2.78 (d, J = 14.2 Hz, 1 H), 2.30 (s, 3 H), 1.13 (d, J = 9.5 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 203.6, 147.5 (two), 134.4, 128.9, 110.6, 106.9, 56.6, 56.0, 55.8, 55.3, 47.0, 46.8, 42.8, 39.6, 38.4, 35.8, 33.0, 28.5, 27.2, 26.8, 25.0; mass spectrum, calcd for $C_{22}H_{29}NO_3S_2$ 419.1589, found 419.1563.

2,3-Dimethoxy-14α-morphinan-6,7-dione (46). Dithioacetal **45** (21.0 mg, 0.050 mmol) was dissolved in dry dichloromethane (0.5 mL) at −75 °C and treated with a solution of *m*-chloroperoxybenzoic acid (0.085 M, 2.06 mL, 0.175 mmol). After the temperature had warmed to −20 °C, the mixture was kept overnight. Quenching with saturated aqueous sodium bisulfite, followed by extraction with dichloromethane and workup in the usual manner gave a crude solid that was dissolved in hydrochloric acid (2 N, 0.7 mL) and heated to 100 °C for 6 h. Upon cooling, the pH was adjusted to 8 with dilute sodium bicarbonate, and the mixture was extracted with dichloromethane. Workup in the usual manner, followed by chromatography on silica gel (ethyl acetate containing 3% *N*-methylpyrrolidine) gave diketone **46** (11.5 mg, 70%) as a colorless foam that was shown by NMR to be a 3:1 mixture of diosphenols: IR ($CDCl_3$) 3440, 1670, 1610, 1510 cm^{-1}; NMR δ 6.82 (s, 0.25 H), 6.78 (s, 0.25 H), 6.63 (s, 0.75 H), 6.61 (s, 0.25 H), 6.58 (s, 0.75 H), 6.09 (d, J = 2 Hz, 0.75 H), 3.90–3.84 (4 singlets, 6 H total); mass spectrum, calcd for $C_{19}H_{23}NO_4$ 329.1627, found 329.1603.

(±)-*O*-Methylpallidinine (47). Diketone **46** (11.5 mg, 0.035 mmol) in dry methanol (0.65 mL) was treated with *p*-toluenesulfonic acid monohydrate (21.5 mg) at room temperature for 100 h. After quenching with saturated sodium bicarbonate solution (15 mL), the reaction mixture was extracted with dichloromethane (3 × 10 mL) and worked up in the usual manner. Chromatography on silica gel (ethyl acetate containing 2% *N*-methylpyrrolidine) gave two fractions: fraction 1 consisted of pure (±)-*O*-methylpallidinine (2.5 mg, 21%, 55% after correction for recovered starting material). Fraction 2 (7 mg, 61%) was largely recovered starting material along with a trace of (±)-*O*-methylisopallidinine (**48**). (±)-*O*-methylpallidinine (**47**) had the following properties: mp 198–202 °C (hydrochloride); IR ($CHCl_3$) 1690, 1620, 1520, 1120 cm^{-1}; NMR ($CDCl_3$, 300 MHz) δ 6.87 (s, 1 H), 6.64 (s, 1 H), 6.37 (s, 1 H), 3.90 (s, 3 H), 3.86 (s, 3 H), 3.70 (s, 3 H), 3.39 (dd, J = 14.1, 16.7 Hz, 1 H), 3.11 (d, J = 17.7 Hz, 1 H), 2.89 (d, J = 5.6 Hz, 1 H), 2.60 (dd, J = 17.7, 5.6 Hz, 1 H), 2.36 (s, 3 H), 2.20–2.00 (m, 2 H), 1.52 (d, J = 11 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 194.7, 151.0, 148.0, 147.6, 132.7, 130.0, 121.6, 111.5, 107.8, 56.7, 56.6, 55.9, 55.1, 45.9, 42.9, 40.2, 36.9, 36.3, 27.2; mass spectrum, calcd for $C_{20}H_{25}NO_4$ 343.1783, found 343.1781. The synthetic material was identical with an authentic sample of the natural product by the above spectral criteria.

Acknowledgment. The latter stages of this work were funded by research Grant GM-28569 from the National Institutes of Health. D.R.S. also acknowledges the Science Research Council (United Kingdom) for a postdoctoral fellowship.

Registry No. **11a**, 91712-86-6; **12a**, 91712-87-7; **12b**, 91712-88-8; **13a**, 91712-89-9; **13b**, 91712-90-2; (±)-**14a**, 91712-91-3; (±)-**14b**, 91712-92-4; (±)-**15a**, 91712-93-5; (±)-**15a** (diketone), 91712-94-6; (±)-**15b**, 91712-95-7; (±)-**15b** (diketone), 91712-96-8; (±)-**16a**, 91712-97-9; (±)-**16b**, 91712-98-0; (±)-**17a**, 91712-99-1; (±)-**17b**, 91713-00-7; (±)-**18a**, 91713-01-8; (±)-**18b**, 91713-02-9; (±)-**19a**, 91713-03-0; (±)-**19b**, 91713-04-1; (±)-**22a**, 91713-06-3; (±)-**22b**, 91713-08-5; (±)-**23a**, 91713-10-9; (±)-**28**, 91713-11-0; **36**, 88176-83-4; (±)-**37**, 91713-12-1; **37**-ol, 91713-13-2; (±)-**38**, 88176-85-6; (±)-**38** (diketone), 91713-14-3; (±)-**39**, 88176-86-7; (±)-**40**, 91713-15-4; (±)-**41**, 88176-88-9; (±)-**42**, 88176-89-0; (±)-**43**, 88176-91-4; (±)-**44**, 91796-76-8; (±)-**44** (hydroxymethylene deriv), 91713-16-5; (±)-**45**, 91713-17-6; (±)-**46**, 91796-77-9; (±)-**47**, 88199-99-9; (±)-48, 91713-18-7; 3-(3,4-dimethoxyphenyl)-2-cyclohexenone, 20036-53-7; (±)-3-(2,3-cyclohexylidenedioxy)phenyl-3-hydroxycyclohexanone ethylene acetal, 91713-19-8; 1,3-cyclohexanedione isopropyl enol ether, 58529-72-9; methallyl chloride, 563-47-3; catechol cyclohexylidene acetal, 182-55-8; 1,3-cyclohexanedione, 504-02-9; veratrole, 91-16-7; *N*-methylhydroxylamine hydrochloride, 4229-44-1; diazomethane, 334-88-3; allyl bromide, 106-95-6; 4-bromoveratrole, 2859-78-1; 3-ethoxy-2-cyclohexenone, 5323-87-5; trimethylene dithiotosylate, 3866-79-3.

Intramolecular *N*-Carbamoyliminium Ion Cyclizations of Unactivated Alkenes and Acetylenes

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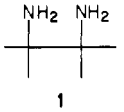
A select series of 3-alkenyl (**7a–e**) and 3-acetylenic (**7f**) 4-hydroxy-5,5-dimethylimidazolidin-2-ones were prepared. Treatment of each substrate except **7e** with acid led to the desired intramolecular amidoalkylation reaction to give the bicyclic imidazolidin-2-ones. The reactions proceeded regio- and stereoselectively in moderate to good yields. The mechanism of these and related transformations are discussed.

The vicinal diamine group (**1**) is incorporated in many natural products and chemotherapeutic agents. Few



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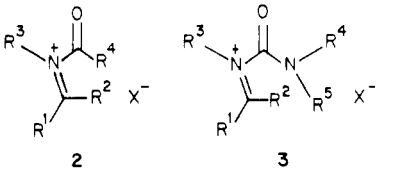
general methods exist for the preparation of this group. Of special interest to us is the development of new procedures for the synthesis of functionalized diamines from readily accessible starting materials.[2-4]

Recently, considerable attention has been focused on intramolecular *N*-acyliminium ion (**2**) initiated cyclization



2 **3**

reactions.[4-8] These transformations have proved partic-

(1) Camille and Henry Dreyfus Teacher-Scholar Grant Recipient, 1977–1982.

(2) Kohn, H.; Jung, S. H. *J. Am. Chem. Soc.* **1983**, *105*, 4106–4108. Jung, S. H.; Kohn, H. *Tetrahedron Lett.* **1984**, *25*, 399–402.
(3) Cortes, S.; Kohn, H. *J. Org. Chem.* **1983**, *48*, 2246–2254.
(4) Kohn, H.; Liao, Z.K. *J. Org. Chem.* **1982**, *47*, 2787–2789.

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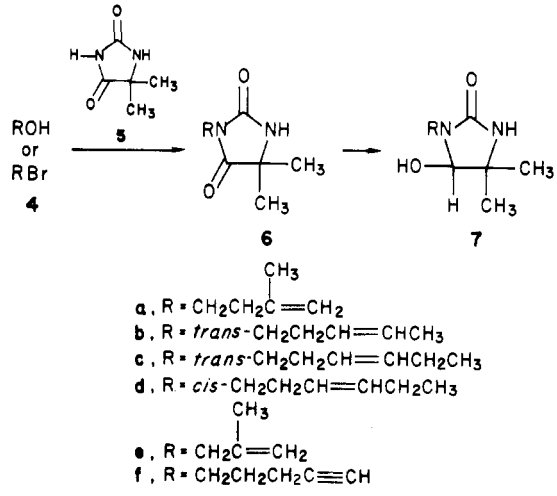
ularly useful for the synthesis of complex natural products. However, little is known about the corresponding transformation beginning with *N*-carbamoyliminium ions **3**.[4,9,10] Previously, we reported the use of *N*-carbamoyl species in intramolecular aromatic annelation reactions.[4] In this paper, we describe the extension of this process to *N*-alkenyl and *N*-acetylenic substrates. Special attention has been placed on delineating the stereospecific and regiospecific features of these cyclization processes.

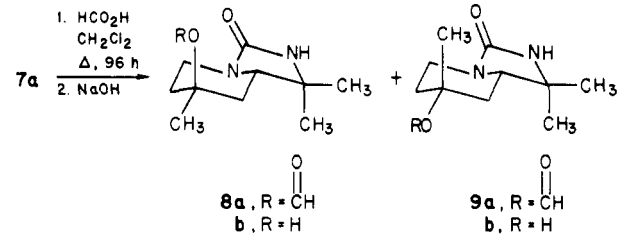
Results

Synthesis. Our study is patterned after the pioneering work of Speckamp and co-workers on α-acyliminium ion **2** initiated condensation reactions of olefins.[5a] The desired *N*-amidoyliminium ions **3** were prepared in situ from the corresponding 4-hydroxy-2-imidazolidinones **7**. These precursors were synthesized in two steps from 5,5-dimethylhydantoin (**5**). In most cases, the oxidative coupling procedure of Mitsunobo[11] was employed, beginning with the appropriate alcohol (**4a,c–f**), diethyl azodicarboxylate, triphenylphosphine, and **5**. Preparation of 3-(*trans*-pent-3-enyl)-5,5-dimethylimidazolidine-2,4-dione (**6b**) was accomplished by alkylation of the hydantoin **5** under basic conditions (KOH, Me_2SO) with alkenyl bromide **4b**.[4] Treatment of **6** with excess $LiAlH_4$ (THF, room temperature, 2 days) afforded the 4-hydroxy adduct **7** in 54–95% yield.[3]

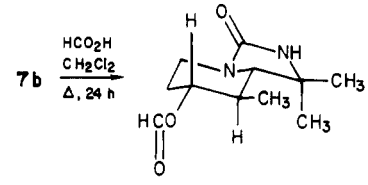


N-Carbamoyliminium ion **3** formation and subsequent intramolecular cyclization was initiated for compounds **7a–d** with formic acid. Stronger acid conditions were employed in the cyclization of the acetylenic adduct **7f** (trifluoroacetic anhydride, trifluoroacetic acid, CH_2Cl_2) and the attempted five-membered annelation reaction beginning with **7e** (trifluoroacetic anhydride, stannic chloride, CH_2Cl_2). In the latter two instances, no detectable reaction was observed with formic acid in CH_2Cl_2.

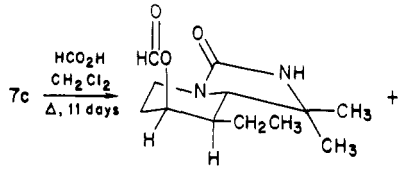
Intramolecular cyclization of **7a** with formic acid produced an approximate 1:1 ratio of **8a** and **9a** (50% yield). Separation of these diastereomers by column chromatography proved difficult. Accordingly, base hydrolysis of the binary mixture gave **8b** and **9b**, which were then separated and identified.

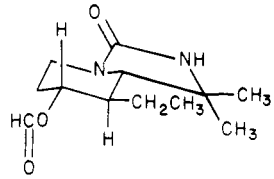


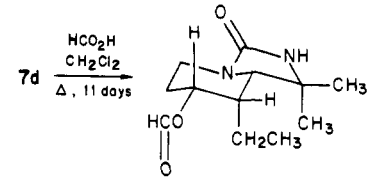
The *trans*-methyl derivative **7b** yielded one major compound **10** (49% yield) upon treatment with formic acid.



Correspondingly, two epimers **11** and **12** were isolated in 23% and 54% yields, respectively, from the *trans*-ethyl adduct **7c**, while the *cis*-ethyl isomer **7d** gave **13** in 42% yield along with unreacted starting material.







Cyclization of the acetylenic derivative **7f** occurred regioselectively to produce the seven-membered ketone **14**

(5) (a) Shoemaker, H. E.; Dijkink, J.; Speckamp, W. N. *Tetrahedron* **1978**, *34*, 163–172. (b) Dijkink, J.; Speckamp, W. N. *Ibid.* **1978**, *34*, 173–178. (c) Veenstra, S. J.; Speckamp, W. N. *J. Am. Chem. Soc.* **1981**, *103*, 4645–4646. (d) Wijnberg, B. P.; Speckamp, W. N. *Tetrahedron Lett.* **1981**, *22*, 5079–5082. (e) Winjberg, B. P.; Speckamp, W. N.; Oostveen, A. R. C. *Tetrahedron* **1982**, *38*, 209–217. (f) Hamersma, J. A. M.; Speckamp, W. N. *Tetrahedron Lett.* **1982**, *23*, 3811–3814. (g) Nossin, P. M. M.; Hamersma, J. A. M.; Speckamp, W. N. *Ibid.* **1982**, *23*, 3807–3810. (h) Winjberg, J. B. P. A.; Speckamp, W. N. *Ibid.* **1975**, 3963–3966. (i) Boer-Terpstra, T.; Dijkink, J.; Shoemaker, H. E.; Speckamp, W. N. *Ibid.* **1977**, 939–942.

(6) (a) Hart, D. J. *J. Org. Chem.* **1981**, *46*, 367–373. (b) Hart, D. J. *Ibid.* **1981**, *46*, 3576–3578. (c) Hart, D. J.; Kanai, K. *Ibid.* **1982**, *47*, 1555–1560. (d) Hart, D. J.; Yang, T.-K. *Tetrahedron Lett.* **1982**, *23*, 2761–2764. (e) Hart, D. J.; Kanai, K. *J. Am. Chem. Soc.* **1983**, *105*, 1255–1263. (f) Hart, D. J.; Tsai, Y.-M. *J. Org. Chem.* **1982**, *47*, 4403–4409.

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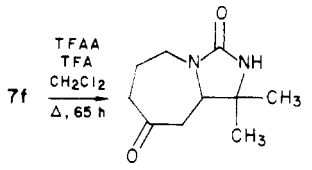
(10) For related reactions, please see: Zaugg, H. F.; Leonard, J. E.; Arendsen, D. L. *J. Heterocycl. Chem.* **1974**, *11*, 833–834. Ben-Et, G.; Ben-Ishai, D. *J. Chem. Soc., Chem. Commun.* **1969**, 376. Ben-Ishai, D.; Ben-Et, G. *Ibid.* **1969**, 1399. Goldstein, E.; Ben-Ishai, D. *Tetrahedron Lett.* **1969**, 2631–2634.

(11) Mitsunobu, O.; Wada, M.; Sano, T. *J. Am. Chem. Soc.* **1972**, *94*, 679–680.

as the major product (46% yield). The acid-mediated



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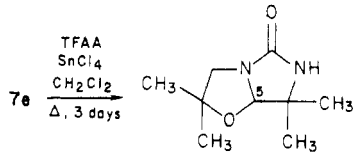
reaction of **7e** did not proceed in the desired sense. In this instance, the cyclic ether **15** was isolated in 30% yield.



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Spectral Properties. The structures of adducts **8b**, **9b**, and **10–13** were readily ascertained from the detailed analysis of the ^1H and ^{13}C NMR spectra (Table I) of these compounds. Moreover, the ^1H NMR spectra for compounds **10**, **11**, and **13** were similar to previously prepared analogues.[5a]

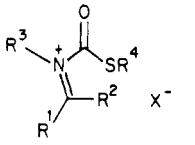
Several features in the ^1H NMR spectra of compounds **8b**, **9b**, and **10–13** were of note. The presence of an equatorial or axial formyloxy (or hydroxy) group at carbon-4 could be ascertained by a series of parameters. First, the chemical shift value for an equatorial carbon-4 hydrogen (compound **11**) appeared downfield (Δppm = 0.38–0.80) from the resonance observed for an axial hydrogen at this ring position (compounds **10**, **12**, and **13**). Second, in compounds **10**, **12**, and **13** the carbon-4 axial hydrogen appeared as a distinctive doublet of doublets of doublets in which there was at least one large coupling interaction. On the other hand, the carbon-4 equatorial proton in **11** appeared as a broad multiplet signal. This pattern was consistent with three small proton–proton coupling interactions.[12] Third, induced downfield shifts were noted for the syn–axial protons at carbons-2 (Δppm $\sim$ 0.11) and 6 (Δppm $\sim$ 0.15) for substrates containing an axial oxygen substituent at carbon-4 vs. an equatorial oxygen moiety (i.e., compare **11** vs. **10** and **12**; **8b** vs. **9b**).[5a,13] Important stereochemical information for these compounds was also deduced from the magnitude of the coupling constant for the carbon-6 proton.[12] Compounds **10–12** all displayed a large proton–proton coupling constant (J = 9–10 Hz) for the carbon-6 methine hydrogen in keeping with the proposed diaxial proton interaction present at carbons-5 and -6. This pattern was in contrast to the smaller coupling constant noted in adduct **13** (J = 3 Hz). This latter value along with the analysis of the carbon-4 methine proton coupling pattern fixed the ethyl substituent at carbon-5 in the axial plane for this adduct.

The composite set of ^{13}C NMR spectra for compounds **8b**, **9b**, and **10–13** proved equally informative. It is well-known that carbon atoms three bonds away from a substituent experience an upfield shift due to sterically induced polarization of the C–H bonds.[14] This effect is generally maximized in rigid systems when the substituent and the carbon in question are in a gauche relationship (γ-gauche effect).[15] Furthermore, heteroatom substituents usually lead to larger upfield shifts than methylene or methyl groups.[14] In light of the relatively rigid nature of these bicyclic ring systems, it was not surprising that pronounced trends were observed in the chemical shift values for various carbon atoms which could be attributed to steric effects and which were in agreement with the assigned structures. These include (1) the upfield shifts noted at carbons-3 and the methylene carbon of the axial ethyl substituent in **13** vs. the chemical shift values for these same carbon atoms in adducts (i.e., compounds **11** and **12**) bearing an equatorial ethyl group; (2) the upfield shifts noted at carbons-2 and -6 upon introduction of a formyloxy group in the axial position (i.e., compound **11**) vs. in the equatorial plane (i.e., compounds **10**, **12**, and **13**); and (3) the upfield shifts noted at carbons-2 and -6 upon substitution of an axial hydroxy moiety (compound **8b**) vs. an axial methyl group (compound **9b**).

Consistent with the proposed regioselective formation of the seven-membered ring adduct **14** from the acetylenic substrate **7f** was the observation of four triplet patterns in the proton-coupled ^{13}C NMR spectrum for the annelated ring methylene units. Several spectral properties supported the structural assignment for cyclic ether **15**. In particular, the downfield singlet at δ 4.83 in the ^1H NMR spectrum is in accord with the anticipated chemical shift value for the carbon-5 methine hydrogen.[3,4] The corresponding carbon resonance was observed at 96.5 ppm. Distinct resonances were also detected between 22.1–28.3 ppm in the ^{13}C NMR spectrum for each of the four different methyl carbon atoms. A significant signal in the mass spectrum of **15** was the peak at m/e 126. This ion has been attributed to the initial cleavage of $(CH_3)_2CO$ from the parent ion (m/e 184).

Discussion

The *N*-carbamoyliminium ion **3** initiated cyclizations were characterized by their high stereoselectivity. These results correlated favorably to those previously described for α-acyliminium[5a] **2** and thiono α-acyliminium[16] **16** ion



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initiated cyclization reactions. Similar stereocontrolled processes have been noted in these systems. These results have been explained in terms of the Stork–Eschenmoser hypothesis in which the reaction proceeds through a chairlike transition state (i.e., **17**).[17] A similar rationale

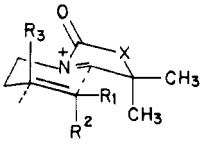

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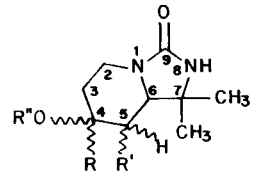
Table I. NMR Spectral Properties of Selectively Substituted Annelated Imidazolidin-2-ones



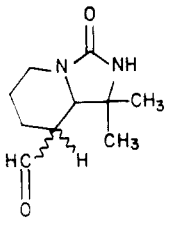
	^{1}H NMR[a]						^{13}C NMR[a]									
compd	C_2				C_7-CH_3								C_7-CH_3			
no.	H_{eq}	H_{ax}	C_4-H	C_6-H	eq	ax	C_2	C_3	C_4	C_5	C_6	C_7	eq	ax	C_9	C_4-OC(O)H
8b[b]	3.40; br dd; 13, 3	2.80; ddd; 16, 13, 3	*c*	3.22; dd; 9, 3	1.14; s	1.12; s	37.0; t	36.1; t	66.6; s; (C_4-CH_3, 27.8 q)	36.6; t	59.6; d	53.5; s	31.5; q	22.3; q	159.4; s	
9b	3.85; ddd; 13, 6, 2	2.68; ddd; 16, 13, 3	*d*	3.09; dd; 9, 4	1.27	1.25	39.5[e]	38.4	69.9, (C_4-CH_3, 24.4, q)	38.8	62.5	54.6	28.4	22.9	159.9	
10	3.88; ddd; 12, 5, 2	2.72; ddd; 12, 12, 5	4.66; ddd; 12, 10, 5	2.90; d; 10	1.38; s	1.25; s	38.5; t	30.1; t	75.8; d	36.5; d; (C_5-CH_3, 13.6, q)	68.6; d	55.4, s	29.2; q	22.8; q	159.6; s	160.5; d
11	3.72; ddd; 13, 5, 3	2.85; ddd; 15, 13, 3	5.45-5.47; br m	3.18; d; 9	1.36; s	1.19; s	35.3; t	29.1; t	67.5; d	41.7; d; (C_5-CH_2CH_3, (20.0 (t), 10.6 (q))	63.8; d	55.0; s	29.5; q	22.7; q	159.6; s	160.1; d
12	3.86; ddd; 13, 5, 2	2.70; ddd; 15, 13 3	4.96; ddd; 15, 11, 4	3.11; d; 9	1.38; s	1.24; s	38.3; t	30.2; t	72.5; d	40.8; d; (C_5-CH_2CH_3, (19.2 (t), 8.5 (q))	64.2; d	55.6; s	29.5; q	23.1; q	159.5; s	160.3; d
13	4.05; ddd; 13, 6, 1	2.90; ddd; 13, 12, 5	5.08; ddd; 12, 9, 5	3.10; d; 3	1.33; s	1.29; s	37.5; t	24.5; t	74.6; d	42.2; d; (C_5-CH_2CH_3, (15.8 (t), 14.7 (q))	66.8; d	54.5; s	31.9; q	21.8; q	159.6; s	160.2; d

[a] ^{1}H and ^{13}C NMR spectrum were taken in $CDCl_3$ unless otherwise noted. The number in each entry is the chemical shift values (δ) observed in parts per million relative to Me_4Si, followed by the multiplicity of the signal, followed by the coupling constant(s) in hertz. [b] The ^{1}H and ^{13}C NMR spectrum were run in Me_2SO-d_6. [c] The chemical shift value for the C_4-CH_3 protons was δ 0.98. [d] The chemical shift value for the C_4-CH_3 protons was δ 1.12. [e] The proton-coupled ^{13}C NMR spectrum for compound **9b** was not taken.

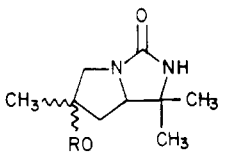
can be offered in this study.[18] Whether or not the entire reaction in some cases (i.e., **7b** → **10**, **7d** → **13**) is concerted or stepwise leading to the stereocontrolled introduction of three chiral centers is not known. Our results do indicate that when the terminal cationic center is sufficiently stabilized (i.e., beginning with **7a**) the reaction process is best explained by a stepwise pathway leading to the eventual formation of two epimers.

The reactions examined in this study proceeded in moderate to good yields. However, slightly lower yields were observed in the α-carbamoyliminium **3** ion initiated reactions than in either the α-acyliminium[5a] **2** or the thiono α-acyliminium[16] **16** ion processes.

The selective formation of the fused seven-membered ring ketone **14** vs. the six-membered ring aldehyde **21** from **7f** may be a reflection of the potential stability of the intermediate vinyl cations (mono- vs. unsubstituted, respectively) that would be generated in each of these reactions.[20] Similar findings have been previously noted.[5i,16a] The inability to detect the desired five-membered cyclized product **22** from **7e** was expected. Formation of this adduct would necessitate an unfavorable 5-Endo-Trig ring closure process.[21]



21



22

Experimental Section

General Methods. Melting points were determined with a Thomas-Hoover melting point apparatus and are uncorrected. Infrared spectra (IR) were run on a Beckman IR 4250 spectrophotometer and calibrated against the 1601-cm^{-1} band of polystyrene. Proton nuclear magnetic resonance (^1H NMR) spectra were recorded on Varian Associates Model XL-100-15, FT-80A, or T-60 instruments as well as by Mrs. Helga Cohen at the Department of Chemistry, University of South Carolina, on a Bruker WH-400 instrument. Carbon-13 nuclear magnetic resonance (^{13}C NMR) spectra were determined on a Varian Associates Model XL-100-15 or FT-80A spectrometer. Chemical shifts are in parts per million relative to Me_4Si, and coupling constants (J values) are in hertz. Mass spectral data were obtained at an ionizing voltage of 70 eV on a Hewlett-Packard 5930 gas chromatograph–mass spectrometer. High-resolution (EI mode) mass spectra were performed by Dr. James Hudson and Dr. John Chinn at the Department of Chemistry, University of Texas at Austin, on a CEC21-110B double-focusing magnetic-sector spectrometer at 70 eV. Exact masses were determined by peak matching. Elemental analyses were obtained at Spang Microanalytical Laboratories, Eagle Harbor, MI.

The solvents and reactants were of the best commercial grade available and were used without further purification unless noted. The 3-methyl-3-buten-1-ol (**4a**), *trans*-3-hexen-1-ol (**4c**), *cis*-3-hexen-1-ol (**4d**), and 2-methyl-2-propen-1-ol (**4e**) were purchased from Aldrich Chemical Co., while 4-pentyn-1-ol (**4f**) was obtained from ICN Pharmaceuticals, Inc. The *trans*-pent-3-enyl bromide was prepared from cyclopropylmethylcarbinol (Aldrich Chemical Co.) by using the method of Julia, Julia, and Tchen.[22] When dry solvents were required, CH_2Cl_2 was distilled from P_2O_5, C_6H_6 was distilled and then stored over Na, and THF was distilled from $LiAlH_4$.

All reactions were run under N_2, and all glassware was dried before use unless otherwise noted. Flash chromatography was run by using Merck silica gel 60 PF-254 (catalog No. 7747). Thin-layer chromatographic analyses were run on Analtech precoated silica G microscope slides (2.5 × 10 cm; catalog no. 01521).

General Procedure for the Preparation of 3-Substituted-5,5-dimethylimidazolidine-2,4-diones 6. Using the Mitsunobu coupling method,[11] 1 equiv of diethyl azodicarboxylate in THF was slowly added to a THF solution containing an equimolar amount of 5,5-dimethylhydantoin (**5**), the appropriate alcohol **4**, and triphenylphosphine at 5–10 °C. The reaction solution was maintained at room temperature (2 days) and then concentrated to dryness in vacuo. A 50% ethyl acetate–hexane solution (100–200 mL) was added to the syrupy residue and the mixture was placed in the refrigerator (18 h). The precipitated triphenylphosphineoxide was filtered, and the solution was concentrated to dryness in vacuo. Purification of the residue by flash chromatography gave the desired 3-substituted-5,5-dimethylimidazolidine-2,4-dione (**6**).

3-(3-Methylbut-3-enyl)-5,5-dimethylimidazolidine-2,4-dione (6a). The Mitsunobu[11] coupling method was employed beginning with a THF solution (150 mL) containing an equimolar amount of **5** (6.40 g, 50 mmol), **4a** (4.30 g, 50 mmol), and triphenylphosphine (13.11 g, 50 mmol), and a 30-mL THF solution of diethyl azodicarboxylate (8.70 g, 50 mmol). After workup and flash chromatography (SiO_2, 50% benzene–ethyl acetate), pure **6a** (R_f 0.60, 50% benzene–ethyl acetate) was obtained in 71% yield (7.45 g): mp 64–66 °C; IR (KBr) 3210, 1770, 1725 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.41 (s, 6 H), 1.78 (s, 3 H), 2.35 (t, 2 H, J = 8 Hz), 3.63 (t, 2 H, J = 8 Hz), 4.69 (d, 1 H, J = 1 Hz), 4.75 (d, 1 H, J = 1 Hz), 7.05 (br s, 1 H, D_2O exchangeable); ^{13}C NMR ($CDCl_3$) 21.8, 25.0, 36.0, 36.5, 58.6, 112.9, 142.1, 156.9, 177.7 ppm. The signal at 25.0 ppm was approximately twice the intensity of neighboring peaks. MS, m/e (relative intensity) 196 (40), 181 (15), 129 (100), 113 (80), 99 (30), 84 (50), 70 (55); M_r 196.1215 (calcd for $C_{10}H_{16}N_2O_2$ 196.1212).

3-(*trans*-Hex-3-enyl)-5,5-dimethylimidazolidine-2,4-dione (6c). Utilizing the procedure described for **6a**, **5** (6.40 g, 50 mmol), **4c** (5.00 g, 50 mmol), and triphenylphosphine (13.11 g, 50 mmol) in THF (150 mL) were treated with diethyl azodicarboxylate (8.70 g, 50 mmol) in THF (30 mL). After workup and flash chromatography (SiO_2, 50% benzene–ethyl acetate), the fractions with a R_f value between 0.61 and 0.68 (TLC analysis, SiO_2, 50% benzene–ethyl acetate) were collected and concentrated to dryness in vacuo. ^1H NMR spectral analysis indicated that these fractions contained **6c** and a small amout of diethyl *N,N'*-hydrazinedicarboxylate. The diethyl *N,N'*-hydrazinedicarboxylate was selectively precipitated from the mixture by using a small amount of benzene. The remaining benzene filtrate was concentrated in vacuo and then further purified by flash chromatography (SiO_2, 50% benzene–ethyl acetate) to give 8.50 g (81% yield) of **6c** (R_f 0.65, 50% benzene–ethyl acetate). Upon standing, the product solidified to a wax: IR (neat, NaCl) 3250, 1770, 1710 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.93 (t, 3 H, J = 7 Hz), 1.42 (s, 6 H), 1.91–2.04 (m, 2 H), 2.17–2.36 (m, 2 H), 3.53 (t, 2 H, J = 7 Hz), 5.39–5.45 (m, 2 H), 7.33 (br s, 1 H, D_2O exchangeable); ^{13}C NMR ($CDCl_3$) 13.6, 24.9, 25.5, 31.2, 38.0, 58.5, 124.8, 135.1, 157.0, 177.8 ppm. The signal at 24.9 ppm was approximately twice the intensity of neighboring peaks. MS, m/e (relative intensity) 210 (3), 141 (2), 129 (100), 113 (10); M_r 210.1373 (calcd for $C_{11}H_{18}N_2O_2$ 210.1368).

3-(*cis*-Hex-3-enyl)-5,5-dimethylimidazolidine-2,4-dione (6d). The preceding method was utilized for the preparation of

(18) An alternative pathway for these reactions is conceivable. Recently, several important examples illustrating the use of the aza-Cope rearrangement in organic synthesis have been reported.[6d,19] An analogous process may have occurred in our transformations prior to final cyclization. Our original choice of *N*-alkenyl substituents do not allow us to distinguish between this and the proposed pathway.

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6d beginning with **5** (6.40 g, 50 mmol), **4d** (5.00 g, 50 mmol), and triphenylphosphine (13.11 g, 50 mmol) in THF (200 mL) and diethyl azodicarboxylate (8.70 g, 50 mmol) in THF (30 mL). After workup and flash chromatography, **6d** (R_f 0.65, SiO_2, 50% benzene–ethyl acetate) was obtained in 64% yield (6.70 g). The desired product solidified upon standing at room temperature: mp 42–45 °C; IR (KBr) 3300, 1765, 1700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.88 (t, 3 H, J = 8 Hz), 1.40 (s, 6 H), 1.77–2.50 (m, 4 H), 3.47 (t, 2 H, J = 8 Hz), 5.25–5.37 (m, 2 H), 5.68 (br s, 1 H, D_2O exchangeable); ^{13}C NMR ($CDCl_3$) 14.3, 20.5, 25.0, 25.9, 38.0, 58.6, 124.3, 134.8, 156.9, 177.6 ppm. The signal at 25.0 ppm was approximately twice the intensity of neighboring peaks. MS (CI), 211 (P + 1); M_r 210.1373 (calcd for $C_{11}H_{18}N_2O_2$ 210.1368).

3-(2-Methylprop-2-enyl)-5,5-dimethylimidazolidine-2,4-dione (6e). The procedure described for the preparation of **6a** was employed using **5** (12.80 g, 100 mmol), **4e** (7.20 g, 100 mmol), and triphenylphosphine (26.20 g, 100 mmol) in THF (250 mL) and diethyl azodicarboxylate (17.40 g, 100 mmol) in THF (50 mL). After workup and flash chromatography (SiO_2, 50% benzene–ethyl acetate), the desired **6e** was isolated as a liquid in 35% yield (6.30g): R_f 0.58 (50% benzene–ethyl acetate); IR (KBr) 3250, 1775, 1730 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.45 (s, 6 H), 1.75 (s, 3 H), 4.03 (s, 2 H), 4.77 (d, 1 H, J = 1 Hz), 4.88 (d, 1 H, J = 1 Hz), 6.77 (br s, 1 H, D_2O exchangeable); ^{13}C NMR ($CDCl_3$) 20.2, 25.0, 43.6, 58.8, 111.7, 139.2, 157.0, 177.5 ppm. The signal at 25.0 ppm was approximately twice the intensity of neighboring peaks. MS, m/e (relative intensity) 182 (100), 167 (10), 154 (32), 139 (11), 124 (5), 113 (11), 97 (35), 96 (38); M_r 182.1050 (calcd for $C_9H_{14}N_2O_2$ 182.1055).

3-(Pent-4-ynyl)-5,5-dimethylimidazolidine-2,4-dione (6f). Diethyl azodicarboxylate (10.50 g, 60 mmol) in THF (50 mL) was slowly added to a THF (250 mL) solution containing **5** (8.30 g, 65 mmol), **4f** (5.00 g, 59 mmol), and triphenylphosphine (15.70 g, 60 mmol) by using the previously described procedure. After workup and flash chromatography (SiO_2, 50% benzene–ethyl acetate), 8.20 g (72% yield) of crystalline product **6f** was isolated: R_f 0.59 (50% benzene–ethyl acetate); mp 87–89 °C; IR (KBr) 3250, 3220, 1750, 1700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.44 (s, 6 H), 1.75–2.50 (m, 5 H), 3.59 (t, 2 H, J = 9 Hz), 7.03 (br s, 1 H, D_2O exchangeable); ^{13}C NMR ($CDCl_3$) 16.1, 25.0, 27.1, 37.8, 58.7, 69.2, 83.0, 156.9, 177.7 ppm. The signal at 25.0 ppm was approximately twice the intensity of neighboring peaks. MS, m/e (relative intensity) 194 (4), 166 (3), 151 (52), 129 (100), 113 (31), 99 (21), 84 (47), 70 (52); M_r 194.1062 (calcd for $C_{10}H_{14}N_2O_2$ 194.1055).

3-(*trans*-Pent-3-enyl)-5,5-dimethylimidazolidine-2,4-dione (6b). A Me_2SO (60 mL, stored via 4 Å molecular sieves, and then freshly distilled from CaH_2) solution containing **5** (6.40 g, 50 mmol) and KOH (3.30 g, 50 mmol) was heated to 100–110 °C (30 min) and then cooled to room temperature. A Me_2SO solution of **4b** (>90% pure, ^{13}C NMR analysis, 8.14 g, 55 mmol) was added, and the solution was maintained at room temperature (2 days). The reaction was quenched by the addition of H_2O (25 mL) and the solution was extracted with Et_2O (3 × 400 mL). The organic layers were combined, washed with H_2O (100 mL), dried ($MgSO_4$), and concentrated in vacuo. The crude product was purified by flash chromatography (SiO_2, 65% benzene–ethyl acetate) to give the desired **6b** which crystallized upon standing (8.50 g, 87% yield): R_f 0.59 (65% benzene–ethyl acetate); mp 34–36 °C; IR (neat, NaCl) 3320, 1790, 1720 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.43 (s, 6 H), 1.65 (d, 3 H, J = 5 Hz), 2.03–2.47 (m, 2 H), 3.48(t, 2 H, J = 6 Hz), 5.25–5.57 (m, 2 H), 6.17 (br s, 1 H, D_2O exchangeable); ^{13}C NMR ($CDCl_3$) 17.8, 25.1, 31.2, 38.0, 58.6, 126.9, 128.2, 156.8, 177.5 ppm. The signal at 25.1 ppm was approximately twice the intensity of neighboring peaks. The ^{13}C NMR spectrum contained two weak signals (<10% of neighboring peaks) at 125.8 and 127.0 ppm. These have been tentatively assigned to the corresponding cis adduct. MS, m/e (relative intensity) 196 (<1), 129 (100), 113 (23), 99 (4), 84 (14); M_r 196.1217 (calcd for $C_{10}H_{16}N_2O_2$ 196.1212).

General Procedure for the Reduction of 3-Substituted-5,5-dimethylimidazolidine-2,4-diones 7. Using the method previously reported,[3,4] an equimolar amount of $LiAlH_4$ was slowly added in increments to a THF (100 mL of THF/0.10 g of $LiAlH_4$) solution of the 3-substituted-5,5-dimethylimidazolidine-2,4-dione **6**. The reaction mixture was allowed to stir at room temperature (2 days) and then the excess $LiAlH_4$ destroyed with H_2O and aqueous 15% NaOH.[23] The reaction mixture was filtered, and the filtrate was dried ($MgSO_4$) and concentrated in vacuo. The desired 3-substituted-4-hydroxy-5,5-dimethylimidazolidin-2-ones **7** were purified by recrystallization or by flash chromatography.

3-(3-Methylbut-3-enyl)-4-hydroxy-5,5-dimethylimidazolidin-2-one (7a). Crude **7a** (3.00 g, 80%) was obtained from the reduction of **6a** (3.70 g, 19 mmol) with $LiAlH_4$. The desired product was purified by recrystallization from CH_2Cl_2 (2.30 g, 62% yield): mp 128–130 °C; IR (KBr) 3300, 3185, 1685 cm^{-1}; ^1H NMR (Me_2SO-d_6) δ 1.08 (s, 6 H), 1.71 (s, 3 H), 2.17 (t, 2 H, J = 7 Hz), 2.88–3.50 (m, 2 H), 4.54 (d, 1 H, J = 7 Hz), 4.70 (s, 2 H), 5.72 (d, 1 H, J = 7 Hz, D_2O exchangeable), 6.37 (br s, 1 H, D_2O exchangeable). Addition of D_2O to the ^1H NMR sample led to a collapse of the doublet at δ 4.54 to a singlet. ^{13}C NMR (Me_2SO-d_6) 21.9, 27.7, 35.8, 36.8, 55.3, 85.5, 111.3, 143.3, 158.7 ppm. The signal at 21.9 ppm was approximately twice the intensity of nearby peaks. MS, m/e (relative intensity) 198 (11), 183 (4), 143 (100); M_r 198.1372 (calcd for $C_{10}H_{18}N_2O_2$ 198.1368).

3-(*trans*-Pent-3-enyl)-4-hydroxy-5,5-dimethylimidazolidin-2-one (7b). Reduction of **6b** (5.80 g, 30 mmol, ^{13}C NMR analysis indicated that the trans/cis isomer ratio was >9:1) by $LiAlH_4$, followed by workup and recrystallization from CH_2Cl_2 gave 5.60 g (95% yield) of **7b** (R_f 0.46, 25% benzene–ethyl acetate). ^{13}C NMR analysis of the product indicated that it was nearly (>95%) pure: mp 98–100 °C; IR (KBr) 3290, 3200, 1690 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.20 (s, 3 H), 1.27 (s, 3 H), 1.63 (d, 3 H, J = 6 Hz), 2.11–2.35 (m, 2 H), 3.09–3.49 (m, 2 H), 4.32 (d, 1 H, J = 11 Hz), 4.60 (d, 1 H, J = 11 Hz, D_2O exchangeable), 4.84 (br s, 1 H, D_2O exchangeable), 5.35–5.48 (m, 2 H). Addition of D_2O to the ^1H NMR sample led to a collapse of the doublet at δ 4.32 to a singlet. ^{13}C NMR ($CDCl_3$) 17.9, 21.8, 28.1, 31.5, 39.4, 56.4, 87.5, 127.4, 128.1, 159.8 ppm; MS, m/e (relative intensity) 198 (8), 143 (100); M_r 198.1364 (calcd for $C_{10}H_{18}N_2O_2$ 198.1368).

3-(*trans*-Hex-3-enyl)-4-hydroxy-5,5-dimethylimidazolidin-2-one (7c). Compound **6c** (6.30 g, 30 mmol) gave 5.40 g (85%) of crude **7c** upon treatment with $LiAlH_4$. Recrystallization of the reaction product from benzene yielded 4.50 g (70%) of pure product: mp 95–98 °C; IR (KBr) 3300, 3200, 1700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.92 (t, 3 H, J = 7 Hz), 1.23 (s, 3 H), 1.28 (s, 3 H), 1.70–2.43 (m, 4 H), 2.75–3.67 (m, 2 H), 4.53 (d, 1 H, J = 10 Hz), 4.90 (d, 1 H, J = 10 Hz, D_2O exchangeable), 5.05 (br s, 1 H, D_2O exchangeable), 5.15–5.60 (m, 2 H). Addition of D_2O to the ^1H NMR sample led to a collapse of the doublet at δ 4.53 to a singlet. ^{13}C NMR ($CDCl_3$) 13.8, 21.8, 25.6, 28.1, 31.5, 39.4, 56.4, 87.4, 125.9, 134.6, 156.8 ppm; MS, m/e (relative intensity) 212 (2), 143 (100), 125 (7).

Anal. Calcd for $C_{11}H_{20}N_2O_2$: C, 62.23; H, 9.50; N, 13.20. Found: C, 62.22; H, 9.42; N, 13.18.

3-(*cis*-Hex-3-enyl)-4-hydroxy-5,5-dimethylimidazolidin-2-one (7d). Beginning with **6d** (5.00 g, 24 mmol), treatment with $LiAlH_4$ followed by workup and flash chromatography (SiO_2, EtOAc) gave pure **7d** (R_f 0.53, EtOAc) in 50% yield (2.55 g): mp 92–94 °C; IR (KBr) 3390, 3220, 1665 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.90 (t, 3 H, J = 6 Hz), 1.18 (s, 3 H), 1.25 (s, 3 H), 1.72–2.47 (m, 4 H), 3.13–3.70 (m, 2 H), 4.00 (d, 1 H, J = 11 Hz), 4.55 (d, 1 H, J = 11 Hz, D_2O exchangeable), 4.70 (br s, 1 H, D_2O exchangeable), 5.23–5.57 (m, 2 H). Addition of D_2O to the ^1H NMR sample led to a collapse of the doublet at δ 4.00 to a singlet. ^{13}C NMR ($CDCl_3$) 14.2, 20.7, 21.9, 26.3, 28.1, 39.7, 56.4, 87.7, 125.8, 134.0, 159.7 ppm; MS, m/e (relative intensity) 212 (11), 143 (100), 125 (3), 99 (5).

Anal. Calcd for $C_{11}H_{20}N_2O_2$: C, 62.23; H, 9.50; N, 13.20. Found: C, 62.30; H, 9.42; N, 13.17.

3-(2-Methylprop-2-enyl)-4-hydroxy-5,5-dimethylimidazolidin-2-one (7e). Beginning with **6e** (6.00 g, 33 mmol), 5.90 g (97%) of crude **7e** was obtained after treatment with $LiAlH_4$. The product was recrystallized from CH_2Cl_2 to yield 3.30 g (54% yield) of purified **7e**: mp 140–143 °C; IR (KBr) 3290, 3200, 1675 cm^{-1}; ^1H NMR ($CDCl_3$–Me_2SO-d_6) δ 1.22 (s, 3 H), 1.25 (s, 3 H), 1.70 (s, 3 H), 3.53 (d, 1 H, J = 16 Hz), 4.06 (d, 1 H, J = 16 Hz), 4.56 (d, 1 H, J = 8 Hz), 4.90 (br s, 2 H), 5.26 (d, 1 H, J = 8 Hz, D_2O exchangeable), 5.46 (br s, 1 H, D_2O exchangeable). Addition of D_2O to the ^1H NMR sample led to a collapse of the doublet at δ 4.56 to a singlet. ^{13}C NMR ($CDCl_3$–Me_2SO-d_6) 20.2, 22.0, 28.3, 45.1, 56.2, 86.5, 112.2, 141.2, 159.7 ppm; MS, m/e (relative in-

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tensity) 184 (36), 169 (9), 167 (11), 129 (10), 115 (7), 114 (6), 113 (36), 112 (7), 111 (16), 100 (100), 99 (62), 98 (16), 84 (29), 82 (32), 72 (61).

Anal. Calcd for $C_9H_{16}N_2O_2$: C, 58.67; H, 8.75; N, 15.21. Found: C, 58.62; H, 8.70; N, 15.26.

3-(Pent-4-ynyl)-4-hydroxy-5,5-dimethylimidazolidin-2-one (7f). Compound **6f** (7.00 g, 36 mmol) gave 5.15 g (73% yield) of **7f** (R_f 0.30, EtOAc) after reduction with $LiAlH_4$, workup, and purification by flash chromatography (SiO_2, EtOAc): mp 105–107 °C; IR (KBr) 3380, 3285, 3250, 1690 cm^{-1}; ^1H NMR ($CDCl_3$–Me_2SO-d_6) δ 1.24 (s, 3 H), 1.33 (s, 3 H), 1.62–2.25 (m, 5 H), 3.08–3.53 (m, 2 H), 4 .58 (d, 1 H, J = 10 Hz), 5.20 (d, 1 H, J = 10 Hz, D_2O exchangeable), 5.25 (br s, 1 H, D_2O exchangeable). Addition of D_2O to the ^1H NMR sample led to a collapse of the doublet at δ 4.58 to a singlet. ^{13}C NMR ($CDCl_3$–Me_2SO-d_6) 16.1 (t), 22.0 (q), 27.3 (t), 28.1 (q), 39.2 (t), 56.3 (s), 68.8 (d), 83.9 (s), 87.4 (d), 159.8 (s) ppm; MS (CI) 197 (P + 1); M_r 196.1217 (calcd for $C_{10}H_{16}N_2O_2$ 196.1212).

Preparation of 4-Hydroxy-4,7,7-trimethyl-1,8-diazabicyclo[4.3.0]nonan-9-one (8b and 9b). A CH_2Cl_2 (50 mL) solution containing **7a** (1.00 g, 25 mmol) and HCO_2H (5 mL) was heated to reflux for 96 h. H_2O (10 mL) was added to the reaction solution, and the mixture was stirred for 10 min at room temperature and then neutralized with 15% aqueous NaOH. The organic layer was separated, dried (Na_2SO_4), and concentrated in vacuo. The residue was recrystallized from benzene to give 0.60 g (50% yield) of a diastereomeric mixture of 4-(formyloxy)-4,7,7-trimethyl-1,8-diazabicyclo[4.3.0]nonan-9-ones **8a** and **9a**: ^{13}C NMR ($CDCl_3$) 21.0, 22.7, 26.7, 28.3, 35.0, 35.4, 35.6, 35.7, 35.9, 36.3, 36.4, 37.5, 54.5, 54.6, 59.8, 61.5, 81.1, 82.4, 159.6, 159.7, 160.0, 160.1 ppm. ^{13}C NMR analysis indicated that the two compounds were present in approximately equal amounts.

The binary mixture was dissolved in a H_2O (10 mL)–CH_3OH (15 mL) solution containing 1.00 g of NaOH and allowed to remain at room temperature for 5 h. The basic solution was extracted with CH_2Cl_2 (3 × 50 mL), and the organic layer was washed with aqueous 2 N HCl, dried (Na_2SO_4), and concentrated to dryness to yield a diastereomeric mixture of **8b** and **9b**. The isomers were separated by flash chromatography (SiO_2, 11% EtOH–EtOAc). The first compound (**8b**) (R_f 0.46, 11% EtOH–EtOAc) was isolated in 17% yield (160 mg): mp 207–209 °C; IR (KBr) 3390, 3245, 1665 cm^{-1}; ^1H NMR (Me_2SO-d_6) δ 0.98 (s, 3 H), 1.12 (s, 3 H), 1.14 (s, 3 H), 1.15–1.28 (m, 2 H), 1.38–1.41 (m, 2 H), 2.80 (ddd, 1 H, J = 16, 13, 3 Hz), 3.22 (dd, 1 H, J = 9, 3 Hz), 3.40 (br dd, 1 H, J = 13, 3 Hz), 4.30 (br s, 1 H), 6.30 (br s, 1 H); ^{13}C NMR (Me_2SO-d_6) 22.3 (q), 27.8 (q), 31.5 (q), 36.1 (t), 36.6 (t), 37.0 (t), 53.5 (s), 59.6 (d), 66.6 (s), 159.4 (s) ppm; MS, m/e (relative intensity) 198 (32), 183 (92), 180 (36), 165 (100), 125 (40), 113 (65), 58 (90), 56 (60).

Anal. Calcd for $C_{10}H_{18}N_2O_2$: C, 60.58; H, 9.15; N, 14.13. Found: C, 60.48; H, 9.20; N, 14.03.

The second adduct (**9b**) (R_f 0.35, 11% EtOH–EtOAc) eluted from the column was isolated in 14% yield (150 mg): mp 179–181 °C; IR (KBr) 3450, 3240, 1695 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.12 (s, 3 H), 1.25 (s, 3 H), 1.27 (s, 3 H), 1.44–1.66 (m, 4 H), 2.40 (br s, 1 H), 2.68 (ddd, 1 H, J = 16, 13, 3 Hz), 3.09 (dd, 1 H, J = 9, 4 Hz), 3.85 (ddd, 1 H, J = 13, 6, 2 Hz), 4.70 (br s, 1 H); ^{13}C NMR ($CDCl_3$) 22.9, 24.4, 28.4, 38.4, 38.8, 39.5, 54.6, 62.5, 69.9, 159.9 ppm; MS, m/e (relative intensity) 198 (16), 183 (100), 180 (34), 165 (60), 125 (43), 114 (45), 113 (79), 58 (67), 56 (46).

Anal. Calcd for $C_{10}H_{18}N_2O_2$: C, 60.58; H, 9.15; N, 14.13. Found: C, 60.31; H, 9.28; N, 13.93.

Preparation of 4-(Formyloxy)-5,7,7-trimethyl-1,8-diazabicyclo[4.3.0]nonan-9-one (10). The procedure utilized for the preparation of **8a** and **9a** was adopted for the synthesis of **10**, beginning with 0.99 g (4.5 mmol) of **7b**, 10 mL of HCO_2H, and CH_2Cl_2 (25 mL). The solution was heated to reflux for 24 h. After workup, thin-layer and ^{13}C NMR spectral analyses indicated the presence of one major adduct (R_f 0.35, EtOAc) and two minor compounds (R_f 0.25–0.30, EtOAc). Purification by flash chromatography (SiO_2, EtOAc) led to the isolation of the major compound: 0.50 g (49%); mp 193.5–195.5 °C; IR (KBr) 3200, 1730, 1710 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.98 (d, 3 H, J = 6 Hz), 1.25 (s, 3 H), 1.38 (s, 3 H), 1.50–2.30 (m, 3 H), 2.72 (ddd, 1 H, J = 12, 12, 5 Hz), 2.90 (d, 1 H, J = 10 Hz), 3.88 (ddd, 1 H, J = 12, 5, 2 Hz), 4.66 (ddd, 1 H, J = 12, 10, 5 Hz), 5.37 (br s, 1 H), 8.12 (s, 1 H); ^{13}C NMR ($CDCl_3$) 13.6 (q), 22.8 (q), 29.2 (q), 30.1 (t), 36.5 (d), 38.5 (t), 55.4 (s), 68.6 (d), 75.8 (d), 159.6 (s), 160.5 (d) ppm; MS, m/e (relative intensity) 226 (30), 211 (35), 181 (100), 103 (94), 96 (63).

Anal. Calcd for $C_{11}H_{18}N_2O_3$: C, 58.39; H, 8.02; N, 12.38. Found: C, 58.32; H, 7.86; N, 12.32.

Preparation of 4-(Formyloxy)-5-ethyl-7,7-dimethyl-1,8-diazabicyclo[4.3.0]nonan-9-one (11 and 12). A CH_2Cl_2 solution (80 mL) containing **7c** (1.50 g, 7 mmol) and HCO_2H (40 mL) was heated to reflux for 11 days. H_2O (20 mL) was added and the mixture was allowed to stir at room temperature (10 min) and then neutralized with 15% aqueous NaOH. The layers were separated and the aqueous phase was extracted with CH_2Cl_2 (3 × 50 mL). The organic layers were combined, dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by flash chromatography (SiO_2, 20% benzene–ethyl acetate). The initial product eluted from the column was identified as **12** (R_f 0.41, 20% benzene–ethyl acetate): 54% yield (0.90g); mp 163–166 °C; IR (KBr) 3200, 1730, 1700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.91 (t, 3 H, J = 7 Hz), 1.24 (s, 3 H), 1.38 (s, 3 H), 0.98–2.12 (m, 5 H), 2.70 (ddd, 1 H, J = 15, 13, 3 Hz), 3.11 (d, 1 H, J = 9 Hz), 3.86 (ddd, 1 H, J = 13, 5, 2 Hz), 4.80 (br s, 1 H), 4.96 (ddd, 1 H, J = 15, 11, 4 Hz), 8.11 (s, 1 H); ^{13}C NMR ($CDCl_3$) 8.5 (q, J = 120 Hz), 19.2 (t, J = 130 Hz), 23.1 (q, J = 120 Hz), 29.5 (q, J = 120 Hz), 30.2 (t, J = 130 Hz), 38.3 (t, J = 130 Hz), 40.8 (d, J = 145 Hz), 55.6 (s), 64.2 (d, J = 140 Hz), 72.5 (d, J = 160 Hz), 159.5 (s), 160.3 (d, J = 226 Hz) ppm; MS, m/e (relative intensity) 240 (14), 225 (13), 195 (56), 179 (13), 156 (3), 125 (11), 113 (100), 110 (36), 109 (10), 83 (10), 82 (12), 58 (14).

Anal. Calcd for $C_{12}H_{20}N_2O_3$: C, 59.98; H, 8.39; N, 11.66. Found: C, 59.93; H, 8.35; N, 11.62.

The second product eluted from the column was **11** (R_f 0.34, 20% benzene–ethyl acetate): 23% yield (0.40 g); mp 211–214 °C; IR (KBr) 3250, 1730, 1700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.92 (t, 3 H, J = 7 Hz), 1.19 (s, 3 H), 1.36 (s, 3 H), 1.46–2.13 (m, 5 H), 2.85 (ddd, 1 H, J = 15, 13, 3 Hz), 3.18 (d, 1 H, J = 9 Hz), 3.72 (ddd, 1 H, J = 13, 5, 3 Hz), 4.80 (br s, 1 H), 5.45–5.47 (br m, 1 H), 8.13 (s, 1 H); ^{13}C NMR ($CDCl_3$) 10.6 (q, J = 120 Hz), 20.0 (t, J = 120 Hz), 22.7 (q, J = 120 Hz), 29.1 (t, J = 120 Hz), 29.5 (q, J = 120 Hz), 35.3 (t, J = 130 Hz), 41.7 (d, J = 130 Hz), 55.0 (s), 63.8 (d, J = 130 Hz), 67.5 (d, J = 149 Hz), 159.6 (s), 160.1 (d, J = 224 Hz) ppm; MS, m/e (relative intensity) 240 (5), 225 (4), 195 (25), 179 (6), 156 (10), 125 (11), 113 (100), 110 (12), 83 (9), 82 (7), 58 (9).

Anal. Calcd for $C_{12}H_{20}N_2O_3$: C, 59.98; H, 8.39; N, 11.66. Found: C, 60.34; H, 8.43; N, 11.68.

Preparation of 4-(Formyloxy)-5-ethyl-7,7-dimethyl-1,8-diazabicyclo[4.3.0]nonan-9-one (13). Using the same procedure described previously for the preparation of **8a** and **9a**, 1.50 g (7 mmol) of **7d** and HCO_2H (50 mL) were heated in CH_2Cl_2 (100 mL) to reflux for 11 days. Thin-layer and ^{13}C NMR spectral analyses of the crude product after workup indicated the presence of only one product (R_f 0.45, EtOAc) together with unreacted starting material (R_f 0.50, EtOAc). Purification of the mixture was accomplished by flash chromatography (SiO_2, EtOAc). The major product isolated in 42% yield (0.70 g) was **13**: mp 140–143 °C; IR (KBr) 3230, 1730, 1700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.97 (t, 3 H, J = 7 Hz), 1.29 (s, 3 H), 1.33 (s, 3 H), 1.50–2.20 (m, 5 H), 2.90 (ddd, 1 H, J = 13, 12, 5 Hz), 3.10 (d, 1 H, J = 3 Hz), 4.05 (ddd, 1 H, J = 13, 6, 1 Hz), 5.08 (ddd, 1 H, J = 12, 9, 5 Hz), 5.10 (br s, 1 H), 8.05 (s, 1 H); ^{13}C NMR ($CDCl_3$) 14.7 (q, J = 130 Hz), 15.8 (t, J = 150 Hz), 21.8 (q, J = 130 Hz), 24.5 (t, J = 150 Hz), 31.9 (q, J = 130 Hz), 37.5 (t, J = 150 Hz), 42.2 (d, J = 130 Hz), 54.5 (s), 66.8 (d, J = 150 Hz), 74.6 (d, J = 160 Hz), 159.6 (s), 160.2 (d, J = 230 Hz) ppm; MS (CI), 241 (P + 1).

Anal. Calcd for $C_{12}H_{20}N_2O_3$: C, 59.98; H, 8.39; N, 11.66. Found: C, 59.91; H, 8.44; N, 11.71.

Preparation of 8,8-Dimethyl-1,9-diazabicyclo[5.3.0]decane-5,10-dione (14). Trifluoroacetic anhydride (0.60 mL, 7 mmol) was added to a CH_2Cl_2 (100 mL) mixture of **7f** (1.10 g, 5.6 mmol) and allowed to stir at room temperature (10 min), 5 mL of trifluoroacetic acid was then added, and the solution was heated to reflux (65 h). The reaction was quenched by the addition of H_2O (20 mL) and then made basic (pH >12) with aqueous 15% NaOH. The mixture was stirred for 3 h and then the two phases were separated. The aqueous layer was extracted with CH_2Cl_2 (2 × 50 mL), and the organic layers were combined and succes-

sively washed with aqueous 2 N HCl (15 mL) and H_2O (2 × 15 mL), dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by flash chromatography (SiO_2). The major product from the reaction was eluted from the column by using 20% EtOH–EtOAc as the eluent and was identified as **14** (R_f 0.22, EtOAc); 46% yield (0.50 g); mp 202–205 °C; IR (KBr) 3220, 1715, 1705 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.17 (s, 3 H), 1.29 (s, 3 H), 1.75–2.06 (m, 2 H), 2.25–2.94 (m, 5 H), 3.25 (dd, 1 H, J = 10, 5 Hz), 4.13 (ddd, 1 H, J = 12, 3, 2 Hz), 5.12 (br s, 1H); ^{13}C NMR ($CDCl_3$) 23.1 (t, J = 130 Hz), 23.2 (q, J = 120 Hz), 28.0 (q, J = 120 Hz), 43.4 (t, J = 130 Hz), 44.1 (t, J = 130 Hz), 45.4 (t, J = 130 Hz), 55.1 (s), 63.3 (d, J = 140 Hz), 160.8 (s), 210.1 (s) ppm; MS, m/e (relative intensity) 196 (92), 181 (100), 153 (36).

Anal. Calcd for $C_{10}H_{16}N_2O_2$: C, 61.20; H, 8.22; N, 14.28. Found: C, 61.02; H, 8.12; N, 14.38.

Preparation of 3,3,6,6-Tetramethyl-4-oxa-1,7-diazabicyclo[3.3.0]octan-8-one (15). A solution of 1.50 g (8 mmol) of **7e**, 0.20 mL (2.5 mmol) of trifluoroacetic anhydride, and 0.18 mL (1.5 mmol) of anhydrous $SnCl_4$ in CH_2Cl_2 (100 mL) was heated to reflux (3 days). A 5% aqueous HCl solution (20 mL) was then added to the solution which was allowed to stir for 10 min at room temperature. The mixture was neutralized with 15% aqueous NaOH, and the organic layer was separated and then washed with H_2O (20 mL), dried (Na_2SO_4) and concentrated in vacuo. Thin-layer and ^{13}C NMR spectral analyses of the crude product showed the presence of both a major (R_f 0.64, EtOAc) and a minor (R_f 0.30, EtOAc) reaction product. The crude product was purified by flash chromatography (SiO_2, EtOAc). The major product (R_f 0.64, EtOAc) was isolated and identified as **15**: 30% yield (0.50 g); mp 128–130 °C; IR (KBr) 3200, 1690, 1300, 1050 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.23 (s, 3 H), 1.30 (s, 9 H), 3.00 (d, 1 H, J = 12 Hz), 3.90 (d, 1 H, J = 12 Hz), 4.83 (s, 1 H), 6.00 (br s, 1 H, D_2O exchangeable); ^{13}C NMR ($CDCl_3$) 22.1 (q, J = 120 Hz), 26.8 (q, J = 120 Hz), 28.0 (q, J = 120 Hz), 28.3 (q, J = 120 Hz), 55.5 (s), 57.0 (t, J = 140 Hz), 88.0 (s), 96.5 (d, J = 170 Hz), 163.7 (s) ppm; MS, m/e (relative intensity) 184 (37), 169 (80), 156 (28), 126 (64), 111 (14), 100 (100), 83 (59), 82 (38), 68 (16).

Anal. Calcd for $C_9H_{16}N_2O_2$: C, 58.67; H, 8.75; N, 15.21. Found: C, 58.61; H, 8.78; N, 15.07.

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Registry No. **4a**, 763-32-6; **4b**, 7515-62-0; **4c**, 928-97-2; **4d**, 928-96-1; **4e**, 513-42-8; **4f**, 5390-04-5; **5**, 77-71-4; **6a**, 91466-51-2; **6b**, 91445-24-8; **6c**, 91445-21-5; **6d**, 91445-22-6; **6e**, 59004-93-2; **6f**, 91445-23-7; **7a**, 91445-25-9; **7b**, 91445-26-0; **7c**, 91445-27-1; **7d**, 91445-28-2; **7e**, 91445-29-3; **7f**, 91445-30-6; **8a**, 91445-31-7; **8b**, 91445-33-9; **9a**, 91445-32-8; **9b**, 91445-34-0; **10**, 91445-35-1; **11**, 91445-36-2; **12**, 91547-55-6; **13**, 91547-56-7; **14**, 91445-37-3; **15**, 91445-38-4.

Reactions of α-Oxo Ketene Dithioacetals with Dimethylsulfonium Methylide: A New Versatile Synthesis of Furans and Butenolides

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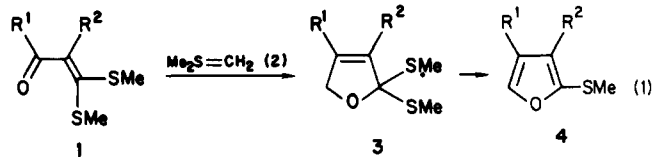
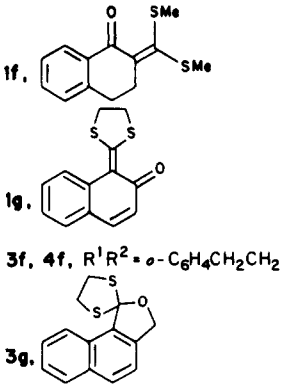
The reaction of 1-mono- and 1,2-disubstituted 3,3-bis(methylthio)-2-propen-1-ones **1** with dimethylsulfonium methylide (**2**) affords 2,2-bis(methylthio)-2,5-dihydrofurans **3** via epoxide **8** which can be isolated in a special case. A couple of methods including acid treatment effected the conversion of **3** to 2-(methylthio)furans **4**, which are found to be useful synthons of a variety of furans and butenolides. Two naturally occurring furans, perillene and rosefuran, were synthesized by this method.

Since many furans and butenolides exist in nature and some of them exhibit interesting biological activities, a number of synthetic methods have been developed.[1] There is a continuing need, however, for simple, versatile synthetic methods for this important class of compounds.

During our study of conjugated ketene dithioacetals,[2] we have found that the reaction of α-oxo ketene dithioacetals **1**, readily available from ketones (or aldehydes) and carbon disulfide,[3] react with dimethylsulfonium methylide (**2**) to give **3**, which is then converted into 2-(methylthio)furans **4** (eq 1). Since one of the α-positions of **4** is masked by a methylthio group which can be substituted by Grignard reagents, removed by Raney nickel, or hydrolyzed into a carbonyl group, **4** was found to be a very



a, R^1 = Ph; R^2 = H
b, R^1, R^2 = $(CH_2)_4$
c, R^1 = Me; R^2 = H
d, R^1 = H; R^2 = Ph
e, R^1 = $Me_2C{=}CH(CH_2)_2$; R^2 = H
h, R^1 = Me; R^2 = $Me_2C{=}CHCH_2$



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