petroleum ether gave 45 mg of 13, mp 151-152 °C (mixture mp), after recrystallization from cyclohexane. Further elution of the column with a mixture (1:4) of chloroform and petroleum ether gave 350 mg (79%) of 9, mp 211-212 °C (mixture mp), after recrystallization from cyclohexane.

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Supplementary Material Available: Summary of crystal data and intensity collection parameters, a complete list of atomic coordinates, anisotropic displacement coefficients, H atom coordinates and isotropic displacement coefficients, and bond distances and bond angles for 9, 13 and 17 (19 pages). Ordering information is given on any current masthead page.

Development of an Asymmetric Approach to the 3,8-Diazabicyclo[3.2.1]octane Moiety of Quinocarcin via Intermolecular 1,3-Dipolar Cycloadditions of Photochemically Generated Azomethine Ylides

Philip Garner,* Wen Bin Ho, Sunitha K. Grandhee, Wiley J. Youngs,† and Vance O. Kennedy

Department of Chemistry, Case Western Reserve University, Cleveland, Ohio 44106-7078

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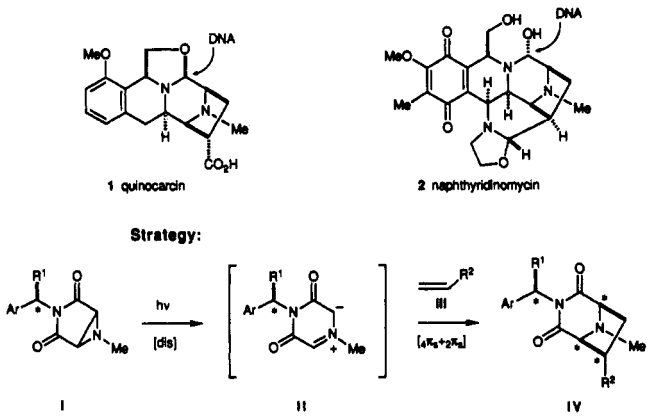
Exploratory work culminating in an enantioselective approach to the DNA-reactive alkaloid quinocarcin (1) is detailed. The key step involves auxiliary-controlled dipolar cycloaddition between photochemically generated azomethine ylides such as 11 and Oppolzer's chiral acryloyl sultam (-)-32 to assemble the 6-exo-substituted 3,8-diazabicyclo[3.2.1]octane core of 1. The synthetic sequence begins with condensation of the benzylamines 3 and maleic anhydride to give the N-alkylated maleimides 6. Triazoline formation (MeN_3) followed by photolytic ($\lambda > 3000$ Å) extrusion of nitrogen leads to the corresponding aziridines 10. Upon irradiation at 2537 Å, these aziridines undergo electrocyclic ring-opening to give azomethine ylides 11, which can be trapped with (-)-32 to give the 6-exo-substituted cycloadduct 33 (diastereoselectivity, ds >25:1). These results stand in sharp contrast to cycloadditions of 11 with (achiral and chiral) acrylate ester dipolarophiles as well as acrylonitrile, which proceed with no appreciable facial selectivity. The expected *re*-face selectivity of (-)-32 was confirmed in one case by X-ray crystallographic analysis of endo-adduct 35a. Removal (and recovery) of the chiral sultam auxiliary can be effected by titanium(IV)-mediated alcoholysis to give ester derivatives of the cycloadducts.

Introduction

Quinocarcin (1) and naphthyridinomycin (2) are potential antitumor antibiotics isolated from *Streptomyces* broths.[1,2] Both of these compounds have been shown to inhibit DNA (and in some systems RNA) synthesis,[3] and the citrate salt of 1 exhibits good activity against a variety of tumor systems.[4] The inhibition of DNA synthesis by 2 appears to occur at the template level via the irreversible and selective binding of these drugs to dG-dC base pairs. Computational studies on quinocarcin support nucleophilic attack of the 2-amino group of guanine onto an imminium species derived from the hemiaminal at C(7).[5] Since the critical DNA-drug interaction (as well as any preceeding recognition step) necessarily involves the combination of chiral molecules, it stands to reason that one of the two possible antipodal forms of the drug (presumably the naturally occurring one) would be more active and/or selective.[6] These considerations provide impetus for the development of asymmetric syntheses of these bioactive molecules and analogues thereof (Scheme I).[7,8]

An attractive strategy for the asymmetric synthesis of 1 and 2 focuses on construction of the 3,8-diazabicyclo-[3.2.1]octane skeleton IV embodied in both targets via the stereocontrolled 1,3-dipolar cycloaddition of an azomethine

Scheme I



ylide II and an olefinic dipolarophile III.[9] If sufficient diastereofacial/topological control could be maintained

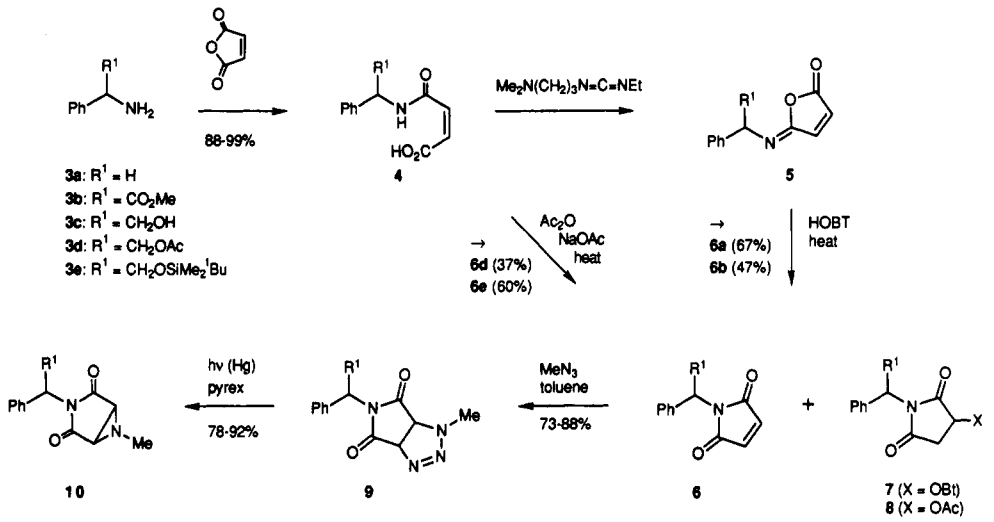
† Address inquiries concerning the X-ray structure determination to this author at the Department of Chemistry, The University of Akron, Akron, OH 44325.

(1) Quinocarcin: Tomita, F.; Takahashi, K.; Shimizu, K. *J. Antibiot.* **1983**, *36*, 463. Takahashi, K.; Tomita, F. *Ibid.* **1983**; *36*, 468. Hirayama, N.; Shirahata, K. *J. Chem. Soc., Perkin Trans. 2* **1983**, 1705.

(2) Naphthyridinomycin: Kluepfel, D.; Baker, H. A.; Piattoni, G.; Sehgal, S. N.; Sidorowicz, A.; Singh, K.; Vezina, C. *J. Antibiot.* **1975**, *28*, 497. Sygusch, J.; Brisse, F.; Hanessian, S.; Kluepfel, D. *Tetrahedron Lett.* **1974**, 4021. Eratta, *Ibid.* **1975**, 170. Cyanocycline A: Zmijewski, M. J., Jr.; Goebel, M. *J. Antibiot.* **1982**, *35*, 524. Hayashi, T.; Noto, T.; Nawata, Y.; Okazaki, H.; Sawada, M.; Ando, K. *Ibid.* **1982**, *35*, 771. SF-1739 HP/naphthocyanidine: Itoh, J.; Omoto, S.; Kodama, Y.; Hisamatsu, T.; Niida, T.; Ogawa, Y. *Ibid.* **1982**, *35*, 642.

0022-3263/91/1956-5893$02.50/0

Scheme II



during this cycloaddition, the resulting adduct IV would possess four of the six (or eight) stereogenic centers present in 1 (or 2) and provide a suitable template for introduction of the remaining functionality and chirality as well. Generation of cyclic azomethine ylides such as II was to be accomplished by means of a photochemically initiated electrocyclic opening of a precursor aziridine I.[10] In this paper, we detail the results of our exploratory work in this area[11] culminating in an enantioselective approach to systems such as IV ("exo" R^2). These results set the stage for a concise asymmetric synthesis of quinocarcin (1) and related substances.[12,13]

Results and Discussion

The first order of business involved the preparation of a series of aziridines **10a–e** corresponding to substructure I. To simplify matters at this stage, we restricted ourselves to commercially available benzylamines (**3a–c**) or simple derivatives thereof (**3e**) as starting materials. These amines were first converted to the maleamic acids **4** in nearly quantitative yield by acylation with maleic anhydride. However, attempts to extend a published maleimide synthesis[14] involving Ac_2O-mediated dehydration to the more highly substituted *N*-alkylmaleamic acids **4b–e** were disappointing in terms of both yield and reproducibility. It was little consolation to learn that at least three other groups had been experiencing similar difficulties in preparing *N-sec*-alkylmaleimides.[15]

After considerable experimentation, two sets of reaction conditions were finally arrived at that did afford acceptable yields of the required maleimides **6**. Method A involves quantitative formation of the (kinetically favored) isoimide **5** with a water-soluble carbodiimide (WSC) and subsequent isomerization to the (thermodynamically favored) male-

(3) Quinocarcin: Tomita, F.; Takahashi, K.; Tamaoka, T. *J. Antibiot.* **1984**, *37*, 1268. Kanamaru, R.; Konishi, Y.; Ishioka, C.; Kakuta, H.; Sato, T.; Ishikawa, A.; Asamura, M.; Wakui, A. *Cancer Chemother. Pharmacol.* **1988**, *22*, 197. Naphthyridinomycin: Zmijewski, M. J., Jr.; Miller-Hatch, K.; Goebel, M. *Antimicrob. Agents Chemother.* **1982**, *21*, 787. Zmijewski, M. J., Jr.; Miller-Hatch, K.; Mikolajczak, M. *Chem.-Biol. Interact.* **1985**, *52*, 361.

(4) Chaing, C.-D.; Kanzawa, F.; Matsushima, Y.; Nakano, H.; Nakagawa, K.; Takahashi, H.; Terada, M.; Morinaga, S.; Tsuchiya, R.; Sasaki, Y.; Saijo, N. *J. Pharmacobio.-Dyn.* **1987**, *10*, 431. Fujimoto, K.; Oka, T.; Morimoto, M. *Cancer Res.* **1987**, *47*, 1516. Inoue, S.; Kubota, T.; Ohishi, T.; Kuzuoka, M.; Oka, S.; Shimoyama, Y.; Kikuyama, S.; Ishibiki, K.; Abe, O. *Keio J. Med.* **1988**, *37*, 355. Inaba, S.; Shimoyama, M. *Cancer Res.* **1988**, *48*, 6029.

(5) Hill, G. C.; Wunz, T. P.; Remers, W. A. *J. Comput.-Aided Mol. Des.* **1988**, *2*, 91.

(6) See, for example: Boger, D. L.; Coleman, R. S.; Invergo, B. J.; Sakya, S. M.; Ishizaki, T.; Munk, S. A.; Zarrinmayeh, H.; Kitos, P. A.; Thompson, S. C. *J. Am. Chem. Soc.* **1990**, *112*, 4623. Hurley, L. H.; Warpehoski, M. A.; Lee, C.-S.; McGovren, J. P.; Scahill, T. A.; Kelly, R. C.; Mitchell, M. A.; Wicnienski, N. A.; Gebhard, I.; Johnson, P. D.; Bradford, V. S. *Ibid.* **1990**, *112*, 4633.

(7) Total synthesis of (±)-quinocarcinol: Danishefsky, S.; Harrison, P. J.; Webb, R. R., II; O'Neill, B. T. *J. Am. Chem. Soc.* **1985**, *107*, 1421. Total synthesis of (±)-quinocarcin: Fukuyama, T.; Nunes, J. J. *Ibid.* **1988**, *110*, 5196. Related synthetic work: Williams, R. M.; Ehrlich, P. P.; Zhai, W., Hendrix, J. *J. Org. Chem.* **1987**, *52*, 2615. Saito, H.; Hirata, T. *Tetrahedron Lett.* **1987**, *28*, 4065. Enantiospecific approaches: Saito, S.; Matsuda, F.; Terashima, S. *Ibid.* **1988**, *29*, 6301. Saito, S.; Tanaka, K.; Nakatani, K.; Matsuda, F.; Terashima, S. *Ibid.* **1989**, *30*, 7423. Lessen, T. A.; Demko, D. M.; Weinreb, S. M. *Ibid.* **1990**, *31*, 2105. Also see refs 11 and 13.

(8) Total synthesis of (±)-cyanocycline A: Evans, D. A.; Illig, C. R.; Saddler, J. C. *J. Am. Chem. Soc.* **1986**, *108*, 2478. Fukuyama, T.; Li, L.; Laird, A. A.; Frank, R. K. *Ibid.* **1987**, *109*, 1587. Related synthetic work: Parker, K. A.; O'Fee, R. *Ibid.* **1983**, *105*, 654. Parker, K. A.; Cohen, I. D.; Babine, R. E. *Tetrahedron Lett.* **1984**, *25*, 3543. Danishefsky, S.; O'Neill, B. T.; Springer, J. P. *Ibid.* **1984**, *25*, 4203. Danishefsky, S.; O'Neill, B. T.; Taniyama, E.; Vaughan, K. *Ibid.* **1984**, *25*, 4199. Evans, D. A.; Biller, S. A. *Ibid.* **1985**, *26*, 1911. *Ibid.* **1985**, *26*, 1907. Fukuyama, T.; Frank, R. K.; Laird, A. A. *Ibid.* **1985**, *26*, 2955. Fukuyama, T.; Laird, A. A. *Ibid.* **1986**, *27*, 6173.

(9) Reviews of azomethine ylide chemistry: Lown, J. W. In 1,3-Dipolar Cycloaddition Chemistry; Padwa, A., Ed.; Wiley-Interscience: New York, 1984; Vol 1, p 653. Tsuge, O.; Kanemasa, S. *Adv. Heterocycl. Chem.* **1989**, *45*, 231.

(10) (a) Huisgen, R.; Mäder, H. *Angew. Chem., Int. Ed. Engl.* **1969**, *8*, 604. (b) Oida, S.; Ohki, E. *Chem. Pharm. Bull.* **1968**, *16*, 764.

(11) Preliminary communications: Garner, P.; Sunitha, K.; Shanthilal, P. *Tetrahedron Lett.* **1988**, *29*, 3525. Garner, P.; Ho, W. B. *J. Org. Chem.* **1990**, *55*, 3973.

(12) Early biosynthetic studies on naphthyridinomycin (Zmijewski, M. J., Jr.; Palaniswamy, V. A.; Gould, S. J. *J. Chem. Soc., Chem. Commun.* **1985**, 1261) suggested that we should be targeting the mirror images of structures **2** (and by analogy **1**—see also ref 5). Recent synthetic work from both Evans' and Fukuyama's groups provide firm chemical evidence on this point: Illig, C. R. The Total Synthesis of (±)-Cyanocycline A and (+)-Cyanocycline A. Ph.D. Dissertation, Harvard University, 1987. Fukuyama, T.; Li, L. Total Synthesis of (+)-Naphthyridinomycin. 21st ACS Central Regional Meeting; May 31–June 2, 1989, Cleveland, OH; American Chemical Society: Washington, DC, 1989; ORGN 272. As will become evident, the protocol outlined in this paper is equally amenable to the enantioselective synthesis of structures corresponding to **ent-1** as well.

(13) For a related approach to the 3,8-diazabicyclo[3.2.1]octane portion of quinocarcin based on 1,3-dipolar cycloaddition to achiral 2-oxidopyrazinium species, see: Kiss, M.; Russell-Maynard, J.; Joule, J. A. *Tetrahedron Lett.* **1987**, *28*, 2187. Allway, P. A.; Sutherland, J. K.; Joule, J. A. *Ibid.* **1990**, *31*, 4781.

(14) Mehta, N. B.; Phillips, A. P.; Lui, F. F.; Brooks, R. E. *J. Org. Chem.* **1960**, *25*, 1012.

(15) Miller, S. A.; Chamberlin, A. R. *J. Org. Chem.* **1989**, *54*, 2505. Meyers, A. I.; Lefker, B. A.; Sowin, T. J.; Westrum, L. J. *Ibid.* **1989**, *54*, 4243. Baldwin, S. W. (Duke University). Personal communication.

Scheme III

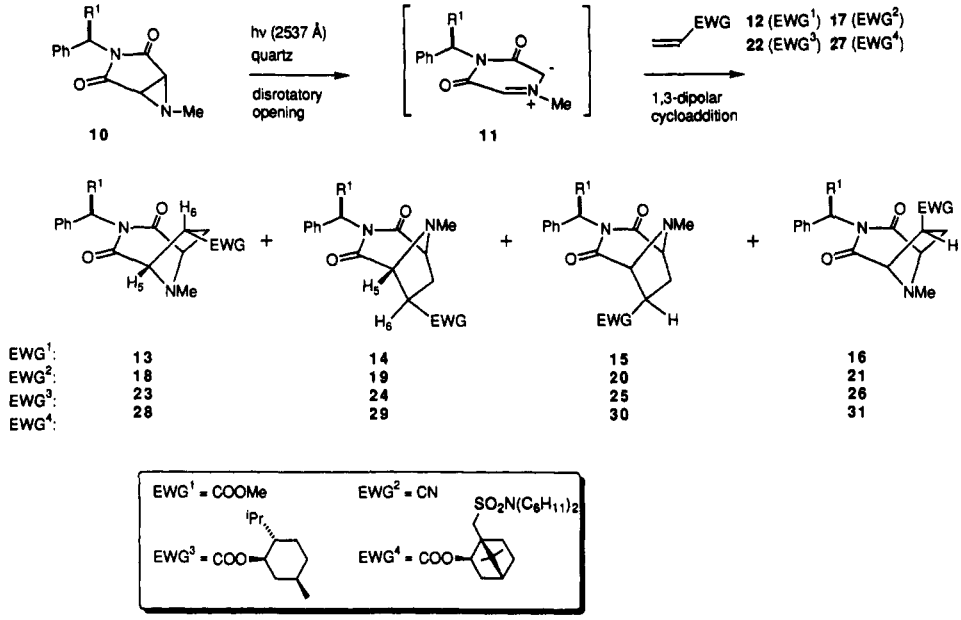


Table I. 1,3-Dipolar Cycloadditions with Acrylate and Acrylonitrile Dipolarophiles

entry	aziridine	dipolarophile	exo adducts	% yield	ratio (ds)	endo adducts	% yield	ratio (ds)
1	**10a**	**12**	**13a/14a**[a]	50		**15a/16a**[a]	11	
2	(±)-**10b**	**12**	(±)-**13b**/(±)-**14b**	73	1:1			
3	**10d**	**12**	**13d/14d**	60	1:1			
4	**10a**	**17**	**18a/19a**	22 (25)[b]		**20a/21a**	36 (40)[b]	
5	**10a**	(−)-**22**	**23a/24a**	64	1:1	**25a/26a**	15	1:1
6	**10a**	(−)-**27**	**28a/29a**	57	1:1			

[a] Enantiomers (**14a** ≡ **ent-13a** and **16a** ≡ **ent-15a**). [b] Corrected yield based on recovered aziridine.

imide **6** by heating the crude isoimides in the presence of the transacylation catalyst, hydroxybenzotriazole (HOBt). Minor amounts of **7**, resulting from formal addition of HOBt across the double bond, were formed during this reaction. The second method (B) resulted from our fine tuning the known Ac_2O-mediated dehydration conditions cited above. Here again, conjugate addition of AcOH across the electron-deficient double bond to give **8** is a side reaction with our *N-sec*-alkyl substrates **4** but is minimized by keeping the concentration of **4** at ≈0.1 M (rather than 2 M as reported in ref 14). The Ac_2O-mediated dehydration of substrate **4c** was accompanied by acetylation of the primary alcohol to give **6d**. Both of these procedures were suitable for large-scale work and reproducibly afforded reasonable yields of the desired maleimides **6** after chromatography starting from the amines **3** (Scheme II).[16]

Treatment of the maleimides **6** with a stock solution of methyl azide[17] in toluene at ambient temperatures resulted in the clean formation of the triazolines **9**. With the chiral maleimides **6b–e** ($R^1 \neq H$), **9b–e** were obtained as mixtures of diastereomers—an observation that we took as a possible foreboding of the inability of the benzylic stereocenter to influence facial selectivity during bimolecular cycloadditions (vide infra). Irradiation of the triazolines **9** using a medium-pressure Hanovia Hg lamp through Pyrex resulted in the clean formation of the aziridines **10**.[18]

These photochemical conditions for the extrusion of N_2 were necessitated by our observation that thermolysis of **9a** resulted in the formation of an isomeric enamine (structure not shown) in addition to the desired aziridine **10a**. With a secure route to the aziridines **10** (≡**I**) in hand, we could now focus on the key photochemically initiated 1,3-dipolar cycloaddition reaction.

Photolysis of aziridines as a means of generating azomethine ylides, while known for some time, has been limited to a few mechanistically oriented reports.[9] Synthetic studies targeting pyrrolidine-containing molecules have generally relied upon thermal methods for azomethine ylide generation.[19] By design, our substrates **10** bore a very close resemblance to one that Huisgen had used to investigate the symmetry controlled nature of electrocyclic ring openings of aziridines.[10a] His photolysis conditions consisted of direct irradiation in aprotic media with a high-pressure mercury arc through quartz with the resulting azomethine ylide being trapped with dimethyl acetylenedicarboxylate and norbornene.

Accordingly, irradiation of the aziridines **10a**, **b**, and **d** at 2537 Å in dioxane resulted in the generation of azomethine ylides **11a**, **b**, and **d**, which underwent clean 1,3-dipolar cycloaddition with electron-withdrawing group (EWG) substituted dipolarophiles (Scheme III, Table I). With methyl acrylate (**12**), the preferential formation of the exo adducts **13/14** was observed, though small amounts of the endo adducts **15a/16a** could be detected in the case

(16) Method A appears to be the milder of the two as evidenced by the fact that the phenylglycine-derived maleimide **6b** was found to have undergone less racemization (45% ee by chiral LSR NMR analysis) than when prepared according to method B (0% ee).

(17) Kovacic, P.; Russell, R. L.; Bennett, R. P. *J. Am. Chem. Soc.* **1964**, *86*, 1588. Gaseous MeN_3 prepared according to this reference was passed through toluene at −78 °C to provide a stock solution (approximately 20% by weight) that could also be assayed by ^1H NMR.

(18) Scheiner, P. *J. Org. Chem.* **1965**, *30*, 7.

(19) For a recent review of pyrrolidine construction via [3 + 2] cycloadditions with an emphasis on application to natural product synthesis, see: Pearson, W. H. In *Studies in Natural Product Chemistry*; Atta-Ur-Rahman, Ed.; Elsevier: Amsterdam, 1988; Vol. 1, Stereoselective Synthesis (Part A), p 323.

Scheme IV

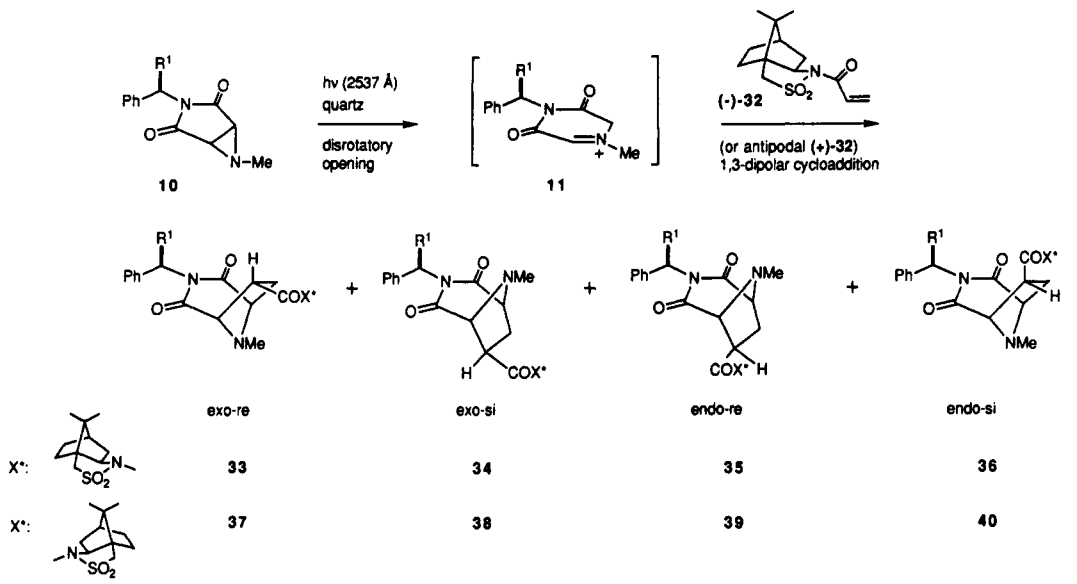


Table II. 1,3-Dipolar Cycloadditions with Chiral Acryloyl Sultam Dipolarophiles

entry	aziridine	dipolarophile	exo adducts	% yield	ratio (ds)	endo adducts	% yield	ratio(ds)
1	**10a**	(−)-**32**[a]	**33a/34a**	39 (42)[b]	>25:1	**35a/36a**	16 (17)[c]	>25:1
2	(±)-**10b**	(−)-**32**[a]	**[33b + ent-38b]/[34b + ent-37b]**	61 (69)[b]	>25:1			
3	**10d**	(−)-**32**[a]	**33d/34d**	58 (65)[b]	>25:1			
4	**10d**	(+)-**32**[a]	**38d/37d**	55 (62)[b]	>25:1			
5	**10e**	(−)-**32**[a]	**33e/34e**	45 (55)[c]	>25:1			
6	**10e**	(+)-**32**[a]	**38e/37e**	46 (56)[c]	>25:1			
7	**10e**	(+)-**32**[d]	**38e/37e**	53 (60)[c]	>25:1			

[a] Portionwise addition of dipolarophile every 30 min. [b] Corrected yield based on recovered aziridine. [c] Corrected yield based on unreacted aziridine in crude ^{1}H NMR spectrum. [d] Continuous slow addition of dipolarophile solution. (See text for details.)

of the "benzylic unsubstituted" substrate **10a**. On the other hand, the endo adducts **20/21** were favored over **18/19** when **11a** was trapped with acrylonitrile (**17**).

The exo/endo ratios appear to correlate with the size of the imide and dipolarophile substituents (vide infra). The diastereomeric exo cycloadducts **13b,d** and **14b,d** were found to be inseparable by flash chromatography and were therefore analyzed as mixtures, their ratios (ds = diastereoselectivity) in each case being determined by careful integration of resolvable ^{1}H NMR signals (see Experimental Section). The topological sense of cycloaddition (that is exo vs endo) was readily determined for each cycloadduct by inspection of the corresponding ^{1}H NMR signal for H-5, which appeared as a singlet for the exo adducts ($\angle$ = 90°) and a doublet ($^3J_{5,6}$ = 7 Hz) for the endo adducts ($\angle$ = 0°).

From these preliminary experiments it was concluded that this 1,3-dipolar cycloaddition approach to the 3,8-diazabicyclo[3.2.1]octane core of **1** (≡ 6-exo-substituted IV) outlined above was viable with ester-activated dipolarophiles. Unfortunately, it was also apparent that those cycloadditions involving the chiral azomethine ylides **11b** and **11d** had proceeded with no appreciable diastereofacial selectivity. In other words, the benzylic stereocenter in II ($R^1 \neq H$) was unable to influence which face of the prochiral olefin III would be attacked by the azomethine ylide.

One possible solution to this dilemma involved rendering the dipolarophile III chiral by virtue of R^2 so that the desired *exo-re* mode of addition would take place preferentially because of conformational biases inherent in the dipolarophile itself.[20] For target **1**, which incorporates the 6-exo carboxylate function,[21] this would amount to identifying a suitable chiral acrylic acid derivative. There were at least two potential problems associated with this plan at the time of its conception. First, the chiral acrylates and/or acrylimides that exhibited high facial selectivity during thermal Diels–Alder cycloadditions were known to require Lewis acids to fix their transition-state conformations and enhance their reactivity. Second, and perhaps more importantly, the behavior of such auxiliaries (with or without Lewis acid additives) under the photochemical conditions used to generate azomethine ylides **11** could not be predicted with certainty.

While the chiral acrylates **22** and **27**, derived from menthol and 10-[dicyclohexyl(sulfonylamido)]isoborneol, respectively, did undergo clean cycloaddition to photochemically generated azomethine ylides **11** (Table I, entries 5 and 6), no facial selectivity was observed. These results were in line with experimental work[22] probing non-Lewis acid catalyzed thermal cycloadditions to these same chiral acrylates as well as theoretical studies[23] addressing the conformation-stabilizing role of Lewis acids on simple

(20) For general surveys of the application of chiral auxiliaries to asymmetric cycloadditions, see: Paquette, L. A. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: Orlando, FL, 1984; Vol. 3, Chapter 7. Oppolzer, W. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 876.

(21) For an intramolecular variant of this cycloaddition strategy that can be used to access the 6-endo-formyl substituted diazabicyclo[3.2.1]-octane system of naphthyridinomycin, see: Garner, P.; Sunitha, K.; Ho, W.-B.; Youngs, W. J.; Kennedy, V. O.; Djebli, A. *J. Org. Chem.* **1989**, *54*, 2041.

(22) Curran, D. P.; Kim, B. H.; Piyasena, H. P.; Loncharich, R. J.; Houk, K. N. *J. Org. Chem.* **1987**, *52*, 2137. In this paper, nitrile oxide cycloadditions with (−)-**22** and (+)-**27** were reported to occur with <4% and 56% de, respectively, while the Diels–Alder reaction of cyclopentadiene and (+)-**27** resulted in a 35% de (endo adducts) and a 23% de (exo adducts). Also see: Olsson, T.; Stern, K.; Sundell, S. *Ibid.* **1988**, *53*, 2468.

(23) Loncharich, R. J.; Schwartz, T. R.; Houk, K. N. *J. Am. Chem. Soc.* **1987**, *109*, 14 and references cited therein.

acrylate esters. Unfortunately, all attempts to incorporate Lewis acids into our photoinduced cycloadditions have been disappointing—presumably due to the adverse effects of complexation on the photophysics of this system.[24]

Thus, we were encouraged by a letter from Curran's laboratory[25] that documented good diastereoselectivity (ds = 9:1) during 1,3-dipolar cycloadditions of Oppolzer's acryloyl sultam **32**[26] and various nitrile oxides. With this chiral dipolarophile, the s-cis rotomer is more stable than the s-trans on steric grounds while the "anti" disposition of the polarized C=O and N → SO_2 groups minimizes an unfavorable dipole–dipole interaction. The partially pyramidalized nitrogen may be responsible for the observed facial selectivity with (–)-**32** since the resulting out-of-plane "bend" of the acrylamide causes the *si*-face of the olefin to be sterically shielded by the methine hydrogen and/or endo sultam oxygen. A stereoelectronic effect involving the nitrogen lone-pair and/or the endo sultam oxygen is also possible.

Irradiation of a dioxane solution containing the aziridine **10a** and 1.5 equiv of the chiral dipolarophile (–)-**32** for 3.5 h led to poor yields of cycloadducts. A comparison of the UV absorption data obtained for **10a**, **12**, **32**, and the cycloadduct eventually identified as **33a** suggested that this result might be due in part to the inherent photoinsensitivity of the reactants and the cycloadducts themselves. At 254 nm, the acryloyl sultam **32** absorbs about 20 times as much light as the acrylate dipolarophiles and about three times as much light as the aziridine **10a**. A control experiment showed that photolysis of a 0.05 M solution of **32** in dioxane for a period of 2 h in the absence of aziridine resulted in its complete decomposition. Furthermore, irradiation of a 0.05 M dioxane solution of the cycloadduct **33a** for 2 h resulted in nondescript decomposition as judged by TLC and only a 31% recovery of unreacted **33a** after chromatography.

We reasoned that the desired reaction might be enhanced if the photolysis could be performed so as to minimize the concentration of dipolarophile **32**. Indeed, when the photolysis of **10a–d** was conducted with (solid) **32** added in 0.2-equiv portions every 30 min until a total of 1.2 equiv was reached, clean cycloaddition was observed (Table II, entries 1–6). The combined (isolated) yield of all cycloadducts produced in each reaction was somewhat substrate dependent but ranged from 45 to 61% with about 6–10% of unreacted **10** being recovered in each case. Prolonged photolysis times did not result in higher yields. Continuous slow addition of a dioxane solution of **32** to a photolyzed solution of **10e** over 2 h resulted in a slightly better yield of **38e** (entry 7). Taken together, these experiments confirm the need to balance dipolarophile concentration and reaction time in order to maximize the yield of cycloadducts. While there is clearly room for improvement, the described procedures do provide a practical means of obtaining synthetically useful yields of sultam-appended cycloadducts.

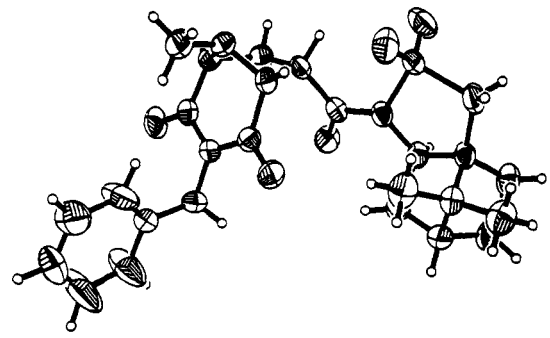


Figure 1. ORTEP plot of **35a**. Thermal ellipsoids are drawn at the 50% probability level with the H atoms in their calculated positions. Atom labeling has been omitted for clarity (see supplementary material).

With the benzylamine-derived aziridine **10a** and (–)-**32**, two products identified as the *exo-re* adduct **33** and *endo-re* adduct **35** were obtained in a ratio of (2.4:1). Only traces of what we believed to be the diastereomeric *exo-si* and *endo-si* addition products **34** and **36** could be detected in unresolved samples of **33** and **35**, respectively. In fact, the dipolarophile facial selectivity associated with all cycloadditions employing **32** was uniformly excellent (ds >25:1) as judged by crude ^1H NMR analysis and in one case by comparison with an independently prepared diastereomeric standard (vide infra). While the endo/exo assignment was readily made by direct inspection of the adducts' proton NMR spectra, the facial selectivity of (–)-**32** in this reaction was presumed to be *re* based on Oppolzer's and Curran's results.[25,27] An X-ray crystallographic analysis of the minor endo adduct confirmed this expectation and unambiguously set its structure as **35** (Figure 1).[28] It should be noted that the eroded exo selectivity observed with **10a** and (–)-32 (versus the acrylate dipolarophiles) was initially of some concern to us since the *endo-re* adduct **35** actually possessed the "wrong" diastereomeric configuration. However, once we turned to the sterically more demanding "benzylic substituted" chiral aziridines **10b**, **d**, and **e** (as required for quinocarcin), the exo mode exclusive.

The usual reductive or basic conditions could not be used for removal of the sultam auxiliary because of the instability of the cyclic imide functionality toward strongly nucleophilic reaction conditions. Fortunately, we found that the cycloadducts could be converted to their corresponding ethyl esters in good yield and the sultam auxiliary efficiently recovered by means of titanium(IV)-mediated alcoholysis (Scheme V).[29] Thus, exposure of adducts **33a,e** and **38e** to 5–8 equiv of $Ti(O^iPr)_4$ in refluxing ethanol led to the isolation of the corresponding ethyl esters **41a,e** and **43e** in 61–75% yield along with 70–90% of the reusable sultam. Alcoholysis of the acetoxymethyl-substituted adducts **33d** and **38d** was accompanied by acetolysis, but the resulting alcohol promoted nonregioselective intramolecular opening of the imide functionality as well. In spite of this particular (substrate-dependent) limitation, we believe that Seebach's transesterification methodology will prove generally useful for removal and recovery of the sultam auxiliary in other contexts as well.[30] Note that

(24) For example, photolysis of **10a** and **22** (2 equiv) in the presence of BF_3·OEt_2 (2 equiv) was sluggish and resulted in the isolation of a (1:1) mixture of **23** and **24**. The possible complexation of BF_3 with the photosubstrate **10a** has not be excluded. For a case where photophysical changes brought on by Lewis acid complexation can be used to advantage, see: Lewis, F. D.; Oxman, J. D.; Huffman, J. C. *J. Am. Chem. Soc.* **1984**, *106*, 466.

(25) Curran, D. P.; Kim, B. H.; Daugherty, J.; Heffner, T. A. *Tetrahedron Lett.* **1988**, *29*, 3555. Curran, D. P.; Heffner, T. A. *J. Org. Chem.* **1990**, *55*, 4585.

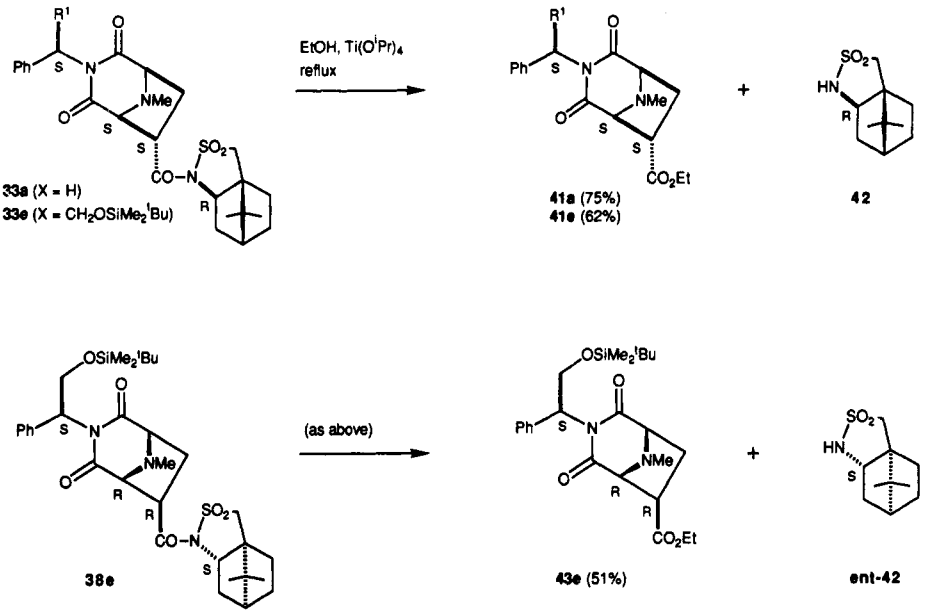
(26) Preparation of **32**: Vandewalle, M.; Van der Eycken, J.; Oppolzer, W.; Vullioud, C. *Tetrahedron* **1986**, *42*, 4035. For a comprehensive review of camphor-derived chiral auxiliaries, see: Oppolzer, W. *Tetrahedron* **1987**, *43*, 1969. (The original article contains printer errors; a corrected version was reprinted in the Errata section of: *Tetrahedron* **1987**, *43*(18).)

(27) Oppolzer, W.; Poli, G.; Starkemann, C.; Bernardinelli, G. *Tetrahedron Lett.* **1988**, *29*, 3559.

(28) **35a** crystallizes from EtOH in the monoclinic space group $P2_1$ (no. 4), with a = 7.1881 (14) Å, b = 13.560 (3) Å, c = 12.540 (3) Å, β = 97.58 (2)°, V = 1211.6 (5) Å, ρ_{calcd} = 1.331 g/cm^3, Z = 2. Standard and direct Fourier methods and least-squares refinement on the basis of 1847 ($F \geq 6.0\ \sigma$) reflections led to a final R = 0.0328.

(29) Seebach, D.; Hungerbühler, E.; Schnurrenberger, P.; Weidmann, B.; Züger, M. *Synthesis* **1982**, 138.

Scheme V



ester **43e** corresponds to the minor diastereomer of reaction **10e** + (−)-**32** and **41e** corresponds to the minor diastereomer of **10e** + (+)-**32**. This relationship permitted us to set the diastereofacial selectivity of these cycloadditions at >25:1 by simply evaluating the level of cross-contamination by ^{1}H NMR spectroscopy.[31]

Experimental Section

Silica gel TLC plates were visualized with UV illumination followed by charring with either 5% anisaldehyde in (95:5:1) EtOH–AcOH–H_2SO_4 (char A) or 2% vanallin + (98:2) EtOH–H_2SO_4 (char B). Melting points are uncorrected. ^{1}H NMR signal assignments[32] were based on selective homonuclear decoupling experiments while the ^{13}C assignments were based on APT (attached proton test) experiments and proton coupling data. High-resolution mass spectral (HRMS) data are reported in units of *m/e* for M^+ or highest mass fragment derived from M^+.

All reactions were performed under inert (N_2 or Ar), moisture-free atmosphere except when working in aqueous media. Photolyses were performed with either a Canrad-Hanovia 450-W medium-pressure Hg lamp or with low-pressure Hg lamps (2537 Å) in a Rayonet Photochemical Reactor RPR-100. Solvents used for photochemical reactions were spectrophotometric grade; 1,4-dioxane was distilled from sodium–benzophenone under N_2 in a recycling still, and acetonitrile was distilled and stored over 4 Å molecular sieves.

General Procedure for Maleamic Acid Synthesis. A solution of maleic anhydride (1.5 equiv) in dry ether (ca. 0.5 M) was added dropwise to an ice-cold solution of amine **3** (1 equiv) in Et_2O (ca. 0.002 M). After the addition was complete (1.5 h), the resulting suspension was stirred at ambient temperature for 20 h. The white solid was collected and washed twice with ether to give the crude product. This crude solid was partitioned between saturated $NaHCO_3$ solution and ether. The aqueous phase was acidified to pH 1–2 with 5 N HCl in an ice bath then extracted with (1:1) EtOAc–THF. The combined organic layers were dried with Na_2SO_4, filtered, and concentrated to give the maleamic acids **4** as white solids.

(*Z*)-4-[(Phenylmethyl)amino]-4-oxo-2-butenoic acid (4a): 99% yield; mp 137–138.5 °C; IR (KBr) 3340, 3150–2940, 1700, 1630, 1580–1430, 1400 cm^{-1}; ^{1}H NMR (200 MHz, DMSO-d_6) δ 9.39 (br s, 1 H, NH), 7.43–7.23 (m, 5 H, Ph), 6.43 (d, J = 12.5 Hz, 1 H, C*H*CO$_2$H), 6.25 (d, J = 12.5 Hz, 1 H, C*H*CONH), 4.38 (m, 2 H, PhCH$_2$); ^{13}C NMR (50.4 MHz, DMSO-d_6): δ 165.8, 165.1 (CO), 138.0 (Ph), 132.2, 131.5 (CH=CH), 128.4, 127.6, 127.2 (Ph), 42.6 (PhCH$_2$); HRMS *m/e* calcd for $C_{11}H_{10}NO_2$ (M^+ − OH) 188.0712, found 188.0712.

[*S*(*Z*)]-4-[[(Methoxycarbonyl)phenylmethyl]amino]-4-oxo-2-butenoic acid (4b): 92% yield; mp 138–139 °C; $[\alpha]_D$ 253.7° (*c* 1.5, $CHCl_3$); IR ($CHCl_3$) 3390, 3260, 1740, 1725, 1600, 1515 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$, 20 °C) δ 7.73 (br d, J = 6.7 Hz, 1 H, NH), 7.35 (br s, 5 H, Ph), 6.40 (d, J = 12.9 Hz, 1 H, C*H*CO$_2$H), 6.33 (d, J = 12.9 Hz, 1 H, C*H*CONH), 5.57 (d, J = 7.0 Hz, 1 H, PhCH), 3.75 (s, 3 H, OCH$_3$); ^{13}C NMR (50.4 MHz, $CDCl_3$) δ 170.1, 165.5, 165.0 (C=O), 136.7 (*C*HCO$_2$H), 134.6 (Ph), 130.7 (*C*HCONH), 129.2, 127.5 (Ph), 57.2 (PhCH), 53.2 (CO$_2$Me); HRMS *m/e* calcd for $C_{11}H_{10}NO_3$ (M^+ − CO$_2$Me) 204.0661, found 204.0667.

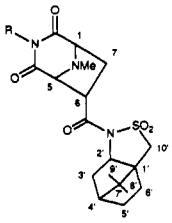
[*S*(*Z*)]-4-[[2-Hydroxy-1-phenylethyl]amino]-4-oxo-2-butenoic acid (4c): 65% yield; $[\alpha]_D$ 118.8° (*c* 1.3, $CHCl_3$); mp 127–128 °C; IR (KBr) 3330 (br), 3220, 1705, 1630, 1550 (br) cm^{-1}; ^{1}H NMR (200 MHz, DMSO-d_6, 90 °C) δ 9.15 (br s, 1 H, NH), 7.43–7.23 (m, 5 H, Ph), 6.56–6.18 (m, 2 H, C*H*=C*H*), 5.21 (m, 0.5 H, $^1/_2$ PhCH), 4.93 (m, 0.5 H, $^1/_2$PhCH), 4.37 (d, J = 6.4 Hz, 1 H, $^1/_2$C*H*$_2$OH), 3.68 (d, J = 6.3 Hz, 1 H, $^1/_2$C*H*$_2$OH); ^{13}C NMR (50.4 MHz, DMSO-d_6, 80 °C): δ 165.6, 165.3, 165.1, 164.8 (CO), 138.4, 137.0 (Ph), 132.5, 132.0, 131.9, 131.7 (CH=CH), 128.4, 128.2, 127.9, 127.6, 127.1, 127.0 (Ph), 65.9, 64.2 (CH$_2$OH), 55.9, 52.0 (PhCH); HRMS *m/e* calcd for $C_{12}H_{13}NO_3$ (M^+ − OH) 218.0817, found 218.0815.

[*S*(*Z*)]-4-[[2-[[(1,1-Dimethylethyl)dimethylsilyl]oxy]-1-phenylethyl]amino]-4-oxo-2-butenoic Acid (4e). The crude gummy product was submitted to the acid–base extraction protocol described above but with 1 N HCl instead of 5 N HCl. The product thus obtained was a colorless oil: 80% yield; $[\alpha]_D$ 97.4° (*c* 1.2, $CHCl_3$); IR ($CHCl_3$) 3420, 3300, 1715, 1600, 1520, 1465 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.36–7.28 (m, 5 H, Ph), 7.22 (br s, 1 H, NH), 6.43 (d, J = 12.8 Hz, 1 H, C*H*CO$_2$H), 6.34 (d, J =

(30) Evans has used this same transesterification methodology to convert analogous carboximides to their corresponding benzyl esters and oxazolidone-based chiral auxiliaries. See: Evans, D. A.; Ellman, J. A.; Dorow, R. L. *Tetrahedron Lett.* **1987**, *28*, 1123.

(31) The use of perhydropyrrolo[1,2-c]imidazol-3-yl β-substituted acrylate as a chiral dipolarophile to control the facial selectivity of N-metalated azomethine ylide cycloaddition was recently reported: Kanemasa, S.; Yamamoto, H. *Tetrahedron Lett.* **1990**, *31*, 3633.

(32) The numbering system used for NMR spectral assignments in the sultam-appendeded cycloadducts is derived from the parent 3,8-diazabicyclo[3.2.1]octane and camphanyl skeleta as follows:



12.8 Hz, 1 H, CHCONH), 5.09 (m, 1 H, PhCH), 4.01 (dd, J = 10.4, 4.3 Hz, 1 H, $^1/_2CH_2OSi$), 3.88 (dd, J = 10.4, 4.3 Hz, 1 H, $^1/_2CH_2OSi$), 0.87 (s, 9 H, $SiC(CH_3)_3$), -0.02 (s, 6 H, $SiMe_2$); ^{13}C NMR (50.4 MHz, $CDCl_3$) δ 165.6, 164.9 (CO), 138.0 (Ph), 137.0, 130.8 (CH=CH), 128.7, 128.1, 126.8 (Ph), 65.5 (CH_2OSi), 55.9 (PhCH), 25.8 ($SiC(CH_3)_3$), 18.2 ($SiC(CH_3)_3$), -5.9, -5.7 ($Si(CH_3)_2$); HRMS, m/e calcd for $C_{14}H_{18}NO_4Si$ (M^+ - $C(CH_3)_3$) 292.1005, found 292.1048.

General Procedures for Maleimide Formation. Method A. A suspension of maleamic acid 4 (1 equiv) and 1-ethyl-3-[3-(dimethylamino)propyl]carbodiimide hydrochloride (1.5–3.0 equiv) in dry CH_2Cl_2 or THF (20 mL/mmol of 4) was stirred at ambient temperature for 20 h. When isoimide formation was complete (NMR analysis), the reaction mixture was partitioned between water and EtOAc. The organic phase was dried with Na_2SO_4 and then filtered and concentrated to give 5 as a gummy product. A solution of crude 5 (1 equiv) and HOBT (0.4 equiv) in dry toluene (12 mL/mmol 5) was heated to 100 °C for 18 h and the reaction was monitored by TLC. The mixture was cooled to room temperature and partitioned between EtOAc and 0.5 N HCl. The organic phase was washed successively with saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4, filtered, and concentrated to a gummy product. This crude material was purified by flash chromatography over silica gel eluting with EtOAc–hexanes to get the desired maleimide 6 along with a small amount of 7.

Method B. A mixture of maleamic acid 4 (1 equiv) and anhydrous NaOAc (0.8 equiv) was heated to 120 °C in an oil bath. Acetic anhydride (8 mL/mmol of 4) was added, and the resulting mixture was stirred at this temperature for 20 h at which time the solvent was removed in vacuo. The residue was partitioned between EtOAc and 0.5 N HCl, and the aqueous layer was extracted two more times with EtOAc. The combined organic solvent was successively washed with saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4, filtered, and concentrated to give the crude gummy product. This material was purified by flash chromatography on silica gel, eluting with EtOAc–hexanes to furnish the desired maleimide product 6 along with a small amount of conjugate addition product 8.

1-(Phenylmethyl)-1*H*-pyrrole-2,5-dione (6a): method A; 67% yield; R_f 0.35 in 3:1 hexanes–EtOAc (char A); mp 68–69 °C; IR ($CHCl_3$) 1710, 1435, 1405 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.29–7.18 (m, 5 H, Ph), 6.62 (s, 2 H, CH=CH), 4.62 (s, 2 H, $PhCH_2$); ^{13}C NMR (50.4 MHz, $CDCl_3$) δ 170.4 (C=O), 136.2 (Ph), 134.2, 128.7, 128.4, 127.8 (C=C, Ph), 41.4 (PhCH); HRMS m/e calcd for $C_{11}H_9NO_2$ (M^+) 187.0633, found 187.0632.

1-(Phenylmethyl)-3-[(benzotriazol-1-yl)oxy]pyrrolidine-2,5-dione (7a): 11% yield; R_f 0.21 in EtOAc (char A); ^1H NMR (200 MHz, $CDCl_3$) δ 8.02–7.29 (m, 9 H, Ph), 5.50 (dd, J = 9.4, 5.7 Hz, 1 H, CHONN=N), 4.77 (d, J = 14.1 Hz, AB, 1 H, $^1/_2PhCH_2$), 4.70 (d, J = 14.1 Hz, AB, 1 H, $^1/_2PhCH_2$), 3.50 (dd, J = 18.5, 5.7 Hz, 1 H, $^1/_2CH_2CO$), 3.36 (dd, J = 18.5, 9.4 Hz, 1 H, $^1/_2CH_2CO$); HRMS m/e calcd for $C_{17}H_{14}N_4O_3$ (M^+) 322.1065, found 322.1065.

(±)-α-Phenyl-2,5-dioxo-1*H*-pyrrole-1-acetic acid, methyl ester (6b): method A; 47% yield; R_f 0.38 in 7:2 hexanes–EtOAc (char A); 45% ee (see text); mp 87–88 °C; IR ($CHCl_3$) 1750, 1720, 1400, 1380 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.46–7.29 (m, 5 H, Ph), 6.71 (s, 2 H, CH=CH), 5.81 (s, 1 H, PhCH), 3.77 (s, 3 H, CO_2CH_3); ^{13}C NMR (50.4 MHz, $CDCl_3$) δ 169.3, 168.3 (C=O), 134.2, 134.1 (Ph, C=C), 129.4, 128.8, 128.5 (Ph), 55.7 (PhCH), 53.0 (CH_3); HRMS m/e calcd for $C_{13}H_{11}NO_4$ (M^+) 245.0688, found 245.0687. Anal. Calcd for $C_{13}H_{11}O_4N$: C, 63.67; H, 4.52; N, 5.71. Found: C, 63.24; H, 4.90; N, 5.75.

(±)-α-Phenyl-2,5-dioxo-3-[(benzotriazol-1-yl)oxy]-pyrrolidine-1-acetic acid, methyl ester (7b): 2 diastereomers, 18% yield; R_f 0.05 in (7:2) hexanes–EtOAc (char A); IR (neat) 1740, 1720, 1500, 1455, 1420, 1380 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 8.03–7.33 (m, 9 H, Ph), 5.94 (s, 1 H, PhCH), 5.59 (m, 1 H, CHONN=N), 3.82 (s, 1.5 H, $^1/_2CO_2CH_3$), 3.80 (s, 1.5 H, $^1/_2CO_2CH_3$), 3.68–3.35 (m, 2 H, CH_2CO); ^{13}C NMR (50.4 MHz, $CDCl_3$) δ 171.0, 170.1, 167.4 (CO), 134.5, 132.6, 132.5, 131.3, 129.9, 129.7, 129.2, 128.7, 124.9, 116.1, 110.3 (Ph), 57.2, 57.0 (PhCH), 55.6, 53.3 (CHONN=N, CO_2CH_3), 33.9, 33.8 (CH_2CO); HRMS m/e calcd for $C_{13}H_{11}NO_4$ (M^+ - HOBt) 245.0688, found 245.0693.

(*S*)-1-[2-(Acetyloxy)-1-phenylethyl]-1*H*-pyrrole-2,5-dione (6d): method B, 37% yield; R_f 0.43 in 3:2 hexanes–EtOAc (char A); $[\alpha]_D$ -2.8° (c 1.1, $CHCl_3$); IR ($CHCl_3$) 1745, 1725 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.43–7.28 (m, 5 H, Ph), 6.67 (s, 2 H, CH=CH), 5.38 (dd, J = 10.2, 5.3 Hz, 1 H, PhCH), 4.96 (t, J = 10.2 Hz, 1 H, $^1/_2CH_2OAc$), 4.67 (dd, J = 10.2, 5.3 Hz, 1 H, $^1/_2CH_2OAc$), 1.99 (s, 3 H, OAc); ^{13}C NMR (50.4 MHz, $CDCl_3$) δ 170.4 (C=O), 135.8 (Ph), 134.1 (C=C), 128.8, 128.5, 127.8 (Ph), 62.3 (CH_2OAc), 53.6 (PhCH), 20.7 (OAc); HRMS m/e calcd for $C_{14}H_{13}NO_4$ (M^+) 259.0845, found 259.0836.

(*S*)-1-[2-(Acetyloxy)-1-phenylethyl]-3-(acetyloxy)-pyrrolidine-2,5-dione (8d): 2 diastereomers; <3% yield; R_f 0.28 in 3:2 hexanes–EtOAc (char A); IR (neat) 1740, 1715 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.43–7.31 (m, 5 H, Ph), 5.47–5.33 (m, 2 H, COCHOAc, PhCH), 5.05 (t, J = 11.4 Hz, 0.5 H, $^1/_4CH_2OAc$), 5.03 (t, J = 11.4 Hz, 0.5 H, $^1/_4CH_2OAc$), 4.74–4.61 (m, 1 H, $^1/_2CH_2OAc$), 3.13 (dd, J = 18.3, 8.8 Hz, 0.5 H, $^1/_4COCH_2$), 3.11 (dd, J = 18.3, 8.8 Hz, 0.5 H, $^1/_4COCH_2$), 2.67 (dd, J = 18.3, 5.2 Hz, 0.5 H, $^1/_4COCH_2$), 2.66 (dd, J = 18.3, 5.2 Hz, 0.5 H, $^1/_4COCH_2$), 2.13 (s, 3 H, OAc), 2.03 (s, 3 H, OAc); ^{13}C NMR (50.4 MHz, $CDCl_3$) δ 173.3, 172.8, 170.4, 169.7 (C=O), 134.8, 134.0, 128.8, 128.3 (Ph), 67.1 (COCHOAc), 61.6, 61.5 (CH_2OAc), 54.8, 54.5 (PhCH), 35.5 ($COCH_2$), 20.7, 20.5 (OAc); HRMS m/e calcd for $C_{14}H_{14}NO_4$ (M^+ - HOAc) 259.0845, found 259.0846.

(*S*)-1-[2-[[(1,1-Dimethylethyl)dimethylsilyl]oxy]-1-phenylethyl]-1*H*-pyrrole-2,5-dione (6e): method B; 60% yield; R_f 0.48 in 5:1 hexanes–EtOAc (char A); mp 52–54 °C; $[\alpha]_D$ -15° (c 1.4, CH_2Cl_2); IR ($CHCl_3$) 1710, 1400, 1370 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.40–7.26 (m, 5 H, Ph), 6.66 (s, 2 H, CH=CH), 5.24 (dd, J = 10.3, 5.6 Hz, 1 H, PhCH), 4.54 (t, J = 10.3 Hz, 1 H, $^1/_2CH_2OSi$), 3.97 (dd, J = 10.3, 5.6 Hz, 1 H, $^1/_2CH_2OSi$), 0.80 (s, 9 H, $SiC(CH_3)_3$), -0.01 (s, 3 H, $SiCH_3$), -0.02 (s, 3 H, $SiCH_3$); ^{13}C NMR (50.4 MHz, $CDCl_3$) δ 170.8 (C=O), 136.8 (Ph), 133.8 (CH=CH), 128.4, 127.9 (Ph), 61.5 (CH_2OSi), 56.9 (PhCH), 25.6 ($SiC(CH_3)_3$), 17.8 ($SiC(CH_3)_3$), -5.6 ($SiCH_3$); HRMS m/e calcd for $C_{18}H_{25}O_3NSi$ (M^+) 331.1603, found 331.1605.

(*S*)-1-[2-[[(1,1-Dimethylethyl)dimethylsilyl]oxy]-1-phenylethyl]-3-(acetyloxy)pyrrolidine-2,5-dione (8e): 2 diastereomers; 8% yield; R_f 0.22 in 5:1 hexanes–EtOAc (char A); IR (neat) 1750 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.46–7.28 (m, 5 H, Ph), 5.43 (dd, J = 8.7, 5.0 Hz, 0.5 H, $^1/_2CHOAc$), 5.42 (dd, J = 8.7, 5.0 Hz, 0.5 H, $^1/_2CHOAc$), 5.32 (dd, J = 10.4, 5.6 Hz, 0.5 H, $^1/_2PhCH$), 5.31 (dd, J = 10.4, 5.6 Hz, 0.5 H, $^1/_2PhCH$), 4.65 (t, J = 10.4 Hz, 0.5 H, $^1/_4CH_2OSi$), 4.63 (t, J = 10.4 Hz, 0.5 H, $^1/_4CH_2OSi$), 3.98 (dd, J = 10.4, 5.6 Hz, 0.5 H, $^1/_4CH_2OSi$), 3.94 (dd, J = 10.4, 5.6 Hz, 0.5 H, $^1/_4CH_2OSi$), 3.12 (dd, J = 18.3, 8.7 H, 0.5 H, $^1/_4CH_2CON$), 3.11 (dd, J = 18.3, 8.7 Hz, 0.5 H, $^1/_4CH_2CON$), 2.60 (dd, J = 18.3, 5.0 Hz, 0.5 H, $^1/_4CH_2CON$), 2.59 (dd, J = 18.3, 5.0 Hz, 0.5 H, $^1/_4CH_2CON$), 2.13 (s, 1.5 H, $^1/_2OAc$), 2.12 (s, 1.5 H, $^1/_2OAc$), 0.83 (s, 9 H, $SiC(CH_3)_3$), 0.01 (s, 6 H, $Si(CH_3)_2$); ^{13}C NMR (50.4 MHz, $CDCl_3$) δ 173.2, 169.8 (C=O), 135.6, 128.8, 128.6, 128.4 (Ph), 66.9 (CHOAc), 60.7 (CH_2OSi), 58.2 ($^1/_2PhCH$), 58.0 ($^1/_2PhCH$), 35.7 (CH_2CON), 25.7 ($SiC(CH_3)_3$), 20.5 (OAc), 18.0 ($SiC(CH_3)_3$), -5.6 ($Si(CH_3)_2$); HRMS m/e calcd for $C_{20}H_{29}NO_5Si$ 334.1111, found 334.1111.

General Procedure for Triazoline Synthesis. To a flask containing maleimide 6 was added a 14% solution of methyl azide[17] in toluene (2.7 mL/mmol of 6). The resulting clear solution was stirred at room temperature for 24 h when TLC analysis showed the clean formation of the product. The excess methyl azide and solvent were removed on a rotary evaporator giving the crude product. This material was chromatographed on silica gel eluting with hexanes–EtOAc to provide the triazoline 9 as a solid.

5-(Phenylmethyl)-3a,6a-dihydro-1-methylpyrrolo[3,4-*d*]-1,2,3-triazole-4,6(1*H*,5*H*)-dione (9a): 73% yield; R_f 0.36 in 1:1 hexanes–EtOAc (char A); mp 142–143 °C (recrystallized from hexanes–CH_2Cl_2); UV (1,4-dioxane) λ_{max} 264 (ϵ 3100) nm; IR ($CHCl_3$) 1720 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.31–7.26 (m, 5 H, Ph), 5.47 (d, J = 12.0 Hz, 1 H, CHN=NN), 4.64 (s, 2 H, $PhCH_2$), 4.21 (d, J = 12.0 Hz, 1 H, CHNN=N), 3.53 (s, 3 H, NCH_3); ^{13}C NMR (50.4 MHz, $CDCl_3$) δ 170.6, 169.6 (C=O), 134.0, 128.0, 127.6 (Ph), 80.7 (CHN=NN), 58.8 (CHNN=N), 42.1 ($PhCH_2$), 35.0 (NCH_3); HRMS m/e calcd for $C_{12}H_{12}N_4O_2$ (M^+) 244.0960, found 244.0961.

(±)-α-Phenyl-3a,6a-dihydro-1-methyl-4,6(1*H*,5*H*)-dioxopyrrolo[3,4-*d*]-1,2,3-triazole-5-acetic acid, methyl ester (9b): 91% yield; R_f 0.20 in 40:1 $CHCl_3$–MeOH (char A); mp 159–160 °C; IR ($CHCl_3$) 1750, 1730 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ

7.44–7.33 (m, 5 H, Ph), 5.80 (s, 0.5 H, PhCH), 5.79 (s, 0.5 H, PhCH), 5.52 (d, J = 10.9 Hz, 1 H, CHNN=N), 4.22 (d, J = 10.9 Hz, 0.5 H, $^1/_2$CHN=NN), 4.21 (d, J = 10.9 Hz, 0.5 H, $^1/_2$CHN=NN), 3.78 (s, 3 H, CO_2CH_3), 3.53 (s, 1.5 H, $^1/_2NCH_3$), 3.50 (s, 1.5 H, $^1/_2NCH_3$); ^{13}C NMR (50.4 MHz, $CDCl_3$) δ 170.2, 169.3 (C=O), 132.7, 129.6, 128.6 (Ph), 81.1 (CHN=NN), 59.3 ($^1/_2$CHNN=N), 59.2 ($^1/_2$CHNN=N), 56.6 (PhCH), 53.1 (CO_2CH_3), 35.5 (NCH_3); HRMS m/e calcd for $C_{14}H_{15}N_4O_4$ (M^+ + 1) 303.1093, found 303.1118. Anal. Calcd for $C_{14}H_{14}N_4O_4$: C, 55.63; H, 4.69; N, 18.53. Found: C, 55.27; H, 4.47; N, 18.10.

5-[2-(Acetyloxy)-1-phenylethyl]-3a,6a-dihydro-1-methylpyrrolo[3,4-*d*]-1,2,3-triazole-4,6(1*H*,5*H*)-dione (9d): 88% yield; R_f 0.27 in 1:1 hexanes–EtOAc (char A); mp 118–120 °C; $[\alpha]_D$ 9.2° (c 3.7, CH_2Cl_2); IR ($CHCl_3$) 1740, 1720 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.40–7.30 (m, 5 H, Ph), 5.48–5.33 (m, 2 H, CHN=NN, PhCH), 5.08 (t, J = 11.3 Hz, 0.5 H, $^1/_4CH_2OAc$), 4.97 (t, J = 11.3 Hz, 0.5 H, $^1/_4CH_2OAc$), 4.63 (dd, J = 11.3, 5.0 Hz, 0.5 H, $^1/_4CH_2OAc$), 4.44 (dd, J = 11.3, 5.0 Hz, 0.5 H, $^1/_4CH_2OAc$), 3.52 (s, 1.5 H, $^1/_2NCH_3$), 3.49 (s, 1.5 H, $^1/_2NCH_3$), 1.98 (s, 1.5 H, $^1/_2OAc$), 1.97 (s, 1.5 H, $^1/_2OAc$); ^{13}C NMR (50.4 MHz, $CDCl_3$) δ 171.3, 170.2 (C=O), 134.2, 134.1, 128.9, 128.1, 128.0 (Ph), 80.9 (CHN=NN), 61.2, 61.0 (CH_2OAc), 59.2, 59.0 (CHNN=N), 54.9, 54.7 (PhCH), 35.6, 35.5 (NCH_3), 20.5 (OAc). Anal. Calcd for $C_{16}H_{16}N_4O_4$: C, 56.95; H, 5.09; N, 17.71. Found: C, 56.81; H, 4.91; N, 17.66.

5-[2-[[(1,1-Dimethylethyl)dimethylsilyl]oxy]-1-phenylethyl]-3a,6a-dihydro-1-methylpyrrolo[3,4-*d*]-1,2,3-triazole-4,6(1*H*,5*H*)-dione (9e): 91% yield; R_f 0.40 in 3:1 hexanes–EtOAc (char A); mp 126–127 °C; $[\alpha]_D$ 7.1° (c 1.3, CH_2Cl_2); IR ($CHCl_3$) 1715 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.31–7.29 (m, 5 H, Ph), 5.44 (d, J = 10.9 Hz, 0.5 H, $^1/_2$CHN=NN), 5.40 (d, J = 10.9 Hz, 0.5 H, $^1/_2$CHN=NN), 5.23 (dd, J = 10.5, 5.4 Hz, 1 H, PhCH), 4.63 (t, J = 10.5 Hz, 0.5 H, $^1/_4CH_2OSi$), 4.62 (t, J = 10.5 Hz, 0.5 H, $^1/_4CH_2OSi$), 4.12 (d, J = 10.9 Hz, 0.5 H, $^1/_2$CHNN=N), 4.09 (d, J = 10.9 Hz, 0.5 H, $^1/_2$CHNN=N), 3.91 (dd, J = 10.5, 5.4 Hz, 0.5 H, $^1/_4CH_2OSi$), 3.90 (dd, J = 10.5, 5.4 Hz, 0.5 H, $^1/_4CH_2OSi$), 3.50 (s, 1.5 H, $^1/_2NCH_3$), 3.49 (s, 1.5 H, $^1/_2NCH_3$), 0.8 (s, 9 H, $SiC(CH_3)_3$), –0.01 (s, 6 H, 2 $SiCH_3$); ^{13}C NMR (50.4 MHz, $CDCl_3$) δ 171.8, 170.7 (C=O), 135.2, 128.6, 128.4, 128.2 (Ph), 80.8 (CHN=NN), 60.5 (CH_2OSi), 59.1 (CHNN=N), 58.2 (PhCH), 35.5 (NCH_3), 25.6 ($SiC(CH_3)_3$), 17.9 ($SiC(CH_3)_3$), –5.6 ($SiCH_3$); HRMS m/e calcd for $C_{19}H_{28}N_4O_3Si$ (M^+) 388.1930, found 388.1914.

General Procedure for Aziridine Synthesis. A 0.2 M solution of triazoline **9** in spectrophotometric-grade 1,4-dioxane in a Pyrex immersion flask was purged with nitrogen gas for 10 min then irradiated with a high-pressure Hg lamp for 5 h. TLC analysis indicated the clean conversion of triazoline to aziridine. The solvent was removed on a rotary evaporator, and the resulting oil was purified by flash chromatography to furnish the desired aziridine **10**.

6-Methyl-3-(phenylmethyl)-3,6-diazabicyclo[3.1.0]hexane-2,4-dione (10a): 83% yield; R_f 0.26 in 30:1 $CHCl_3$–MeCN (char A); mp 114–115 °C; IR ($CHCl_3$) 1710 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.30–7.26 (m, 5 H, Ph), 4.51 (s, 2 H, $PhCH_2$), 2.83 (s, 2 H, COCHCHCO), 2.47 (s, 3 H, NCH_3); ^{13}C NMR (50.4 MHz, $CDCl_3$) δ 171.6 (C=O), 135.4, 128.6, 128.2, 127.7 (Ph), 45.3 (NCH_3), 41.8 ($PhCH_2$), 41.7 (COCHCHCO). Anal. Calcd for $C_{21}H_{12}N_2O_2$: C, 66.65; H, 5.59; N, 12.95. Found: C, 66.31; H, 5.41; N, 12.75.

(±)-6-Methyl-2,4-dioxo-α-phenyl-3,6-diazabicyclo[3.1.0]hexane-3-acetic acid, methyl ester (10b): racemic; 82% yield; R_f 0.50 in 40:1 $CHCl_3$–MeOH (char A); mp 125–126 °C; IR ($CHCl_3$) 1750, 1730 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.41–7.31 (m, 5 H, Ph), 5.66 (s, 1 H, PhCH), 3.78 (s, 3 H, CO_2CH_3), 2.85 (s, 2 H, COCHCHCO), 2.47 (s, 3 H, NCH_3); ^{13}C NMR (50.4 MHz, $CDCl_3$) δ 170.7, 170.6, 167.8 (C=O), 133.4, 129.3, 128.6, 128.5 (Ph), 55.6 (PhCH), 53.0 (CO_2CH_3), 45.3 (NCH_3), 41.7 (COCHCHCO); HRMS m/e calcd for $C_{14}H_{14}O_4N_2$ (M^+) 274.0953; found, 274.0952.

(*S*)-3-[2-(Acetyloxy)-1-phenylethyl]-6-methyl-3,6-diazabicyclo[3.1.0]hexane-2,4-dione (10d): gum; 90% yield; R_f 0.50 (tailed) in 35:1 $CHCl_3$–MeOH (char A); $[\alpha]_D$ 17.2° (c 1.3, $CHCl_3$); IR ($CHCl_3$) 1740, 1720 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.33–7.7.20 (m, 5 H, Ph), 5.20 (dd, J = 10.0, 5.6 Hz, 1 H, PhCH), 4.84 (dd, J = 11.3, 10.0 Hz, 1 H, $^1/_2CH_2OAc$), 4.60 (dd, J = 11.3, 5.6 Hz, 1 H, $^1/_2CH_2OAc$), 2.73 (s, 2 H, COCHCHCO), 2.39 (s, 3 H, NCH_3), 1.97 (s, 3 H, OAc); ^{13}C NMR (50.4 MHz, $CDCl_3$) δ 172.4, 171.0 (C=O), 135.7, 129.2, 128.9, 128.3 (Ph), 62.2 (CH_2OAc), 53.9 (PhCH), 45.7 (NCH_3), 42.1 (COCHCHCO), 21.2 (OAc); HRMS m/e calcd for $C_{13}H_{12}N_2O_2$ (M^+ – HOAc) 228.0899, found 228.0899.

(*S*)-3-[2-[[(1,1-Dimethylethyl)dimethylsilyl]oxy]-1-phenylethyl]-6-methyl-3,6-diazabicyclo[3.1.0]hexane-2,4-dione (10e): 93% yield; R_f 0.35 in 3:1 hexanes–EtOAc (char A); mp 78–79.5 °C; $[\alpha]_D$ 0.7° (c 2.3, $CHCl_3$); IR ($CHCl_3$) 1715 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.24–7.21 (m, 5 H, Ph), 5.02 (dd, J = 9.8, 5.9 Hz, 1 H, PhCH), 4.36 (t, J = 9.8 Hz, 1 H, $^1/_2CH_2OSi$), 3.93 (dd, J = 9.8, 5.9 Hz, 1 H, $^1/_2CH_2OSi$), 2.68 (s, 2 H, COCHCHCO), 2.34 (s, 3 H, NCH_3), 0.76 (s, 9 H, $SiC(CH_3)_3$), –0.07 (s, 3 H, $SiCH_3$), –0.08 (s, 3 H, $SiCH_3$); ^{13}C NMR (50.4 MHz, $CDCl_3$) δ 172.2 (C=O), 136.3, 128.5, 128.4, 127.8 (Ph), 61.1 (CH_2OSi), 56.9 (PhCH), 45.0 (NCH_3), 41.5 (COCHCHCO), 25.6 ($SiC(CH_3)_3$), 18.0 ($SiC(CH_3)_3$), –5.6 ($SiCH_3$); HRMS m/e calcd for $C_{18}H_{25}O_3N_2Si$ (M^+ – CH_3) 345.1634, found 345.1644.

General Procedure for 1,3-Dipolar Cycloadditions with Simple Acrylate Dipolarophiles. A nitrogen-purged dioxane solution of aziridine **10** (0.2 M) and methyl acrylate (2.0 equiv) in a quartz tube (diameter 1.5 cm) was irradiated at 2537 Å in a Rayonet photochemical reactor. After the reaction was judged to be complete by TLC analysis, the solvent was removed on a rotary evaporator. The resulting crude gum was flash chromatographed over silica gel, eluting with hexanes–EtOAc to provide the pure cycloadducts.

(±)-*exo*-8-Methyl-2,4-dioxo-3-(phenylmethyl)-3,8-diazabicyclo[3.2.1]octane-6-carboxylic Acid, Methyl Ester (13a/14a) and (±)-*endo*-8-Methyl-2,4-dioxo-3-(phenylmethyl)-3,8-diazabicyclo[3.2.1]octane-6-carboxylic Acid, Methyl Ester (15a/16a). Reaction time, 10 h. **13a/14a**: 50% yield; R_f 0.41 in 3:2 hexanes–EtOAc (char A); mp 69–70 °C; IR ($CHCl_3$) 1735, 1680 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33–7.22 (m, 5 H, Ph), 4.84 (s, 2 H, $PhCH_2$), 4.13 (s, 1 H, H-5), 3.81 (d, J = 7.4 Hz, 1 H, H-1), 3.74 (s, 3 H, CO_2CH_3), 2.98 (dd, J = 9.8, 5.1 Hz, 1 H, H-6), 2.70 (ddd, J = 13.7, 7.4, 5.1 Hz, 1 H, H-7a), 2.41 (s, 3 H, NCH_3), 2.15 (dd, J = 13.7, 9.8 Hz, 1 H, H-7b); ^{13}C NMR (50.4 MHz, $CDCl_3$) δ 172.6, 172.1, 171.2 (C=O), 136.4, 128.8, 128.5, 127.7 (Ph), 68.2 (C-5), 65.4 (C-1), 52.7 ($COOCH_3$), 45.1 (C-6), 41.5 ($PhCH_2$), 35.6 (NCH_3), 30.9 (C-7); HRMS m/e calcd for $C_{16}H_{18}N_2O_4$ (M^+) 302.1267, found 302.1271. **15a/16a**: gum; 11% yield; R_f 0.24 (3:2) hexanes–EtOAc; IR ($CHCl_3$) 1735, 1680 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37–7.20 (m, 5 H, Ph), 4.82 (d, J = 13.9 Hz, 1 H, AB, $^1/_2PhCH_2$), 4.77 (d, J = 13.9 Hz, 1 H, AB, $^1/_2PhCH_2$), 3.95 (d, J = 6.8 Hz, 1 H, H-5), 3.77 (d, J = 7.4 Hz, 1 H, H-1), 3.51 (s, 3 H, CO_2Me), 3.46 (m, 1 H, H-6), 2.51 (ddd, J = 13.6, 10.8, 7.4 Hz, 1 H, H-7a), 2.33 (s, 3 H, NCH_3), 2.26 (dd, J = 13.6, 5.4 Hz, 1 H, H-7b); ^{13}C NMR (50.4 MHz, $CDCl_3$) δ 172.7, 171.0, 170.1 (C=O), 136.7, 129.0, 128.3, 127.5 (Ph), 69.0 (C-5), 65.8 (C-1), 52.4 (CO_2CH_3), 45.2 (C-6), 41.8 ($PhCH_2$), 35.9 (NCH_3), 30.2 (C-7); HRMS m/e calcd for $C_{16}H_{18}N_2O_4$ 302.1267, found 302.1267.

[1*R*,*S*[1α,3(*S),5α,6α]]-3-[(Methoxycarbonyl)phenylmethyl]-8-methyl-2,4-dioxo-3,8-diazabicyclo[3.2.1]octane-6-carboxylic Acid, Methyl Ester (13b/ent-13b) and [1*R*,*S*-[1α,3(*R**),5α,6α]]-3-[(Methoxycarbonyl)phenylmethyl]-8-methyl-2,4-dioxo-3,8-diazabicyclo[3.2.1]octane-6-carboxylic Acid, Methyl Ester (14b/ent-14b).** Reaction time, 8 h. **13b/ent-13b and 14b/ent-14b**: gum; 73% yield; IR ($CHCl_3$) 1740, 1695 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45–7.29 (m, 5 H, Ph), 6.25 (s, 1 H, PhCH), 4.16 (s, 0.5 H, $^1/_2$H-5), 4.15 (s, 0.5 H, $^1/_2$H-5), 3.85 (d, J = 6.8 Hz, 0.5 H, $^1/_2$H-1), 3.83 (d, J = 6.8 Hz, 0.5 H, $^1/_2$H-1), 3.76 (s, 3 H, CO_2CH_3), 3.73 (s, 3 H, CO_2CH_3), 3.05 (dd, J = 9.7, 5.1 Hz, 0.5 H, $^1/_2$H-6), 3.00 (dd, J = 9.7, 5.1 Hz, 0.5 H, H-6), 2.71 (m, 1 H, H-7a), 2.46 (s, 3 H, NCH_3), 2.20 (dd, J = 13.7, 9.7 Hz, 0.5 H, $^1/_2$H-7b), 2.18 (dd, J = 13.7, 9.7 Hz, 0.5 H, $^1/_2$H-7b); ^{13}C NMR (50.4 MHz, $CDCl_3$) δ 172.0, 170.7, 168.3 (C=O), 134.4, 129.9, 128.4, 128.3 (Ph), 68.0 (C-5), 65.3 (C-1), 54.9 (PhCH), 52.8 (CO_2CH_3), 45.0 ($^1/_2$C-6), 44.9 ($^1/_2$C-6), 35.3 (NCH_3), 30.9 ($^1/_2$C-7), 30.8 ($^1/_2$C-7); HRMS m/e calcd for $C_{18}H_{20}O_6N_2$ (M^+) 360.1321, found 360.1316.

[1*R*[1α,3(*S),5α,6α]]-3-[2-(Acetyloxy)-1-phenylethyl]-8-methyl-2,4-dioxo-3,8-diazabicyclo[3.2.1]octane-6-carboxylic Acid, Methyl Ester (13d) and [1*S*[1α,3(*R**),5α,6α]]-3-[2-(Acetyloxy)-1-phenylethyl]-8-methyl-2,4-dioxo-3,8-diazabicyclo[3.2.1]octane-6-carboxylic Acid, Methyl Ester (14d).** Reaction time, 3 h. **13d/14d**: gum; 61% yield; R_f 0.20 in 2:1 hexanes–EtOAc (char A); IR ($CHCl_3$) 1730, 1680 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.33–7.23 (m, 5 H, Ph), 5.95 (dd, J = 9.8, 5.4

Hz, 1 H, PhCH), 5.00 (dd, J = 11.2, 9.8 Hz, 0.5 H, $^1/_4CH_2OAc$), 4.97 (dd, J = 11.2, 9.8 Hz, 0.5 H, $^1/_4CH_2OAc$), 4.81 (dd, J = 11.2, 5.4 Hz, 0.5 H, $^1/_4CH_2OAc$), 4.78 (dd, J = 11.2, 5.4 Hz, 0.5 H, $^1/_4CH_2OAc$), 4.10 (s, 1 H, H-5), 3.80 (d, J = 7.3 Hz, 1 H, H-1), 3.74 (s, 1.5 H, $^1/_2CO_2CH_3$), 3.72 (s, 1.5 H, $^1/_2CO_2CH_3$), 3.05 (dd, J = 9.7, 5.0 Hz, 0.5 H, $^1/_2$H-6), 2.91 (dd, J = 9.7, 5.0 Hz, 0.5 H, $^1/_2$H-6), 2.78–2.63 (m, 1 H, H-7a), 2.50 (s, 1.5 H, $^1/_2NCH_3$), 2.49 (s, 1.5 H, $^1/_2NCH_3$), 2.15 (m, 1 H, H-7b), 2.01 (s, 3 H, OAc); ^{13}C NMR (50.4 MHz, $CDCl_3$) δ 173.0, 172.9, 172.1, 171.7, 171.4, 170.3 (C=O), 136.0, 128.5, 128.1, 127.8 (Ph), 68.6 (C-5), 65.7 (C-1), 62.3 (CH_2OAc), 52.8, 52.3, 52.2 (PhCH, CO_2CH_3), 45.1, 45.0 (C-6), 35.5 (NCH_3), 31.1, 30.8 (C-7), 20.8 (OAc); HRMS m/e calcd for $C_{19}H_{21}N_2O_6$ (M^+ – H) 373.1400, found 373.1400.

(±)-*exo*-6-Cyano-8-methyl-2,4-dioxo-3-(phenylmethyl)-3,8-diazabicyclo[3.2.1]octane (18a/19a) and (±)-*endo*-6-Cyano-8-methyl-2,4-dioxo-3-(phenylmethyl)-3,8-diazabicyclo[3.2.1]octane (20a/21a). A mixture of aziridine **10a** (103 mg, 0.480 mmol) and acrylonitrile (17; 50 mg, 0.95 mmol) in MeCN (5.0 mL) was purged with N_2 and irradiated as described above. Reaction time, 4.5 h. **18a/19a**: 25% yield (based on 10% recovered **10a**); R_f 0.62 in 1:1 hexanes–EtOAc (char A); mp 108–110 °C; IR ($CHCl_3$) 2240 (weak), 1740 (weak), 1690 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.34–7.26 (m, 5 H, Ph), 4.8 (s, 2 H, $PhCH_2$), 4.08 (s, 1 H, H-5), 3.95 (d, J = 7.3 Hz, 1 H, H-1), 3.08 (dd, J = 9.4, 4.7 Hz, 1 H, H-6), 2.67 (ddd, J = 13.7, 7.4, 4.7 Hz, 1 H, H-7a), 2.50 (s, 3 H, NCH_3), 2.35 (dd, J = 13.7, 9.4 Hz, 1 H, H-7b); ^{13}C NMR (50.4 MHz, $CDCl_3$) δ 171.3, 169.1 (C=O), 136.2, 128.9, 128.6, 127.9 (Ph), 119.9 (CN), 69.3 (C-5), 64.9 (C-1), 41.8 ($PhCH_2$), 35.7 (C-6), 33.3 (C-7), 30.3 (NCH_3); HRMS m/e calcd for $C_{15}H_{15}N_3O_2$ (M^+) 269.1164, found 269.1149. **20a/21a**: 40% yield (based on 10% recovered **10a**); R_f 0.24 in 1:1 hexanes–EtOAc (char A); mp 147–148 °C; IR ($CHCl_3$) 2240 (weak), 1740 (weak), 1690 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.44–7.25 (m, 5 H, Ph), 4.99 (d, J = 13.8 Hz, 1 H, AB, $^1/_2PhCH_2$), 4.86 (d, J = 13.8 Hz, 1 H, AB, $^1/_2PhCH_2$), 4.03 (d, J = 6.8 Hz, 1 H, H-5), 3.84 (d, J = 7.4 Hz, 1 H, H-1), 3.45 (ddd, J = 11.3, 6.8, 5.3 Hz, 1 H, H-6), 2.80 (ddd, J = 13.7, 11.3, 7.4 Hz, 1 H, H-7a), 2.40 (s, 3 H, NCH_3), 2.16 (dd, J = 13.7, 5.3 Hz, 1 H, H-7b); ^{13}C NMR (50.4 MHz, $CDCl_3$), δ 171.5, 168.5 (C=O), 136.2, 129.1, 128.5, 127.8 (Ph), 117.4 (CN), 68.1 (C-5), 65.0 (C-1), 42.1 ($PhCH_2$), 35.8 (C-6), 32.4 (C-7), 28.9 (NCH_3); HRMS m/e calcd for $C_{15}H_{15}N_3O_2$ (M^+) 269.1164, found 269.1159.

General Procedure for 1,3-Dipolar Cycloadditions with *N*-Acryloyl Sultam 32. Portionwise Addition of Dipolarophile. To a quartz tube (diameter 1.5 cm) containing aziridine **10** in 1.4-dioxane (0.1 M) was added 0.2 equiv of solid **32**. The resulting solution was purged with nitrogen and photolyzed at 2537 Å for 30 min with TLC monitoring. This procedure was repeated until a total of 1.2 equiv of **32** had been introduced.

Continuous Slow Addition of Dipolarophile. A vigorously stirred dioxane solution containing **10** (0.1 M) and **32** (0.2 equiv) was purged with nitrogen and photolyzed as described above. To the photolyzed mixture was added a degassed 0.15 M dioxane solution of **10** (1 equiv) over 2 h via a submerged opaque plastic cannula using a syringe pump. At this point the solvent was evaporated and the crude product purified by flash chromatography on silica gel, eluting with EtOAc–hexanes.

[3a*S*[1[1*S,5*R**,6*R**],3aα,6α,7aβ]]-Hexahydro-8,8-dimethyl-1-[[8-methyl-2,4-dioxo-3-(phenylmethyl)-3,8-diazabicyclo[3.2.1]oct-6-yl]carbonyl]-3*H*-3a,6-methano-2,1-benzisothiazole 2,2-Dioxide (33a) and [3a*S*[1-[1*R**,5*R**,6*R**],3aα,6α,7aβ]]-Hexahydro-8,8-dimethyl-1-[[8-methyl-2,4-dioxo-3-(phenylmethyl)-3,8-diazabicyclo[3.2.1]-oct-6-yl]carbonyl]-3*H*-3a,6-methano-2,1-benzisothiazole 2,2-Dioxide (35a). (10a + (–)-32) 33a**: 42% yield (based on 6% recovered **10a**); R_f 0.50 in 1:1 hexane–EtOAc (char B); mp 227–228 °C (recrystallized from EtOH); $[\alpha]_D$ –58.5° (c 1.6, $CHCl_3$); IR ($CHCl_3$) 1690 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, rt) δ 7.38–7.23 (m, 5 H, Ph), 4.89 (d, J = 13.9 Hz, AB, 1 H, $PhCH_2$), 4.84 (d, J = 13.9 Hz, AB, 1 H, $PhCH_2$) 3.96 (s, 1 H, H-5), 3.87 (m, 2 H, H-1, $(SO_2)NCH$), 3.67 (dd, J = 9.3, 5.3 Hz, 1 H, H-6), 3.52 (d, J = 13.9 Hz, AB, 1 H, CH_2SO_2), 3.45 (d, J = 13.9 Hz, AB, 1 H, CH_2SO_2), 2.78 (m, 1 H, H-7a), 2.40 (s, 3 H, NCH_3), 2.27 (dd, J = 13.7, 9.3 Hz, 1 H, H-7b), 2.1–1.3 (m, 7 H), 1.16 (s, 3 H, $^1/_2C(CH_3)_2$), 0.98 (s, 3 H, $^1/_2C(CH_3)_2$); ^{13}C NMR (50.4 MHz, $CDCl_3$, 20 °C) δ 172.7, 170.4, 170.3 (C=O), 136.8, 128.9, 128.5, 127.6 (Ph), 69.2 (C-5), 65.7, 65.5 (C-1, C-2′), 52.9 (C-10′), 48.6 (C-1′), 47.8 (C-3′), 45.4 (C-6), 44.4 (C-4′), 41.8 ($PhCH_2$), 38.3 (C-6′), 35.6 (NCH_3), 32.7 (C-5′), 31.5 (C-7), 26.4 (C-7′), 20.8, 19.8 (C-8′, C-9′); HRMS m/e calcd for $C_{25}H_{31}N_3O_5S$ (M^+) 485.1984, found 485.1983. **35a**: 17% yield (based on recovered **10a**); R_f 0.63 in 1:1 hexane–EtOAc (char B); mp 202–203 °C (recrystallized from EtOH); $[\alpha]_D$ –80.2° (c 1.8, $CHCl_3$); IR ($CHCl_3$) 1690 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, rt) δ 7.30–7.19 (m, 5 H, Ph), 4.83 (d, J = 14.0 Hz, AB, 1 H, $PhCH_2$), 4.79 (d, J = 14.0 Hz, AB, 1 H, $PhCH_2$), 4.20 (d, J = 6.7 Hz, 1 H, H-5), 4.12 (m, 1 H, H-6), 3.82 (br d, 2 H, H-1, $(SO_2)NCH$), 3.54 (d, J = 13.8 Hz, AB, 1 H, CH_2SO_2), 3.47 (d, J = 13.8 Hz, AB, 1 H, CH_2SO_2), 2.52 (ddd, J = 13.6, 9.7, 7.7 Hz, 1 H, H-7a), 2.43 (dd, J = 13.6, 5.6 Hz, 1 H, H-7b), 2.37 (s, 3 H, NCH_3), 2.1–1.3 (m, 7 H), 1.29 (s, 3 H, $^1/_2C(CH_3)_2$), 0.98 (s, 3 H, $^1/_2C(CH_3)_2$); ^{13}C NMR (50.4 MHz, $CDCl_3$, 21 °C) δ 172.7, 170.2, 168.8 (C=O), 136.7, 129.0, 128.2, 127.4 (Ph), 70.4 (C-5), 66.2, 65.5 (C-1 & C-2′), 53.2 (C-10′), 48.4 (C-1′), 47.8 (C-3′), 45.7 (C-6), 44.5 (C-4′), 41.9 ($PhCH_2$), 38.1 (C-6′), 36.2 (NCH_3), 32.9 (C-5′), 29.2 (C-7), 26.5 (C-7′), 20.6, 20.1 (C8′, C-9′); HRMS m/e calcd for $C_{25}H_{31}N_3O_5S$ (M^+) 485.1984, found 485.1986. Anal. Calcd for $C_{25}H_{31}N_3O_5S$: C, 61.83; H, 6.43; N, 8.66; found: C, 61.55; H, 6.47; N, 9.03.

[3a*S*[1[1*S,3(*R**),5*R**,6*R**],3aα,6α,7aβ]]-1-[[3-[2-(Acetyloxy)-1-phenylethyl]-8-methyl-2,4-dioxo-3,8-diazabicyclo[3.2.1]oct-6-yl]carbonyl]hexahydro-8,8-dimethyl-3*H*-3a,6-methano-2,1-benzisothiazole 2,2-Dioxide (33d). 10d + (–)-32**: 65% yield (based on 11% recovered **10d**); R_f 0.42 in 1:1 hexane–EtOAc (char B); $[\alpha]_D$ – 6.9° (c 1.1, $CHCl_3$); IR ($CHCl_3$) 1740, 1690 cm^{-1}; ^1H NMR (400 MHz (1:1) $CDCl_3$–C_6D_6, rt) δ 7.35–7.12 (m, 5 H, Ph), 6.05 (dd, J = 10.8, 5.3 Hz, 1 H, PhCH), 5.05 (t, J = 10.8 Hz, 1 H, $^1/_2CH_2OAc$), 4.75 (dd, J = 10.8, 5.3 Hz, 1 H, $^1/_2CH_2OAc$), 3.91 (s, 1 H, H-5), 3.83 (dd, J = 9.3, 5.7 Hz, 1 H, H-6), 3.74 (d, J = 7.0 Hz, 1 H, H-1), 3.64 (dd, J = 7.7, 5.0 Hz, 1 H, $(SO_2)NCH$), 3.06 (d, J = 13.8 Hz, AB, 1 H, CH_2SO_2), 2.95 (d, J = 13.8 Hz, AB, 1 H, CH_2SO_2), 2.72 (ddd, J = 13.3, 7.0, 5.7 Hz, 1 H, H-7a), 2.29 (s, 3 H, NCH_3), 2.18 (dd, J = 13.3, 9.3 Hz, 1 H, H-7b), 1.93 (s, 3 H, OAc), 2.0–0.9 (m, 7 H), 0.79 (s, 3 H, $^1/_2C(CH_3)_2$), 0.64 (s, 3 H, $^1/_2C(CH_3)_2$); ^{13}C NMR (50.4 MHz, $CDCl_3$, 21 °C) δ 173.0, 170.7, 170.3 (C=O), 136.1, 128.5, 128.0, 127.8 (Ph), 69.7 (C-5), 66.1, 65.5 (C-1, C-2′), 61.9 (CH_2OAc), 52.8 (C-10′), 52.1 (PhCH), 48.6 (C-1′), 47.9 (C-3′), 45.4 (C-6), 44.4 (C-4′), 38.3 (C-6′), 35.7 (NCH_3), 32.7 (C-5′), 31.7 (C-7), 26.4 (C-7′), 21.0, 20.7, 19.8 (OAc, C-8′, C-9′); HRMS m/e calcd for $C_{28}H_{35}N_3O_7S$ (M^+) 557.2196, found 557.2179.

[3a*R*[1[1*S,3(*R**),5*R**,6*R**],3aα,6α,7aβ]]-1-[[3-[2-(Acetyloxy)-1-phenylethyl]-8-methyl-2,4-dioxo-3,8-diazabicyclo[3.2.1]oct-6-yl]carbonyl]hexahydro-8,8-dimethyl-3*H*-3a,6-methano-2,1-benzisothiazole 2,2-Dioxide (38d). 10d + (+)-32**: 64% yield (based on 14% recovered **10d**); R_f 0.34 in 1:1 hexanes–EtOAc (char B); $[\alpha]_D$ 71.4° (c 1.3, $CHCl_3$); IR ($CHCl_3$) 1740, 1690 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, rt) δ 7.29–7.18 (m, 5 H, Ph), 5.92 (dd, J = 10.8, 5.1 Hz, 1 H, PhCH), 4.94 (t, J = 10.8 Hz, 1 H, $^1/_2CH_2OAc$), 4.73 (dd, J = 10.8, 5.1 Hz, 1 H, $^1/_2CH_2OAc$), 3.89 (s, 1 H, H-5), 3.80 (dd, J = 7.6, 5.2 Hz, 1 H, $(SO_2)NCH$), 3.74 (d, J = 7.0 Hz, 1 H, H-1), 3.59 (br dd, J = 9.1, 5.6 Hz, 1 H, H-6), 3.43 (d, J = 13.8 Hz, AB, 1 H, CH_2SO_2), 3.37 (d, J = 13.8 Hz, AB, 1 H, CH_2SO_2), 2.69 (ddd, J = 13.3, 7.0, 5.6 Hz, 1 H, H-7a), 2.44 (s, 3 H, NCH_3), 2.28 (dd, J = 13.3, 9.1 Hz, 1 H, H-7b), 1.99 (s, 3 H, OAc), 2.1–1.1 (m, 7 H), 1.09 (s, 3 H, $^1/_2C(CH_3)_2$), 0.90 (s, 3 H, $^1/_2C(CH_3)_2$); ^{13}C NMR (50.4 MHz, $CDCl_3$, 20 °C) δ 173.0, 170.9, 170.7 (C=O), 136.1, 128.5, 128.0, 127.8 (Ph), 69.4 (C-5), 66.4, 65.6 (C-1 & C-2′), 62.1 (CH_2OAc), 52.9 (C-10′), 52.3 (PhCH), 48.6 (C-1′), 47.9 (C-3′), 45.2 (C-6), 44.5 (C-4′), 38.3 (C-6′), 35.7 (NCH_3), 32.8 (C-5′), 32.0 (C-7), 26.4 (C-7′), 21.0, 20.7, 19.8 (OAc, C-8′, C-9′); HRMS m/e calcd for $C_{28}H_{35}N_3O_7S$ (M^+) 557.2196, found 557.2201.

[3a*S*[1[1*S,3(*R**),5*R**,6*R**],3aα,6α,7aβ]]-8-Methyl-2,4-dioxo-α-phenyl-6-[(tetrahydro-8,8-dimethyl-3*H*-3a,6-methano-2,1-benzisothiazol-1(4*H*)-yl)carbonyl]-3,8-diazabicyclo[3.2.1]octane-3-acetic Acid, Methyl Ester, *S*,*S*-Dioxide (33b) and [3a*S*[1[1*S**,3(*S**),5*R**,6*R**],3aα,6α,7aβ]]-8-Methyl-2,4-dioxo-α-phenyl-6-[(tetrahydro-8,8-dimethyl-3*H*-3a,6-methano-2,1-benzisothiazol-1(4*H*)-yl)carbonyl]-3,8-diazabicyclo[3.2.1]octane-3-acetic Acid, Methyl Ester, *S*,*S*-Dioxide (ent-38b). (±)-10b + (–)-32**: 69% yield (based on 11% recovered **10b**); R_f 0.45 in 1:1 hexanes–EtOAc (char B); mp 197–198 °C; IR ($CHCl_3$) 1750, 1695 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, rt) δ 7.29–7.18 (m, 5 H, Ph), 6.24 (s, 0.5 H, $^1/_2PhCH$), 6.23 (s, 0.5 H, $^1/_2PhCH$), 4.00 (s, 0.5 H, $^1/_2$H-5), 3.91 (s, 0.5 H, $^1/_2$H-5),

3.88 (m, 2 H, H-1, $(SO_2)NCH$), 3.76 (s, 1.5 H, $^1/_2CO_2Me$), 3.75 (s, 1.5 H, $^1/_2CO_2Me$), 3.67 (dd, J = 9.2, 5.1 Hz, 1 H, H-6) 3.49 (d, J = 13.8 Hz, AB, 0.5 H, $^1/_4CH_2SO_2$), 3.48 (d, J = 13.8 Hz, AB, 0.5 H, $^1/_4CH_2SO_2$), 3.43 (d, J = 13.8 Hz, AB, 0.5 H, $^1/_4CH_2SO_2$), 3.42 (d, J = 13.8 Hz, AB, 0.5 H, $^1/_4CH_2SO_2$), 2.78 (m, 1 H, H-7a), 2.45 (s, 1.5 H, $^1/_2NCH_3$), 2.42 (s, 1.5 H, $^1/_2NCH_3$), 2.29 (dd, J = 13.6, 9.2 Hz, 0.5 H, $^1/_2$H-7b), 2.25 (dd, J = 13.6, 9.2 Hz, 0.5 H, $^1/_2$H-7b), 2.1–1.2 (m, 7 H), 1.14 (s, 3 H, $^1/_2C(CH_3)_2$), 0.86 (s, 3 H, $^1/_2C(CH_3)_2$); ^{13}C NMR (50.4 MHz, $CDCl_3$, 20 °C) δ 172.1, 170.4, 170.2, 169.8, 169.7, 168.3 (C=O), 134.4, 130.0, 129.9, 128.3 (Ph), 69.2, 69.1 (C-5), 65.7, 65.5 (C-2′), 55.0, 54.9 (PhCH), 52.8 (C-10′), 52.7 (CO_2CH_3), 48.6 (C-1′), 47.9 (C-3′), 45.4, 45.0 (C-6), 44.4 (C-4′), 38.3 (C-6′), 35.6 (NCH_3), 32.7 (C-5′), 31.6, 31.1 (C-7), 26.4 (C-7′), 20.8, 19.8 (C-8′, C-9′); HRMS m/e calcd for $C_{27}H_{32}O_7N_3S$ (M^+ – H) 542.1960, found 542.1962.

[3a*S*[1[1*S,3(*R**),5*R**,6*R**],3aα,6aα,7a$\alpha\beta$]]-1-[[3-[2-[[(1,1-Dimethylethyl)dimethylsilyl]oxy]-1-phenylethyl]-8-methyl-2,4-dioxo-3,8-diazabicyclo[3.2.1]oct-6-yl]carbonyl]-hexahydro-8,8-dimethyl-3*H*-3a,6-methano-2,1-benzisothiazole 2,2-Dioxide (33e).** **10e + (–)-32**: 55% yield (based on 18% recovered **10e**); R_f 0.27 in 2:1 hexanes–EtOAc (char B); mp 274–275 °C (recrystallized from EtOAc); $[\alpha]_D$ – 4.5° (*c* 1.2, $CHCl_3$); IR ($CHCl_3$) 1685, 1340 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, rt) δ 7.33–7.22 (m, 5 H, Ph), 5.80 (dd, J = 10.1, 5.5 Hz, 1 H, PhCH), 4.66 (t, J = 10.1 Hz, 1 H, $^1/_2CH_2OSi$), 4.11 (dd, J = 10.1, 5.5 Hz, 1 H, $^1/_2CH_2OSi$), 3.91 (s, 1 H, H-5), 3.86 (m, 2 H, H-1, $(SO_2)NCH$), 3.70 (dd, J = 9.2, 5.1 Hz, 1 H, H-6), 3.48 (d, J = 13.8 Hz, AB, 1 H, $^1/_2CH_2SO_2$), 3.41 (d, J = 13.8 Hz, AB, 1 H, $^1/_2CH_2SO_2$), 2.81 (ddd, J = 13.2, 7.1, 5.1 Hz, 1 H, H-7a), 2.51 (s, 3 H, NCH_3), 2.19 (dd, J = 13.2, 9.2 Hz, 1 H, H-7b), 2.1–1.2 (m, 7 H), 1.14 (s, 3 H, $^1/_2C(CH_3)_2$), 0.95 (s, 3 H, $^1/_2C(CH_3)_2$), 0.85 (s, 9 H, $SiC(CH_3)_3$), 0.04 (s, 3 H, $SiCH_3$), 0.03 (s, 3 H, $SiCH_3$); ^{13}C NMR (50.4 MHz, $CDCl_3$, 20 °C) δ 173.1, 170.6, 170.5 (C=O), 137.3, 128.3, 128.1, 127.6 (Ph), 69.9 (C-5), 65.9, 65.4 (C-1, C-2′), 61.3 (CH_2OSi), 55.6 (PhCH), 52.8 (C-10′), 48.6 (C-1′), 47.8 (C-3′), 45.6 (C-6), 44.4 (C-4′), 38.3 (C-6′), 35.6 (NCH_3), 32.7 (C-5′), 30.9 (C-7), 26.4 (C-7′), 25.9 ($SiC(CH_3)_3$), 20.8, 19.8 (C-8′, C-9′), 18.3 ($SiC(CH_3)_3$), –5.4 ($Si(CH_3)_2$); HRMS m/e calcd for $C_{32}H_{47}O_6N_3SSi$ (M^+) 629.2955, found 629.2952.

[3a*R*[1[1*S,3(*R**),5*R**,6*R**],3aα,6aα,7a$\alpha\beta$]]-1-[[3-[2-[[(1,1-Dimethylethyl)dimethylsilyl]oxy]-1-phenylethyl]-8-methyl-2,4-dioxo-3,8-diazabicyclo[3.2.1]oct-6-yl]carbonyl]-hexahydro-8,8-dimethyl-3*H*-3a,6-methano-2,1-benzisothiazole 2,2-Dioxide (38e).** **10e + (+)-32**: 55% yield (based on 16% recovered **10e**); R_f 0.28 in 2:1 hexanes–EtOAc (char B); mp 243–244 °C (recrystallized from 5:2 hexanes–EtOAc); $[\alpha]_D$ 52.8° (*c* 1.5, $CHCl_3$); IR ($CHCl_3$) 1685, 1340 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, rt) δ 7.33–7.22 (m, 5 H, Ph), 5.78 (dd, J = 9.9, 5.8 Hz, 1 H, PhCH), 4.63 (t, J = 9.9 Hz, 1 H, $^1/_2CH_2OSi$), 4.11 (dd, J = 9.9, 5.8 Hz, 1 H, $^1/_2CH_2OSi$), 3.89 (s, 1 H, H-5), 3.83 (m, 2 H, H-1, $(SO_2)NCH$), 3.59 (dd, J = 9.0, 5.0 Hz, 1 H, H-6), 3.48 (d, J = 13.8 Hz, AB, 1 H, $^1/_2CH_2SO_2$), 3.40 (d, J = 13.8 Hz, AB, 1 H, $^1/_2CH_2SO_2$), 2.81 (ddd, J = 13.2, 7.0, 5.0 Hz, 1 H, H-7a), 2.50 (s, 3 H, NCH_3), 2.27 (dd, J = 13.2, 9.0 Hz, 1 H, H-7b), 2.1–1.2 (m, 7 H), 1.12 (s, 3 H, $^1/_2C(CH_3)_2$), 0.94 (s, 3 H, $^1/_2C(CH_3)_2$), 0.85 (s, 9 H, $SiC(CH_3)_3$), 0.03 (s, 3 H, $SiCH_3$), 0.02 (s, 3 H, $SiCH_3$); ^{13}C NMR (50.4 MHz, $CDCl_3$, 20 °C) δ 173.5, 170.6, 170.5 (C=O), 137.7, 128.4, 127.9, 127.7 (Ph), 69.7 (C-5), 66.1, 65.5 (C-1 & C-2′), 61.8 (CH_2OSi), 56.1 (PhCH), 52.8 (C-10′), 48.6 (C-1′), 47.8 (C-3′), 45.3 (C-6), 44.4 (C-4′), 38.3 (C-6′), 35.6 (NCH_3), 32.7 (C-5′), 31.5 (C-7), 26.4 (C-7′), 25.9 ($SiC(CH_3)_3$), 20.8, 19.8 (C-8′ & C-9′), 18.3 ($SiC(CH_3)_3$), –5.4 ($SiCH_3$); HRMS m/e calcd for $C_{32}H_{47}O_6N_3SSi$ (M^+) 629.2955, found 629.2952.

General Procedure for Alcoholysis of Sultam Auxiliary. To a 0.01 M solution of cycloadduct **33** (→**41**) or **38** (→**43**) in absolute EtOH was added $Ti(O^iPr)_4$ (8 equiv), and the resulting heterogeneous mixture was heated under reflux (100 °C oil bath) until judged complete by TLC. During this time, the reaction had become homogeneous. After being cooled in an ice bath, the mixture was quenched with 1 N HCl then basified with saturated $NaHCO_3$ solution and extracted with Et_2O or CH_2Cl_2. The combined extracts were washed with brine, dried with $MgSO_4$, filtered, and evaporated to give a mixture of ethyl ester and recovered sultam. Preparative TLC furnished the desired ethyl ester **41** or **43** (51–75% yield) and recovered (–)- or (+)-sultam (84–90% yield).

(1*R*-*exo*)-8-Methyl-2,4-dioxo-3-(phenylmethyl)-3,8-diazabicyclo[3.2.1]octane-6-carboxylic acid, ethyl ester (41a): reaction time 40 h; PTLC eluting with 7:1 hexanes–Me_2CO (R_f 0.14, char B); 75% yield; $[\alpha]_D$ 49.5° (*c* 1.9, $CHCl_3$); IR ($CHCl_3$) 1735, 1685 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$, 20 °C) δ 7.31–7.17 (m, 5 H, Ph), 4.80 (s, 2 H, $PhCH_2$), 4.14 (q, J = 7.1 Hz, 2 H, OCH_2CH_3), 4.09 (s, 1 H, H-5), 3.77 (d, J = 7.3 Hz, 1 H, H-1), 2.92 (dd, J = 9.7, 5.1 Hz, 1 H, H-6), 2.66 (ddd, J = 13.8, 7.3, 5.1 Hz, 1 H, H-7a), 2.34 (s, 3 H, NCH_3), 2.10 (dd, J = 13.8, 9.7 Hz, 1 H, H-7b), 1.21 (t, J = 7.1 Hz, 3 H, OCH_2CH_3); ^{13}C NMR (50.4 MHz, $CDCl_3$, 20 °C) δ 172.7, 171.7, 171.3 (C=O), 136.7, 128.8, 128.5, 127.7 (Ph), 68.3 (C-5), 65.5 (C-1), 61.8 (OCH_2CH_3), 45.2 (C-6), 41.5 ($PhCH_2$), 35.6 (NCH_3), 30.9 (C-7), 14.1 (OCH_2CH_3); HRMS m/e calcd for $C_{17}H_{20}O_4N_2$ (M^+) 316.1423, found 316.1410.

[1*R*[1α,3(*S),5aα,6aα]]-3-[2-[[(1,1-Dimethylethyl)dimethylsilyl]oxy]-1-phenylethyl]-8-methyl-2,4-dioxo-3,8-diazabicyclo[3.2.1]octane-6-carboxylic acid, ethyl ester (41e)**: reaction time 23 h; PTLC eluting with 2:1 hexanes–EtOAc (R_f 0.53, char B); 62% yield; $[\alpha]_D$ 59° (*c* 1.1, $CHCl_3$); IR ($CHCl_3$) 1730, 1680 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, rt) δ 7.33–7.23 (m, 5 H, Ph), 5.78 (dd, J = 10.2, 5.5 Hz, 1 H, PhCH), 4.66 (t, J = 10.2 Hz, 1 H, $^1/_2CH_2OSi$), 4.18 (q, J = 7.2 Hz, 2 H, OCH_2CH_3), 4.06 (m, 2 H, H-5, $^1/_2CH_2OSi$), 3.78 (d, J = 7.1 Hz, 1 H, H-1), 3.04 (dd, J = 9.8, 5.1 Hz, 1 H, H-6), 2.65 (ddd, J = 13.5, 7.1, 5.1 Hz, 1 H, H-7a), 2.50 (s, 3 H, NCH_3), 2.14 (dd, J = 13.5, 9.8 Hz, 1 H, H-7b), 1.25 (t, J = 7.2 Hz, 3 H, OCH_2CH_3), 0.85 (s, 9 H, $SiC(CH_3)_3$), 0.03 (s, 6 H, $Si(CH_3)_2$); ^{13}C NMR (50.4 MHz, $CDCl_3$, 20 °C) δ 172.9, 172.1, 171.7 (C=O), 137.2, 128.4, 128.1, 127.8 (Ph), 68.8 (C-5), 66.0 (C-1), 61.7, 61.5 (CH_2OSi, OCH_2CH_3), 55.8 (PhCH), 45.4 (C-6), 35.7 (NCH_3), 31.0 (C-7), 25.9 ($SiC(CH_3)_3$), 18.3 ($SiC(CH_3)_3$), 14.2 (OCH_2CH_3), –5.4 ($SiCH_3$); HRMS m/e calcd for $C_{24}H_{36}N_2O_5Si$ (M^+) 460.2394, found 460.2400.

[1*S*[1α,3(*R),5aα,6aα]]-3-[2-[[(1,1-Dimethylethyl)dimethylsilyl]oxy]-1-phenylethyl]-8-methyl-2,4-dioxo-3,8-diazabicyclo[3.2.1]octane-6-carboxylic acid, ethyl ester (43e)**: reaction time 23 h; PTLC eluting with 2:1 hexanes–EtOAc (R_f 0.52, char B); 51% yield; $[\alpha]_D$ 5.7° (*c* 0.8, $CHCl_3$); IR ($CHCl_3$) 1730, 1680 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, rt) δ 7.33–7.23 (m, 5 H, Ph), 5.79 (dd, J = 10.2, 5.5 Hz, 1 H, PhCH), 4.67 (t, J = 10.2 Hz, 1 H, $^1/_2CH_2OSi$), 4.17 (q, J = 7.2 Hz, 2 H, OCH_2CH_3), 4.07 (m, 2 H, H-5, $^1/_2CH_2OSi$), 3.77 (d, J = 7.1 Hz, 1 H, H-1), 2.95 (dd, J = 9.8, 5.1 Hz, 1 H, H-6), 2.65 (ddd, J = 13.5, 7.1, 5.0 Hz, 1 H, H-7a), 2.51 (s, 3 H, NCH_3), 2.20 (dd, J = 13.5, 9.8 Hz, 1 H, H-7b), 1.25 (t, J = 7.2 Hz, 3 H, OCH_2CH_3), 0.85 (s, 9 H, $SiC(CH_3)_3$), 0.03 (s, 6 H, $Si(CH_3)_2$); ^{13}C NMR (50.4 MHz, $CDCl_3$, 20 °C) δ 172.9, 172.1, 171.7 (C=O), 137.2, 128.4, 128.0, 127.8 (Ph), 68.8 (C-5), 66.0 (C-1), 61.7, 61.4 (CH_2OSi, OCH_2CH_3), 55.7 (PhCH), 45.2 (C-6), 35.7 (NCH_3), 31.2 (C-7), 25.9 ($SiC(CH_3)_3$), 18.3 ($SiC(CH_3)_3$), 14.1 (OCH_2CH_3), –5.4 ($SiCH_3$); HRMS m/e calcd for $C_{24}H_{36}N_2O_5Si$ (M^+) 460.2394, found 460.2396.

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Registry No. 1, 84573-33-1; **3a**, 100-46-9; **3b**, 37760-98-8; **3c**, 20989-17-7; **3e**, 120417-13-2; **4a**, 15329-69-8; **4b**, 120566-65-6; **4c**, 120566-66-7; **4e**, 120417-14-3; **6a**, 1631-26-1; (±)-**6b**, 135557-49-2; **6d**, 120566-68-9; **6e**, 120417-15-4; (±)-**7a**, 135457-83-9; (±)-**7b** (isomer 1), 135457-84-0; (±)-**7b** (isomer 2), 135457-85-1; **8d** (isomer 1), 135457-86-2; **8d** (isomer 2), 135457-87-3; **8e** (isomer 1), 135457-88-4; **8e** (isomer 2), 135457-89-5; (±)-**9a**, 120566-60-1; (±)-**9b** (isomer 1), 135557-50-5; (±)-**9b** (isomer 2), 135557-51-6; **9d** (isomer 1), 120566-70-3; **9d** (isomer 2), 120662-95-5; **9e** (isomer 1), 135557-52-7; **9e** (isomer 2), 135557-53-8; **10a**, 120566-61-2; (±)-**10b**, 135457-90-8; **10d**, 120566-72-5; **10e**, 127381-60-6; **12**, 96-33-3; (±)-**13a**, 120566-63-4; (±)-**13b**, 135557-54-9; **13d**, 120566-77-0; (±)-**14b**, 135557-55-0; **14d**, 120662-98-8; (±)-**15a**, 120566-64-5; **17**, 107-13-1; (±)-**18a**, 135457-91-9; (±)-**20a**,

135457-92-0; (–)-22, 4835-96-5; 23a, 135457-93-1; 24a, 135558-14-4; 25a, 135557-56-1; 26a, 135557-57-2; (–)-27, 96303-89-8; 28a, 135481-27-5; 29a, 135558-15-5; (–)-32, 94594-91-9; (+)-32, 119944-89-7; 33a, 127470-56-8; 33b, 127420-42-2; 33d, 127381-63-9; 33e, 127381-65-1; 35a, 127381-61-7; ent-38b, 127381-62-8; 38d, 127381-64-0; 38e, 127470-57-9; 41a, 127381-66-2; 41e, 127381-68-4; 43e, 127420-41-1; maleic anhydride, 108-31-6.

Supplementary Material Available: Tables of data collection details, fractional atomic coordinates, bond distances, bond and torsional angles, as well as anisotropic and isotropic thermal parameters associated with the X-ray structure determination of 35a; ^{1}H NMR spectra for all new compounds; UV spectra for compounds 10a, 12, (–)-32, and 33a (46 pages). Ordering information is given on any current masthead page.

Direct Polyiodination of Benzenesulfonic Acid

Daniell Lewis Mattern* and Xinhua Chen

Chemistry Department, University of Mississippi, University, Mississippi 38677

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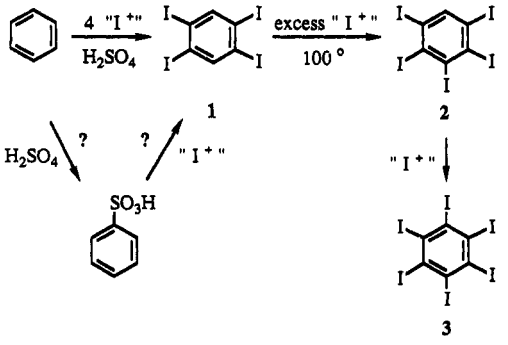
Direct aromatic polyiodination of benzenesulfonic acid (using I_2 and H_5IO_6 in H_2SO_4 at room temperature) was performed to test the possible intermediacy of $C_6H_5SO_3H$ in the corresponding direct polyiodination of benzene to $C_6H_2I_4$. The major product from $C_6H_5SO_3H$ was 3,4,5-triiodobenzenesulfonic acid (4). In contrast, no 4 was formed in the C_6H_6 reaction, showing that no significant sulfonation of C_6H_6 to $C_6H_5SO_3H$ occurred during benzene iodination. Compound 4 itself was shown to be inert under the reaction conditions. A pathway is proposed from $C_6H_5SO_3H$ to the other reaction products (C_6I_6, C_6I_5H, two $C_6I_4H_2$ isomers, and 3,4,5-triiodophenol), which therefore avoids the intermediacy of 4.

We have recently described a powerful system for the direct polyiodination and periodination of a variety of unactivated aromatic substrates.[1,2] This mixture, 3:1 iodine:periodic acid in concentrated sulfuric acid, may be thought of as producing iodonium ion, I^+, although the actual electrophilic species may be more complex.[3] Thus, 4 equiv of "I^+" at room temperature convert benzene to 1,2,4,5-tetraiodobenzene (1) in good yield, whereas forcing conditions (2-fold excess of "I^+" at 100 °C) produce hexaiodobenzene (3) in moderate yield. The presumed intermediate pentaiodobenzene (2) is not observed in substantial yield in either case.[2]



Since aromatics can undergo sulfonation in concentrated sulfuric acid,[4] the question arises whether the substrates become sulfonated during the course of direct polyiodinations. Such sulfonated intermediates would be deactivated toward subsequent iodination but would not be expected to be inert, since iodination can proceed on deactivated substrates such as nitrobenzene and benzoic acid.[2] We did not observe sulfonated products in our earlier studies, but sulfonated intermediates could escape detection by undergoing subsequent iododesulfonation[5,6] during the reaction or protiodesulfonation[5] during the aqueous isolation of products.

To test this possibility, we studied the polyiodination reaction of the prototypical aromatic substrate, benzene. Benzene is more apt to be sulfonated than any of the deactivated substrates (including iodinated benzenes),[4] and in fact is known to form benzenesulfonic acid, $C_6H_5SO_3H$, in concentrated H_2SO_4.[7] We subjected benzene and its sulfonation product, $C_6H_5SO_3H$, to the same iodination conditions and examined the product mixtures. If sulfonation of benzene is an initial step during benzene's polyiodination to 1, then the room-temperature reaction starting with $C_6H_5SO_3H$ should also give the product 1. In the event, the two substrates gave quite different product mixtures, prompting us to propose separate pathways for their polyiodination.

Results and Discussion

Iodination Conditions. Iodinations were performed with the appropriate quantities of 3:1 I_2/H_5IO_6 in concentrated H_2SO_4 to provide the relative equivalents of "I^+" shown in Table I. After cooling this reagent mixture on ice, the substrate was added with stirring; $C_6H_5SO_3H$ was supplied as its sodium salt. Reactions were allowed to stir at room temperature for 2 days or were heated to 55 °C for 1 day as shown in Table I. Benzene reactions typically produced voluminous precipitates; in contrast, no precipitates were apparent in the $C_6H_5SO_3H$ reactions.

Each completed reaction mixture was poured onto ice, and any precipitate was collected by filtration. The aqueous filtrate was concentrated; any resulting pearly paste was collected by centrifugation and purified by the HCl precipitation method of Boyle.[8] This paste was identified by its NMR and mass spectra as 3,4,5-triiodobenzenesulfonic acid (4); it was the only arenesulfonic acid

(1) Mattern, D. L. *J. Org. Chem.* **1983**, *48*, 4772.
(2) Mattern, D. L. *J. Org. Chem.* **1984**, *49*, 3051.
(3) Garrett, R. A.; Gillespie, R. J.; Senior, J. B. *Inorg. Chem.* **1965**, *4*, 563.
(4) Sutter, C. M.; Weston, A. W. *Org. React.* **1946**, *3*, 141.
(5) Cerfontain, H. *Mechanistic Aspects in Aromatic Sulfonation and Desulfonation*; Wiley-Interscience: New York, 1968; pp 185–198.
(6) Boyle, M. *J. Chem. Soc.* **1911**, *99*, 325.
(7) Gold, V.; Satchell, D. P. N. *J. Chem. Soc.* **1956**, 1635.
(8) Boyle, M. *J. Chem. Soc.* **1909**, *95*, 1683.

0022-3263/91/1956-5903$02.50/0