of the olefin coupling constants (14 and 10.7 Hz, respectively). A single attempt was made to close **67** by using lithium diisopropylamide in THF,[30] but it was unsuccessful. Finally, phenyl vinyl sulfone gave the addition product **69** in low yield, but no product of ring closure was observed.

Conclusion. The synthesis of a series of iodo lactams from the unsaturated amides has been achieved by a new cyclization method that depends on generating the *N*,*O*-bis(trimethylsilyl) derivatives as intermediates. In general, iodo lactams undergo direct S_N2 reactions with reactive (but weakly basic) nucleophiles like azide and triphenylphosphine and elimination or decomposition in the pres-

(27) A radical coupling reaction of **3** has been reported. See ref 5f.
(28) Reaction of lithium dibutylcuprate with an *N*-acylaziridine: Aratani, M.; Dunkerton, L. V.; Fukuyama, T.; Kishi, Y.; Karoi, H.; Sugiura, S.; Inoue, S. *J. Org. Chem.* **1975**, *40*, 2009.
(29) Knapp, S.; Patel, D. V. *J. Org. Chem.* **1984**, *49*, 5072.
(30) McCombie, S. W.; Shankar, R. B.; Ganguly, A. K. *Tetrahedron Lett.* **1985**, *26*, 6301; **1987**, *28*, 4123 and 4127.



ence of bases or basic nucleophiles. Sodium hydride may be used to generate an *N*-acylaziridine intermediate, which can be opened with azide to deliver an azido lactam with overall retention of stereochemistry. Silver-assisted solvolysis of iodo lactams gives the hydroxy lactams with retention of configuration, probably also because of participation by the lactam nitrogen. The sodium salt of 5-(iodomethyl)-2-pyrrolidinone (**3**), generated at −20 °C, undergoes an annulation reaction with unsaturated esters (but not sulfones), leading to pyrrolizidine derivatives.

Experimental Section

Apparatus and Reagents. Melting points were obtained on an Electrothermal apparatus and are uncorrected. Proton nuclear magnetic resonance (NMR) spectra were obtained on a Varian Associates XL-400 or VXR-200 spectrometer. Carbon-13 NMR spectra were obtained on the latter instrument at 50 MHz. Chemical shifts are reported in parts per million downfield from tetramethylsilane, and coupling constants (*J*) are in hertz. ^{1}H NMR and ^{13}C NMR measurements were made on deuteriochloroform solutions unless otherwise specified. Infrared (IR) spectra were recorded on a Perkin-Elmer Model 727B spectrophotometer. Chemical ionization mass spectra (CI-MS) were obtained on a VG Analytical Model 7070EQ spectrometer, using isobutane as the carrier gas. Elemental analyses were performed by Robertson Laboratories.

Precoated silica gel plates (E. Merck 5715-7) were used for analytical thin layer chromatography (TLC). Machery Nagel silica gel 60 (230–400 mesh) was employed for column chromatography. THF was distilled from benzophenone ketyl. Nitromethane was distilled from anhydrous calcium sulfate. Pentane, dichloromethane, DMF, triethylamine, and pyridine were distilled from calcium hydride. Bulk grade ether and petroleum ether were distilled prior to use. *endo*-2-Norbornene-6-carboxamide (**25**),[31] mp 201–202 °C, was a gift from Professor R. R. Sauers of this department. 3-[(Phenylmethoxy)methyl]-4-pentenoic acid, the precursor to **22**, was made by Claisen rearrangement[32] from 4-(phenylmethoxy)-2-buten-1-ol.[33] Other solvents and reagents were obtained commercially and used as received. Organic solutions were dried over anhydrous sodium sulfate, and all reactions were performed under an argon atmosphere.

General Procedure for Formation of Unsaturated Amides. For a 10–100-mmol scale, oxalyl chloride (1.5 equiv) was added to a stirred solution or suspension of the unsaturated carboxylic acid (1 equiv) in toluene at 23 °C over a 30-min period. The solution was stirred for 30 min after evolution of gas was no longer apparent (total reaction time about 1.5 h). The reaction mixture was concentrated to about half the original volume by using a vacuum pump equipped with a sodium hydroxide trap and then added over a 30-min period to a stirred mixture of toluene and excess liquid ammonia cooled with a dry ice/acetone bath. The reaction mixture was allowed to warm to room temperature and then was concentrated to a residue on a rotary evaporator. The solids were partitioned between 10% aqueous sodium hydroxide and dichloromethane, and the aqueous phase was washed three times with additional dichloromethane. The combined organic extract was washed with brine, dried, and concentrated to a solid, which was crystallized from isopropyl ether or isopropyl ether/hexane to give the pure unsaturated amide in 80–95% yield.

Using this procedure the unsaturated amides 3-butenamide[34] (**10**), 4-pentenamide[34] (**1**), 5-hexenamide[34] (**8**), 2-(2-cyclopentenyl)acetamide[35] (**12**), 2-(2-cyclohexenyl)acetamide[36] (**14**), 3-methyl-4-pentenamide[15] (**16**), 3-phenyl-4-pentenamide[15] (**19**), and 3-[(phenylmethoxy)methyl]-4-pentenamide (**22**) were prepared from the corresponding unsaturated acids. Compound **22** was obtained as an oil: ^{1}H NMR (200 MHz) 7.32 (br s, 5 H), 5.72–5.89 (m, 1 H), 5.49–5.62 (br s, 1 H), 5.38–5.48 (br s, 1 H), 5.13 (dd, 2 H, J = 11, 5), 4.51 (s, 2 H), 3.42–3.56 (m, 2 H), 2.81–2.91 (m, 1 H), 2.49 (dd, 1 H, J = 14.4, 6.1), 2.27 (dd, 1 H, J = 14.4, 7.7); IR (film) 3400, 3200, 3120, 2930, 2850, 1660, 1610, 1500, 1460, 1400, 1360, 1280, 1210, 1120, 1070, 1030, 1000, 920, 740, 700.

General Procedure for Iodolactamization. For a 1–5-mmol scale, a solution of 1 equiv of the unsaturated amide and 2.2 equiv of triethylamine in dry pentane was treated at 0 °C with 2.2 equiv of trimethylsilyl trifluoromethanesulfonate and stirred under argon for 30 min at 23 °C. The supernatant, which contained the *N,O*-bis-silylated amide, was transferred to a second dry flask under an argon atmosphere. The residue was rinsed with additional pentane, which was combined with the supernatant in the second flask, and the pentane (in total about 5 mL/mmol of substrate) was carefully removed by using an aspirator equipped with a calcium sulfate drying tube. THF was added, the solution was cooled to 0 °C, and a solution of 2.2 equiv of iodine in THF was added in one portion. After 10 min, the solution was quenched with aqueous sodium bicarbonate and then aqueous sodium sulfite and extracted with three portions of ethyl acetate. The organic solution was dried with sodium sulfate, concentrated, and chromatographed on silica without delay by using ether/petroleum ether as the eluant, affording the iodo lactam as a stable, white solid. Efficient crystallization of the product could normally be achieved by using ether/hexane.

5-(Iodomethyl)-2-pyrrolidinone[37] **(3)**: yield 0.977 g from ether/hexane, mp 68–70 °C; ^{1}H NMR (400 MHz) 6.0–6.1 (br s, 1 H), 3.85 (app quint, 1 H, J = 5), 3.23 (dd, 1 H, J = 10.0, 5.2), 3.14 (dd, 1 H, J = 10.0, 7.1), 2.28–2.50 (m, 3 H), 1.75–1.85 (m, 1 H); IR (film) 3200, 2930, 2850, 1685, 1460, 1415, 1370, 1310, 1280, 1255. Anal. Calcd for C_5H_8INO: C, 26.69; H, 3.58; N, 6.22; I, 56.39. Found: C, 26.75; H, 3.52; N, 6.00; I, 56.49.

6-(Iodomethyl)-2-piperidone (9): yield 0.069 g from ether/hexane, mp 157–158 °C; ^{1}H NMR (400 MHz) 6.60–6.75 (br s, 1 H), 3.49 (app quint, 1 H, J = 5), 3.24 (dd, 1 H, J = 10, 5), 3.13 (dd, 1 H, J = 10, 7), 2.2–2.4 (m, 3 H), 1.95–2.05 (m, 1 H), 1.83–1.90 (m, 1 H), 1.69–1.77 (m, 1 H); IR (film) 3230, 2960, 2860, 1660, 1500, 1440, 1410, 1340, 1320, 1195, 1170, 1090, 970, 940.

4-(Iodomethyl)-2-azetidinone (11):[13,14] yield 0.191 g from ether/hexane, mp 98–99 °C (lit.[13] mp 106–106.5 °C); ^{1}H NMR (400 MHz) 5.98 (br s, 1 H), 3.87–4.05 (m, 1 H), 3.27–3.45 (m, 2 H), 3.15 (dd, 1 H, J = 14.5, 4.5), 2.70 (d, 1 H, J = 14.5); IR (KBr) 3325, 2940, 1740, 1720, 1435, 1417, 1350, 1255, 1190, 1160, 957, 940, 855, 800.

***8-exo*-Iodo-2-azabicyclo[3.3.0]octan-3-one (13)**: yield 0.863 g from ether/hexane, mp 138–139 °C; ^{1}H NMR (400 MHz) 5.75–5.85 (br s, 1 H), 4.47 (d, 1 H, J = 3.7), 4.16 (br s, 1 H), 3.05–3.13 (m, 1 H), 2.70 (dd, 1 H, J = 18, 10), 2.33–2.45 (m, 1 H), 2.10–2.20 (m, 2 H), 1.99–2.06 (m, 1 H), 1.55–1.60 (m, 1 H); IR (film) 3050, 2925, 2830, 1680, 1430, 1410, 1365, 1315, 1300, 1260, 1180,

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(36) 3-Cyclohexeneacetic acid: Cristol, S. J.; Freeman, P. K. *J. Am. Chem. Soc.* **1961**, *83*, 4427.
(37) Ott, H.; Hardessere, E. *Helv. Chim. Acta* **1955**, *36*, 312.

1155, 1105, 880, 820, 770, 640. Anal. Calcd for $C_7H_{10}INO$: C, 33.49; H, 4.02; N, 5.58; I, 50.58. Found: C, 33.51; H, 3.79; N, 5.39; I, 50.88.

7-Iodo-2-oxo-2,3,3aα,4,5,6,7β,7aα-octahydroindole (15): yield 0.837 g from ether/hexane, mp 115–116 °C; ^{1}H NMR (400 MHz) 5.9–6.0 (br s, 1 H), 3.9–4.0 (m, 1 H), 3.81 (t, 1 H, J = 9.1), 2.6–2.7 (m, 1 H), 2.88 (dd, 1 H, J = 16.3, 7.4), 2.13 (dd, 1 H, J = 16.3, 7.7), 1.77–1.90 (m, 2 H), 1.65–1.75 (m, 2 H), 1.52–1.58 (m, 1 h), 1.4–1.5 (m, 1 H); IR (film) 3200, 2900, 2845, 1685, 1440, 1415, 1335, 1300, 1255, 1220, 1170, 1125, 1100, 1095, 1060, 1020, 980, 920, 900. Anal. Calcd for $C_8H_{12}INO$: C, 36.25; H, 4.56; N, 5.28; I, 47.87. Found: C, 36.09; H, 4.53; N, 5.00; I, 48.46.

5-(Iodomethyl)-4-methyl-2-pyrrolidinone (17 and 18). A mixture of cis/trans isomers (3:1 by quantitative ^{13}C NMR analysis[38]) was obtained after chromatography. Attempts at further purification were unsuccessful. Crystallization from ether/hexane gave 0.088 g of the same 3:1 cis/trans mixture, mp 60–61 °C: ^{13}C NMR of the mixture (cis is starred) 177.45*, 177,12, 62.28, 58.62*, 38.50, 38.24*, 35.21, 32.59*, 19.61, 13.91*, 10.46, 6.37*; IR (film) 3200, 2960, 2870, 1690, 1430, 1380, 1350, 1300, 1270, 1240, 1190, 1080, 950, 900. Anal. Calcd for $C_6H_{10}INO$: C, 30.15; H, 4.21; N, 5.86; I, 53.09. Found: C, 30.31; H, 4.03; N, 5.71; I, 52.97.

5-(Iodomethyl)-4-phenyl-2-pyrrolidinone (20 and 21). A mixture of cis/trans isomers (2:1 by quantitative ^{13}C NMR analysis[38]) was obtained after chromatography. Crystallization from ether/hexane gave 0.197 g (28%) of pure **20**, mp 90–91 °C, and 0.395 g (58%) of the remaining mixture from the mother liquor as an oil: ^{1}H NMR of **20** (400 MHz) 7.32–7.40 (m, 2 H), 7.19–7.28 (m, 3 H), 5.95–5.99 (br s, 1 H), 4.20–4.24 (m, 1 H), 3.86 (app q, 1 H, J = 8.0), 2.68–2.87 (m, 4 H); ^{13}C NMR (**20**) 176.82, 137.08, 128.93, 128.73, 127.88, 58.70, 43.00, 35.03, 8.08 [Anal. Calcd for $C_{11}H_{12}INO$: C, 43.88; H, 4.02; N, 4.65; I, 42.15. Found: C, 43.81; H, 4.15; N, 4.51; I, 42.24]. ^{13}C NMR of **21** (in mixture with **20**) 176.48, 137.00, 128.91, 127.57, 62.47, 46.71, 39.00, 10.40; partial ^{1}H NMR of **21** (in mixture with **20**, 400 MHz) 6.68 (br s, 1 H), 3.71–3.76 (m, 1 H), 3.33 (dd, 1 H, J = 12, 8), 3.23–3.29 (m, 1 H), 3.20 (dd, 1 H, J = 12, 8).

5-(Iodomethyl)-4-[(phenylmethoxy)methyl]-2-pyrrolidinone (23 and 24): yield 0.116 g of an otherwise uncontaminated mixture of cis/trans isomers (1:1 by quantitative ^{13}C NMR analysis[38]), obtained after chromatography. Attempts to crystallize or separate the isomers were unsuccessful: ^{13}C NMR of the mixture (cis is starred) 177.23, 176.99*, 138.33*, 138.05, 129.12, 128.96, 128.55, 128.42, 128.36, 128.20, 73.94, 73.79*, 72.09, 68.71*, 58.78, 58.06*, 41.24, 38.88*, 34.19, 33.58*, 12.72, 8.49*; IR (film) 3210, 2920, 2850, 1700, 1610, 1500, 1450, 1410, 1360, 1260, 1190, 1100, 1070, 1020, 800, 740, 700.

4-*exo*-Iodo-6-azatricyclo[3.2.1.1^{3,8}]nonan-7-one (26). Three changes were made in the general procedure: (1) *tert*-butyldimethylsilyl trifluoromethanesulfonate[19] was used as the silylating agent, (2) dichloromethane was used as the solvent for the silylation step, and (3) the reaction was quenched by using 10% aqueous sodium sulfite only. The *N*-*tert*-butyldimethylsilyl iodo lactam **32** was obtained after chromatography as an oil (61 mg, 88%): ^{1}H NMR (400 MHz) 4.09 (d, 1 H, J = 4.8), 3.64 (s, 1 H), 3.00 (t, 1 H, J = 4.1), 2.70 (s, 1 H), 2.30–2.36 (m, 2 H), 1.96 (td, 1 H, J = 11.0, 4.1), 1.72–1.76 (m, 2 H), 0.935 (s, 9 H), 0.319 (s, 3 H), 0.245 (s, 3 H); IR (film) 2950, 2920, 2860, 2840, 1695, 1470, 1385, 1310, 1275, 1255, 1230, 1140, 1105, 1030, 940, 850, 835, 740.

The *tert*-butyldimethylsilyl ether of 4-iodobutanol (**34**) was also isolated from this reaction (34.1 mg, 61%): ^{1}H NMR (400 MHz) 3.62 (t, 2 H, J = 8), 3.20 (t, 2 H, J = 7.7), 1.86–1.96 (m, 2 H), 1.57–1.65 (m, 2 H), 0.86 (s, 9 H), 0.03 (s, 6 H). Removal of the silyl group by using aqueous hydrogen fluoride in acetonitrile solution[20] gave 4-iodobutanol (**35**), which was converted to its known *p*-nitrobenzoyl ester **36**, mp 104–104.5 °C (lit.[21] mp 104–105 °C).

The silyl group of **32** was removed by using aqueous hydrogen fluoride in acetonitrile solution,[20] giving the iodo lactam **26** (38.3 mg, 91%; 80% overall from **25**), mp 155–156 °C: ^{1}H NMR (400 MHz) 6.55–6.66 (br s, 1 H), 4.14 (d, 1 H, J = 4), 3.78 (br s, 1 H), 3.09 (s, 1 H), 2.70 (s, 1 H), 2.30 (d, 1 H, J = 11), 1.96 (td, 1 H, J = 10.8, 4.2), 1.78–1.82 (m, 2 H), 1.71 (d, 1 H, J = 11); IR (KBr) 3100, 3000, 2900, 1660, 1415, 1410, 1325, 1280, 1240, 1215, 1115, 1080, 1030, 1020, 900, 800, 730. Anal. Calcd for $C_8H_{10}INO$: C, 36.50; H, 3.80; I, 48.29; N, 5.32. Found: C, 36.57; H, 3.59; I, 48.07; N, 5.61.

General Procedure for Azido Lactams. For a 0.05–0.66-mmol scale, a solution of the iodo lactam (1 equiv) and sodium azide (10 equiv) in DMF solution was (A) heated until TLC analysis indicated the disappearance of iodo lactam or (B) treated with 0.1 equiv of sodium hydride (60% oil dispersion) and stirred at room temperature. The DMF was removed under reduced pressure, and the residue was partitioned between dichloromethane and 10% aqueous sodium hydroxide. The aqueous layer was washed with two additional portions of dichloromethane, and the combined organic extract was dried, concentrated, and chromatographed by using ether/petroleum ether mixtures as the eluant. Normally any unsaturated lactam, if present, eluted before the azido lactam. Crystallization of the solid azido lactams occurred from ether solution.

5-(Azidomethyl)-2-pyrrolidinone (38): yield 85 mg of an oil; ^{1}H NMR (400 MHz) 5.80–5.84 (br s, 1 H), 3.79–3.85 (m, 1 H), 3.49 (dd, 1 H, J = 12.2, 4.2), 3.30 (dd, 1 H, J = 12.0, 7.6), 2.26–2.40 (m, 3 H), 1.79–1.88 (m, 1 H); IR (film) 3220, 2900, 2830, 2090, 1680, 1455, 1435, 1415, 1280, 1260, 1220, 1090, 1009, 980, 910. Anal. Calcd for $C_5H_8N_4O$: C, 42.85; H, 5.71; N, 40.00. Found: C, 42.89; H, 5.63; N, 40.15.

6-(Azidomethyl)-2-piperidone (39): yield 13 mg, mp 93–94 °C; ^{1}H NMR (400 MHz) 5.83–5.95 (br, s 1 H), 3.35–3.47 (m, 2 H), 3.18 (app t, 1 H, J = 7), 2.16–2.40 (m, 2 H), 1.83–1.93 (m, 2 H), 1.64–1.70 (m, 1 H), 1.30–1.40 (m, 1 H); IR (film) 3210, 2940, 2860, 2100, 1665, 1500, 1460, 1410, 1390, 1300, 1280, 1190, 1120, 980, 930.

4-(Azidomethyl)-2-azetidinone (40): yield 5.8 mg of an oil; ^{1}H NMR (400 MHz) 6.13–6.20 (br s, 1 H), 3.77–3.80 (m, 1 H), 3.63 (dd, 1 H, J = 14, 8), 3.41 (dt, 1 H, J = 12, 8), 3.14 (dd, 1 H, J = 19, 8.1), 2.77 (d, 1 H, J = 19); IR (film) 3250, 2960, 2930, 2850, 2100, 1740, 1445, 1420, 1370, 1260, 1220, 1180, 1100, 1075, 1030, 965, 910, 880.

8-*exo*-Azido-2-azabicyclo[3.3.0]octan-3-one (41): yield 30 mg, mp 67–68 °C; ^{1}H NMR (400 MHz) 5.6–5.7 (br s, 1 H), 3.94 (d, 1 H, J = 8), 3.79–3.80 (br s, 1 H), 2.97–3.05 (m, 1 H), 2.64 (dd, 1 H, J = 18, 12), 2.0–2.2 (m, 3 H), 1.8–1.9 (m, 1 H), 1.62–1.70 (m, 1 H); IR (film) 3200, 2950, 2850, 2100, 1690, 1455, 1425, 1360, 1320, 1295, 1260, 1080, 1018, 775, 710.

8-*endo*-Azido-2-azabicyclo[3.3.0]octan-3-one (42). Azido lactam **42** was obtained as an oily inseparable mixture with the unsaturated lactam **46** (25 mg total, ratio 2:3 by NMR analysis). The mixture was hydrogenated to give a mixture of the saturated lactam **49** and the cis amino lactam **53**, which were separated and characterized independently (see below).

7-Azido-2-oxo-2,3,3aα,4,5,6,7β,7aα-octahydroindole (43): yield 66 mg of the exo azide, mp 69–70 °C; ^{1}H NMR (400 MHz), 6.14–6.23 (br s, 1 H), 3.29–3.49 (m, 1 H), 3.27 (t, 1 H, J = 8), 2.65–2.73 (m, 1 H), 2.14–2.30 (m, 2 H), 1.98–2.05 (m, 1 H), 1.58–1.70 (m, 2 H), 1.47–1.55 (m, 1 H), 1.43–1.49 (m, 2 H), IR (Nujol) 3200, 2910, 2850, 2100, 1690, 1440, 1420, 1375, 1340, 1300, 1255, 1240, 1175, 1170, 1060, 1000, 955, 915, 985, 880, 850, 810, 710. Anal. Calcd for $C_8H_{12}N_4O$: C, 53.32; H, 6.71; N, 31.09. Found: C, 52.46; H, 6.61; N, 30.17.

7-Azido-2-oxo-2,3,3aα,4,5,6,7α,7aα-octahydroindole (44). yield 57 mg of the endo azide, mp 91–92 °C; ^{1}H NMR (400 MHz) 5.5–5.6 (br s, 1 H), 3.85 (app t, 1 H, J = 4.3), 3.6–3.7 (m, 1 H), 2.50 (dd, 1 H, J = 16, 7), 2.20–2.30 (m, 1 H), 2.00 (d, 1 H, J = 16), 1.83–1.90 (m, 2 H), 1.57–1.65 (m, 2 H), 1.21–1.33 (m, 2 H); IR (Nujol) 3200, 2920, 2850, 2100, 1690, 1440, 1420, 1385, 1370, 1315, 1300, 1260, 1240, 1200, 1180, 1130, 1100, 1075, 1015, 960, 910, 835.

General Procedure for Unsaturated Lactams. For a 0.1–0.4-mmol scale, a solution of the iodo lactam (1 equiv) and 1,8-diazabicyclo[5.4.0]undec-7-ene (1.1 equiv) in toluene was heated at reflux until TLC analysis showed the disappearance of starting material (6–12 h). The solution was concentrated to a residue, which was chromatographed by using 1:1 ether/petroleum ether as the eluant to give the pure product.

6-Methyl-3,4-dihydro-2(1*H*)-pyridone (45): yield from **9**, 41 mg, mp 105–107 °C (ether) (lit.[39] mp 108 °C); the 400-MHz

(38) Shoolery, J. N. *Prog. NMR Spectrosc.* **1977**, *11*, 79.

^{1}H NMR spectrum matched the literature values;[39] IR (film) 3200, 2960, 2930, 2850, 1680, 1620, 1520, 1380, 1270, 1240, 1170, 1040, 810.

2-Azabicyclo[3.3.0]oct-7-en-3-one (46): yield from **13**, 29 mg of an oil: ^{1}H NMR (400 MHz) 6.8–6.9 (br s, 1 H), 5.80 (d, 1 H, J = 5), 5.77 (d, 1 H, J = 5.7), 4.59 (d, 1 H, J = 10), 2.98–3.09 (m, 1 H), 2.65 (dd, 1 H, J = 16, 10), 2.61 (dd, 1 H, J = 15, 11), 2.24 (d, 1 H, J = 20), 2.15 (dd, 1 H, J = 18, 5); IR (film) 3220, 2900, 2855, 1690, 1620, 1460, 1430, 1380, 1300, 1280, 1210, 1155, 1120, 1085, 1020, 850, 800, 780, 710.

2-Oxo-2,3,3aα,4,5,7aα-hexahydroindole (47): yield from **15**, 11.3 mg of an oil; ^{1}H NMR (400 MHz), 6.24–6.31 (br s, 1 H), 5.94 (d, 1 H, J = 10), 5.67 (d, 1 H, J = 10), 4.04 (s, 1 H), 2.50–2.60 (m, 1 H), 2.47 (dd, 1 H, J = 16, 7.5), 1.95–2.15 (m, 3 H), 1.66–1.70 (m, 1 H), 1.55–1.60 (m, 1 H); IR (film) 3200, 3000, 2910, 2840, 1690, 1660, 1435, 1400, 1365, 1310, 1295, 1265, 1155, 1100, 1060, 980, 940, 910, 875, 760.

1-Azatricyclo[4.2.1.0^{2,9}]nonan-8-one (50). A solution of 60 mg (0.226 mmol) of iodo lactam **15** in 1 mL of THF was added in one portion to a stirred suspension of oil-free sodium hydride in 5 mL of THF. After 1 h the reaction mixture was concentrated and chromatographed by using 1:1 ether/petroleum ether as the eluant, giving 24 mg (77%) of *N*-acylaziridine **50**: mp 112–114 °C; ^{1}H NMR (400 MHz) 3.18–3.37 (m, 1 H), 3.03–3.14 (m, 1 H), 2.75–2.86 (m, 1 H), 2.33 (dd, 1 H, J = 12, 10), 2.19 (d, 1 H, J = 18), 1.97–2.15 (m, 1 H), 1.21–1.59 (m, 5 H); IR (film) 2940, 2850, 1735, 1475, 1420, 1310, 1275, 1140, 1040, 990, 960, 880, 860, 730.

General Procedure for Amino Lactams. For a 0.2–0.4-mmol scale, a solution of the azido lactam in ethanol was hydrogenated by using 10% palladium-on-carbon at 1 atm hydrogen pressure and 23 °C for 12 h. The catalyst was removed by filtration through Celite, and the filtrate was acidified with saturated ethanolic hydrogen chloride. Concentration gave a semisolid residue, which was crystallized from ethanol/ether to afford the product as its hydrochloride salt.

5-(Aminomethyl)-2-pyrrolidinone hydrochloride (51): yield 56 mg, mp 164–165 °C; ^{1}H NMR (D_2O, 400 MHz) 3.91–3.94 (m, 1 H), 2.97–3.05 (m, 2 H), 2.20–2.35 (m, 3 H), 1.75–1.77 (m, 1 H); IR (Nujol) 3400, 2900, 2720, 2650, 1680, 1600, 1460, 1380, 1340, 1275, 1160, 1120, 1085, 1035, 1000, 960, 880.

8-*exo*-Amino-2-azabicyclo[3.3.0]octan-3-one hydrochloride (52): yield 30 mg, mp 164–166 °C; ^{1}H NMR (D_2O, 400 MHz) 3.93 (d, 1 H, J = 8), 3.40 (s, 1 H), 2.87 (app t, 1 H, J = 10), 2.49 (dd, 1 H, J = 18, 9.2), 1.90–2.16 (m, 3 H), 1.58–1.64 (m, 1 H), 1.40–1.46 (m, 1 H); IR (Nujol) 3400, 2900, 2760, 1670, 1540, 1460, 1420, 1380, 1360, 1318, 1275, 1220, 1165, 1105, 1075, 1060, 1010, 960, 915, 880, 840, 800, 735. Anal. Calcd for $C_7H_{13}ClN_2O$: C, 47.59; H, 7.37; N, 15.86. Found: C, 47.36; H, 7.27; N, 15.62.

8-*endo*-Amino-2-azabicyclo[3.3.0]octan-3-one Hydrochloride (53). The mixture of azido lactam **42** and unsaturated lactam **46** (see above) was hydrogenated according to the general procedure: yield 10 mg of **53**, mp 183–185 °C; ^{1}H NMR (D_2O, 400 MHz) 4.13 (app t, 1 H, J = 5.5), 3.30–3.37 (m, 1 H), 2.86–2.94 (m, 1 H), 2.57 (dd, 1 H, J = 18, 10), 2.00 (dd, 1 H, J = 18, 5), 1.83–1.88 (m, 1 H), 1.65–1.74 (m, 1 H), 1.43–1.60 (m, 2 H); IR (Nujol) 3400, 2920, 2850, 1660, 1480, 1420, 1380, 1330, 1270, 1190, 1160, 1095, 1070, 1030, 900, 930.

2-Azabicyclo[3.3.0]octan-3-one (49). The hydrogenation of the mixture of **42** and **46** (see above) gave, in addition to the amino lactam **53**, 26 mg (95%) of saturated lactam **49** as an oil. The structure of **49** was confirmed by independent reduction of pure **46**, which gave the same compound in 98% yield: ^{1}H NMR (400 MHz) 7.68–7.79 (br s, 1 H), 4.17 (s, 1 H), 2.67–2.85 (m, 2 H), 2.12 (d, 1 H, J = 18), 1.60–1.77 (m, 4 H), 1.49–1.53 (m, 2 H); IR (film) 3260, 2950, 2855, 1690, 1470, 1455, 1438, 1420, 1380, 1325, 1305, 1270, 1180, 1140, 1100, 1045, 910, 855.

5-[2,2-Bis(ethoxycarbonyl)ethyl]-2-pyrrolidinone (54). Diethyl malonate (32.2 μL, 0.215 mmol) was added to a stirred suspension of oil free sodium hydride (5.7 mg, 0.24 mmol) in 1 mL of DMF. After gas evolution ceased (about 10 min) a solution of 48 mg (0.215 mmol) of iodo lactam **3** in 1 mL of DMF was added in one portion, and the resulting mixture was stirred for 12 h at room temperature. The reaction mixture was concentrated to a residue, which was partitioned between 1 mL of saturated aqueous sodium bicarbonate and 3 mL of dichloromethane. The aqueous phase was washed with three additional 3-mL portions of dichloromethane, and the combined organic extracts were dried, concentrated, and chromatographed by using 1:1 ether/petroleum ether as the eluant, affording 51 mg (92%) of **54** as an oil: ^{1}H NMR (200 MHz) 6.10–6.15 (br s, 1 H), 4.23 (q, 4 H, J = 8), 3.65–3.70 (m, 1 H), 3.38 (t, 1 H, J = 8), 2.25–2.37 (m, 3 H), 2.00–2.12 (m, 2 H), 1.70–1.80 (m, 1 H), 1.26 (t, 6 H, J = 8); IR (film) 3200, 2960, 2930, 2850, 1730, 1690, 1460, 1440, 1420, 1365, 1300, 1260, 1235, 1175, 1155, 1095, 1025, 860, 800.

5-[2-(Ethoxycarbonyl)-3-oxobutyl]-2-pyrrolidinone (55). By the procedure for **54**, 57 μL (0.444 mmol) of ethyl acetoacetate gave 52 mg (52%) of **55** as a roughly equal mixture of diastereomers: ^{1}H NMR (400 MHz) 6.30–6.40 (br s, 1 H), 4.23 (app sextet, 2 H, J = 7), 3.82–3.92 (m, 1 H), 3.16–3.26 (m, 2 H), 2.30–2.49 (m, 5 H), 2.26 (s, 1.5 H), 2.21 (s, 1.5 H), 1.27 (t, 1.5 H, J = 7), 1.31, t, 1.5 H, J = 7); IR (film) 3250, 2980, 2940, 1740, 1720, 1690, 1460, 1420, 1360, 1290, 1210, 1145, 1100, 1045.

[(2-Oxopyrrolidin-5-yl)methyl]triphenylphosphonium Iodide (56). A mixture of 100 mg (0.44 mmol) of iodo lactam **3**, 1.16 g (4.44 mmol) of triphenylphosphine, and 5 mL of DMF was heated at 100 °C for 15 h. The reaction mixture was cooled, concentrated to a residue, and partitioned between 100 mL of ether and 100 mL of water. The aqueous phase, which contained the product, was washed with two additional portions of ether to removed excess triphenylphosphine and then concentrated to a residue. Crystallization from ethanol/ether gave 158 mg (73%): mp 211–213 °C; ^{1}H NMR (400 MHz, D_2O) 7.55–7.75 (m, 15 H), 4.11–4.15 (app quint, 1 H, J = 5), 3.62 (td, 1 H, J = 16.2, 6.3), 3.49 (td, 1 H, J = 16, 9), 2.21–2.29 (m, 1 H), 2.07–2.15 (m, 1 H), 1.96–2.04 (m, 1 H), 1.54–1.60 (m, 1 H).

General Procedure for Acetoxy Lactams. For a 0.1–0.5-mmol scale, silver trifluoroacetate (1.5 equiv) was added in one portion to a stirred solution of the iodo lactam (1 equiv) and 1 equiv of water in nitromethane at 0 °C. During the next 1–3 h at 0 °C, the formation of insoluble silver iodide was observed. The reaction mixture was filtered through Celite, concentrated to a residue, and dissolved in pyridine (about 2 mL). Acetic anhydride (2 equiv) was added, and the solution was stirred for 12 h. Aqueous sodium bicarbonate was added, and the resulting mixture was extracted with dichloromethane (3 × 5 mL). The organic layer was dried, concentrated, and chromatographed by using 1:1 ether/petroleum ether as the eluant. The resulting acetoxy lactam normally crystallized from ether solution. The (known) unsaturated lactam and/or unsaturated amide, when present as a byproduct, eluted after the acetoxy lactam.

5-(Acetoxymethyl)-2-pyrrolidinone (58):[40] yield 56 mg (80%) of an oil: ^{1}H NMR (400 MHz) 6.30–6.40 (br s, 1 H), 4.17 (app quint, 1 H, J = 7.4), 3.80 (d, 2 H, J = 7.7), 2.34 (dd, 2 H, J = 12, 7.6), 2.21–2.28 (m, 1 H), 2.06 (s, 3 H), 1.77–1.83 (m, 1 H); IR (film) 3300, 2950, 2920, 2840, 1720, 1680, 1460, 1435, 1420, 1370, 1235, 1050, 975, 795. Anal. Calcd for $C_7H_{11}NO_3$: C, 53.50; H, 7.01; N, 8.92. Found: C 53.21; H, 7.05; N, 8.50.

8-*exo*-Acetoxy-3-oxo-2-azabicyclo[3.3.0]octane (59): yield 24 mg (32%), mp 63–64 °C: ^{1}H NMR (400 MHz) 5.89–5.95 (br s, 1 H), 4.69–4.72 (m, 1 H), 3.80 (d, 1 H, J = 8), 2.90–2.94 (m, 1 H), 2.58 (dd, 1 H, J = 18, 10), 2.07–2.14 (m, 1 H), 2.05 (s, 3 H), 1.98–2.03 (m, 1 H), 1.73–1.81 (m, 1 H), 1.48–1.61 m, 1 H); IR (Nujol) 3240, 2955, 2870, 1735, 1695, 1450, 1425, 1380, 1250, 1200, 1150, 1110, 1085, 1030, 980, 915. Anal. Calcd for $C_9H_{13}NO_3$: C, 59.02; H, 7.10; N, 7.65. Found: C, 58.94; H, 7.09; N, 7.53. The unsaturated lactam **46** and the unsaturated amide **12** were also isolated from this reaction (46 and 22%, respectively).

7-Acetoxy-2-oxo-2,3,3aα,4,5,6,7β,7aα-octahydroindole (60): yield 31 mg (42%), mp 78–80 °C: ^{1}H NMR (400 MHz) 5.80–5.85 (br s, 1 H), 4.63–4.66 (m, 1 H), 3.45 (app t, 1 H, J = 7), 2.66–2.77 (m, 1 H), 2.25 (dd, 1 H, J = 16.6, 8), 2.21 (dd, 1 H, J = 16.6, 10), 2.05 (s, 3 H), 1.91–1.94 (m, 1 H), 1.50–1.72 (m, 4 H), 1.30–1.48 (m, 1 H); IR (Nujol) 3200, 2950, 2860, 1735, 1680, 1460, 1438, 1385, 1370, 1325, 1250, 1240, 1045, 975, 955, 810, 735. Anal. Calcd for $C_{10}H_{15}NO_3$: C, 60.91; H, 7.61; N, 7.11. Found: C, 60.62; H, 7.64; N, 6.76. The unsaturated lactam **47** and the unsaturated amide

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14 were also isolated from this reaction as a mixture representing 55% yield.

2,7-Dioxo-2,3,3aα,4,5,6,7,7aα-octahydroindole (61). A solution of 50 mg of the crude hydroxy lactam, prepared as in the synthesis of acetoxy lactam **60**, in 1 mL of dichloromethane was oxidized with pyridinium chlorochromate following the procedure previously reported.[29] Chromatography using 1:1 ether/petroleum ether as the eluant gave keto lactam **61** (35 mg, 71% yield) as an oil: ^{1}H NMR (400 MHz) 5.95–6.15 (br s, 1 H), 3.96 (d, 1 H, J = 7), 3.05–3.15 (m, 1 H), 2.30–2.45 (m, 2 H), 1.94–2.08 (m, 2 H), 1.47–1.85 (m, 4 H); IR (film) 3400, 2940, 2860, 1720, 1680, 1460, 1375, 1320, 1270, 1230, 1210, 1160, 1140, 1080, 910, 810, 735; CI-MS 154 (M + 1).

7-Acetoxy-2-oxo-2,3,3aα,4,5,6,7a,7aα-octahydroindole (62). A solution of 34 mg (0.22 mmol) of keto lactam **61** in 1 mL of THF was reduced with L-Selectride (Aldrich) following the published procedure.[29] The crude hydroxy lactam was acetylated as for **60** and chromatographed to produce 31 mg (70% yield from **61**) of **62**, mp 140–141 °C: ^{1}H NMR (400 MHz) 5.53–5.54 (br s, 1 H), 4.95–4.98 (m, 1 H), 3.88 (app t, 1 H, J = 4.7), 3.08 (s, 3 H), 2.42–2.47 (m, 2 H), 1.67–1.77 (m, 3 H), 1.22–1.49 (m, 4 H); IR (film) 3200, 2900, 2850, 1725, 1690, 1435, 1380, 1320, 1260, 1235, 1040, 980, 770. Anal. Calcd for $C_{10}H_{15}NO_3$: C, 60.91; H, 7.61; N, 7.11. Found: C, 60.73; H, 7.44; N, 6.88.

General Procedure for Conjugate Additions. For a 0.1–1.0-mmol scale, a solution of iodo lactam **3** (1 equiv) in THF was added to a stirred suspension of oil free sodium hydride (1 equiv) in THF at −20 °C. After gas evolution ceased, a solution of the Michael acceptor (3 equiv) in THF was added at −20 °C, and the reaction mixture was allowed to warm to room temperature over 30 min. Sodium bicarbonate was added, and the aqueous phase was extracted with four portions of ethyl acetate. The combined organic extracts were dried, concentrated, and chromatographed by using 1:1 ether/petroleum ether as the eluant to afford the products.

2,3-Bis(methoxycarbonyl)-8-oxo-5,6,7,8-tetrahydro-4*H*-pyrrolizine (64): yield 30.5 mg (95%) of an oil: ^{1}H NMR (200 MHz) 4.76–4.81 (app quint, 1 H, J = 5), 4.17 (s, 3 H), 4.08 (s, 3 H), 3.57 (dd, 1 H, J = 11, 4), 3.45 (t, 1 H, J = 10), 2.75–2.90 (m, 3 H), 2.35–2.37 (m, 1 H); IR (film) 2950, 2850, 1735, 1645, 1440, 1400, 1360, 1275, 1245, 1220, 1180, 1165, 1100, 1025, 890, 800, 780, 695.

2,3-Bis(methoxycarbonyl)-8-oxo-3,4,5,6,7,8-hexahydro-2*H*-pyrrolizine (65): yield 11 mg of a high R_f isomer and 11 mg of a mixture of three isomers (about 3:2:1) of lower R_f, total 70%. ^{1}H NMR of high R_f isomer (200 MHz) 4.48 (app t, 1 H, J = 8), 3.72 (s, 3 H), 3.70 (s, 3 H), 3.42 (dd, 1 H, J = 12, 2.3), 3.19–3.31 (m, 2 H), 2.92–3.19 (m, 1 H), 2.25–2.59 (m, 3 H), 1.77–1.88 (m, 1 H); IR of high R_f isomer (film) 2945, 2850, 1735, 1690, 1435, 1415, 1360, 1265, 1225, 1200, 1175, 1090, 1010, 900, 850, 810. Partial ^{1}H NMR of mixture of lower isomers (400 MHz) 3.73 and 3.68, 3.72 and 3.70, 3.74 and 3.77 (methyl singlets for 3:2:1 isomers, respectively); the IR spectrum of the lower isomers closely resembles that of the higher isomer; CI-MS 424 (M + 1).

2-(Ethoxycarbonyl)-8-oxo-3,4,5,6,7,8-hexahydro-2*H*-pyrrolizine (66): yield 119 mg (68%) of a roughly 1:1 mixture of two diasteriomers: ^{1}H NMR (200 MHz) 4.13 (app quint, 2 H, J = 7.1), 3.13–3.98 (m, 3 H), 2.00–2.86 (m, 4 H), 1.47–1.95 (m, 3 H), 1.27 (t, 1.5 H, J = 7.1), 1.25 (t, 1.5 H, J = 8); IR (film) 2960, 2930, 2850, 1735, 1690, 1455, 1420, 1375, 1280, 1250, 1180, 1100, 1030, 855; CI-MS 198 (M + 1).

1-[(*E*)-2-(Phenylsulfonyl)ethenyl]-5-(iodomethyl)-2-pyrrolidinone (67): yield 96 mg (79%), mp 123–124 °C (ether): ^{1}H NMR (200 MHz) 7.86–7.95 (m, 2 H), 7.51–7.72 (m, 4 H), 5.94 (d, 1 H, J = 14), 3.93–4.03 (m, 1 H), 3.14–3.34 (m, 2 H), 2.61–2.75 (m, 1 H), 2.02–2.52 (m, 3 H); IR (Nujol) 2940, 2900, 2860, 1715, 1610, 1480, 1440, 1375, 1295, 1255, 1180, 1140, 1080, 975, 910, 840, 825, 780, 750, 730, 680.

1-[(*Z*)-2-(Phenylsulfonyl)ethenyl]-5-(iodomethyl)-2-pyrrolidinone (68): yield 169 mg (70%), mp 207–210 °C (ether): ^{1}H NMR (200 MHz) 7.87 (d, 2 H, J = 7), 7.53–7.73 (m, 3 H), 7.04 (d, 1 H, J = 10), 5.59 (d, 1 H, J = 10.7), 5.11 (s, 1 H), 3.62 (dd, 1 H, J = 10.4, 6.5), 3.45 (d, 1 H, J = 9.4), 2.61–2.75 (m, 1 H), 2.25–2.58 (m, 2 H), 1.99–2.70 (m, 1 H); IR 2950, 2850, 1725, 1610, 1480, 1445, 1430, 1355, 1290, 1230, 1140, 1085, 1025, 1000, 985, 930, 740, 675. Anal. Calcd for $C_{13}H_{14}INO_3S$: C, 39.9; H, 3.58; N, 3.58; I, 32.48. Found: C, 40.48; H, 3.53; N, 3.42; I, 32.09.

1-[2-(Phenylsulfonyl)ethyl]-5-(iodomethyl)-2-pyrrolidinone (69): yield 15 mg; NMR (400 MHz) 7.88 (d, 2 H, J = 8), 7.50–7.73 (m, 3 H), 3.84–3.93 (m, 1 H), 3.67–3.79 (m, 1 H), 3.58 (app quint, 1 H, J = 7), 3.30–3.44 (m, 3 H), 3.19–3.29 (m, 1 H), 2.39–2.48 (m, 1 H), 2.20–2.26 (m, 1 H), 2.07–2.18 (m, 1 H), 1.73–1.80 (m, 1 H); IR (film) 3060, 2930, 1695, 1580, 1445, 1415, 1305, 1150, 1090, 745, 695; CI-MS 394 (M + 1).

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Registry No. **1**, 6852-94-4; **2**, 100556-54-5; **3**, 5831-75-4; **4**, 100556-55-6; **6**, 1729-32-4; **8**, 28487-09-4; **9**, 100556-63-6; **10**, 28446-58-4; **11**, 74694-50-1; **12**, 72845-09-1; **13**, 100556-58-9; **14**, 100556-65-8; **15**, 100556-57-8; **16**, 87168-54-5; **17**, 100556-60-3; **18**, 100556-59-0; **19**, 100556-66-9; **20**, 100556-62-5; **21**, 100556-61-4; **22**, 115307-09-0; **23**, 115307-10-3; **24**, 115307-11-4; **25**, 51757-85-8; **26**, 100556-56-7; **32**, 100556-64-7; **34**, 92511-12-1; **35**, 3210-08-0; **36**, 3210-36-4; **38**, 113466-82-3; **39**, 113466-90-3; **40**, 115307-12-5; **41**, 113466-85-6; **42**, 113532-06-2; **43**, 113466-84-5; **44**, 113466-86-7; **45**, 10333-14-9; **46**, 113466-88-9; **47**, 113466-87-8; **49**, 72845-14-8; **50**, 113466-89-0; **51**, 115307-13-6; **52**, 113466-91-4; **53**, 113532-07-3; **54**, 115307-14-7; **55** (isomer 1), 115307-15-8; **55** (isomer 2), 115307-16-9; **56**, 115307-17-0; **58**, 60216-38-8; **59**, 115307-18-1; **60**, 115307-19-2; **61**, 115307-20-5; **62**, 115307-21-6; **64**, 115307-22-7; **65** (isomer 1), 115307-23-8; **65** (isomer 2), 115307-24-9; **65** (isomer 3), 115307-25-0; **65** (isomer 4), 115307-26-1; *cis*-**66**, 115307-27-2; *trans*-**66**, 115307-28-3; **67**, 115307-29-4; **68**, 115307-30-7; **69**, 115307-31-8; H_2C=$CHCH_2CO_2H$, 625-38-7; H_2C=$CH(CH_2)_2CO_2H$, 591-80-0; H_2C=$CH(CH_2)_3CO_2H$, 1577-22-6; H_2C=$CHCH(CH_3)CH_2CO_2H$, 1879-03-4; H_2C=$CHCH(Ph)CH_2CO_2H$, 5703-57-1; $PhCH_2OCH_2CH(CH$=$CH_2)CH_2CO_2H$, 115307-32-9; crotonamide, 23350-58-5; dimethyl acetylenedicarboxylate, 762-42-5; dimethyl fumarate, 624-49-7; ethyl acrylate, 140-88-5; *trans*-bis(phenylsulfonyl)ethylene, 963-16-6; *cis*-bis(phenylsulfonyl)ethylene, 963-15-5; phenyl vinyl sulfone, 5535-48-8; 2-(2-cyclopentenyl)acetic acid, 13668-61-6; 2-(2-cyclohexenyl)acetic acid, 3675-31-8; diethyl malonate, 105-53-3; ethyl acetoacetate, 141-97-9.