

H, CH=), 2.30 (t, $J = 8.7$ Hz, 1 H, CHC_6H_5), 1.89 (q, $J = 8.7$ Hz, 1 H, $\text{CH}-\text{C}=\text{CH}_2$), 1.66 (d, $J = 0.9$ Hz, 3 H, CH_3), 1.50 (d, $J = 0.9$ Hz, 3 H, CH_3), 1.20 (t, $J = 8.5$ Hz, 1 H, CHD). For *trans*-**19-d** ($(\text{CD}_3)_2\text{SO}$, 270 MHz) δ 7.2 (m, 5 H, C_6H_5), 4.73 (dm, $J = 8.7$ Hz, 1 H, $\text{CH}=\text{CH}$), 1.80 (dd, $J = 4.3, 8.4$ Hz, 1 H, CHC_6H_5), 1.69 (m, 1 H, $\text{CH}-\text{C}=\text{CH}_2$), 1.63 (br s, 6 H, CH_3), 0.92 (dd, $J = 5.4, 8.5$ Hz, 1 H, CHD).

Isomerization of *cis*-19**.** $(\text{C}_5\text{H}_5)(\text{CO})_2\text{FeI}$ (0.043 g, 0.14 mmol) and AgBF_4 (0.030 g, 0.15 mmol) were stirred in 2 mL of CH_2Cl_2 for 30 min at room temperature. *cis*-**19** (0.025 g, 0.15 mmol; *cis*-**19**-*trans*-**19**, 9-1) was added to the dark solution containing precipitated AgI , and the mixture was stirred for 1 h. Diethyl ether (15 mL) was added to oil out the crude alkene complex $(\text{C}_5\text{H}_5)(\text{CO})_2\text{Fe}(\text{cis- and trans-19})^+\text{BF}_4^-$ (**21**), which was washed with diethyl ether (2×10 mL). The diethyl ether washes contained 5 mg of *cis*- and *trans*-**19** (2-1). Alkene complex **21** was dried under high vacuum for 1 h and became increasingly dark. NaI (21 mg, 0.15 mmol) in acetone (0.5 mL) was added to alkene complex **21**, and the mixture was stirred for 15 min. Chromatography (silica gel, hexane) gave **19**. Analysis by analytical gas chromatography (10% DEGS, 130 °C; heptadecane internal standard) indicated that 0.008 g of **19** (*cis*-**19**-*trans*-**19**, 1-3.5) was present.

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Registry No. **1a**, 81939-62-0; **1b**, 95615-87-5; **2**, 89486-58-8; **3**, 81939-65-3; **4**, 95615-88-6; **5**, 81939-66-4; **6**, 12108-22-4; **7**, 82246-54-6; **8**, 81939-68-6; **9**, 70569-00-5; **10a**, 37668-14-7; **11a**, 81939-70-0; **11b**, 95615-89-7; **12a**, 81939-64-2; **12b**, 95615-90-0; **13**, 12288-63-0; **14**, 95721-03-2; **15**, 33422-32-1; **16**, 89486-60-2; *syn*-**17**, 89576-67-0; *anti*-**17**, 37151-61-4; *syn*-**18**, 53235-18-0; *anti*-**18**, 53276-22-5; *cis*-**19**, 89486-56-6; *trans*-**19**, 89486-57-7; *cis*-**19d**, 95615-94-4; *trans*-**19d**, 95615-95-5; *cis*-**21**, 95615-92-2; *trans*-**21**, 95721-05-4; $(\text{C}_5\text{H}_5)(\text{CO})_2\text{Fe}^+\text{BF}_4^-$, 93757-32-5; $(\text{C}_5\text{H}_5)(\text{CO})_2\text{Fe}^-\text{Na}^+$, 12152-20-4; $(\text{C}_5\text{H}_5)(\text{CO})_2\text{FeI}$, 12078-28-3; $[(\text{C}_5\text{H}_5)(\text{CO})_2\text{Fe}]_2$, 12154-95-9; $(\text{C}_5\text{H}_5)[\text{P}(\text{C}_6\text{H}_5)_3](\text{CO})\text{FeC}(\text{CH}_3)_2(\text{OCH}_3)$, 95615-93-3; $\text{ClCOC}(\text{CH}_3)=\text{CH}_2$, 920-46-7; CH_3Li , 917-54-4; $\text{N}_2\text{CHC}-\text{O}_2\text{CH}_2\text{CH}_3$, 623-73-4; *cis*-CHD=CHC₆H₅, 21370-59-2; MeI, 74-88-4; $\text{C}_6\text{H}_5\text{COCH}=\text{C}(\text{CH}_3)_2$, 5650-07-7; 1,1,2,2-tetramethylcyclopropane, 4127-47-3; 1,1-dimethyl-2-phenylcyclopropane, 7653-94-3; lithium dimethylcuprate, 15681-48-8; isobutylene, 115-11-7; styrene, 100-42-5; cyclooctene, 931-88-4; 4-chlorobut-3-en-2-one, 7119-27-9.

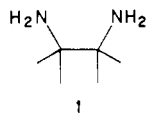
Stereoselective Synthesis of Vicinal Diamines from Alkenes and Cyanamide

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Contribution from the Department of Chemistry, University of Houston, Houston, Texas 77004. Received October 5, 1984

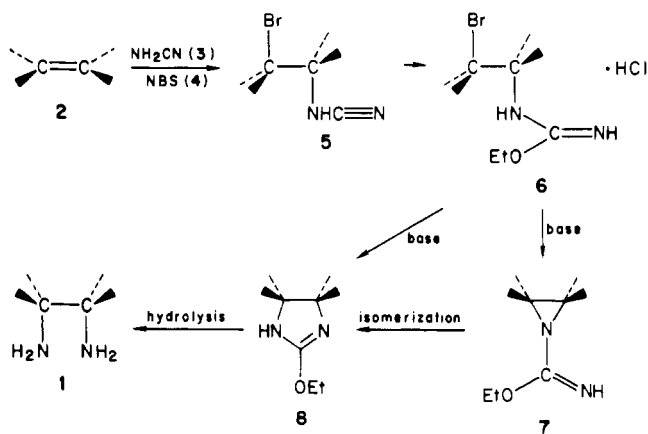
Abstract: A new procedure for the preparation of vicinal diamines is described beginning with unactivated olefins, cyanamide, and *N*-bromosuccinimide. Diamination proceeded stereospecifically and permitted access to nitrogen-unsubstituted diamines. With this procedure, 1-hexene (**2a**), 2-methylpropene (**2b**), *trans*-2-butene (**2c**), *trans*-4-octene (**2d**), *cis*-2-butene (**2e**), and cyclohexene (**2f**) were converted to the corresponding vicinal diamines in 47–71% overall yield. In the initial step, treatment of the alkene (**2**) with cyanamide (**3**) and *N*-bromosuccinimide (**4**) yielded the bromo cyanamide **5**. This adduct is then converted to the isourea salt **6** in situ with ethanolic hydrochloric acid. Treatment of **6** with mild bases (i.e., triethylamine, NaHCO_3) in select cases gave the 2-ethoxyimidazoline **8**. Alternatively, use of more basic conditions (i.e., sodium ethoxide, NaOH) led to ethyl aziridinecarboximate **7** formation. The aziridine **7** could be stereospecifically transformed to the isomeric imidazoline **8** with nucleophilic catalysts (i.e., NaI , triethylamine-hydroiodide). Basic hydrolysis of the imidazoline **8** in the last step generated the desired vicinal diamine **1**. The mechanism and scope of each step in this diamination procedure are discussed.

The vicinal diamine unit (**1**) is commonly observed in naturally occurring compounds and medicinal agents. Despite the importance of this functional group, few general diamination methods exist. This is astonishing in light of the many eloquent ways available for the synthesis of vicinal glycols,² vicinal halohydrins,² vicinal dihalides,² and vicinal oxyamino compounds.³



Conceptually, the simplest procedure for the generation of **1** is the ammonolysis of the corresponding vicinal dihalide.⁴ Un-

Scheme I. Synthesis of Vicinal Diamines



fortunately, this method which was applied in the preparation of 1,2-diaminoethane yields predominantly elimination products in more complex systems.⁵ As a result, a variety of other dis-

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Table I. Synthesis of Vicinal Bromo Cyanamides 5

alkenes 2					products 5							
2	R ₁	R ₂	R ₃	R ₄	5	R ₁	R ₂	R ₃	R ₄	yield, ^a %		bp, °C (torr) ^b ; state
a	<i>n</i> -Bu	H	H	H	a ₁	<i>n</i> -Bu	H	H	H	78	{ 2 1	–; pale brownish oil
					a ₂		H	H	<i>n</i> -Bu			
b	Me	Me	H	H	b	Me	Me	H	H	50 ^c		67–70 (0.005); colorless oil
c	Me	H	H	Me	c	Me	H	H	Me	66 ^d		60–70 (0.03); colorless oil
d	<i>n</i> -Pr	H	H	<i>n</i> -Pr	d	<i>n</i> -Pr	H	H	<i>n</i> -Pr	93		60–70 (0.0005); colorless oil
e	Me	H	Me	H	e	Me	H	Me	H	73		67–70 (0.0005); colorless oil
f	R ^e	H	R ^e	H	f	R ^e	H	R ^e	H	80 ^f		70–80 (0.0005); waxy solid (mp 40–42 °C)
g	Me	Et	H	Me	g	Me	Et	H	Me	67 ^g		pale brownish oil
h	Me	Me	Me	Me	h	Me	Me	Me	Me	71		mp 109–110 °C; white solid

^a Numbers reported are the yields obtained after preparative workup, but prior to final purification. ^b The number in each entry is the boiling point at which the product distilled during the bulb-to-bulb distillation unless otherwise indicated. Boiling points and melting points are uncorrected. ^c Carbodiimide 9a was also formed in 10% yield. ^d The ¹³C NMR spectrum of crude 5e indicated the possible presence of a small amount of the erythro isomer 5c. We have attributed this minor product to the *trans*-2-butene (2c) potentially present in the starting material. ^e R, R = (CH₂)₄. ^f *trans*-2-Bromocyclohexanol (10) was observed (10% yield). ^g Carbodiimide 9b was also formed in 7% yield.

placement reactions (i.e., with azide,⁶ amines,⁷ *N*-aromatic-substituted amides⁸), rearrangements (i.e., Curtius⁹), intramolecular cyclizations,¹⁰ and reductive procedures (i.e., vicinal dinitro alkanes,¹¹ dioximes,¹² and α -aminonitriles¹³) have been examined. Recently, several procedures have appeared that utilize organometallic reagents¹⁴ and select starting materials.¹⁵ These approaches generally provide routes for the *N,N'*-disubstituted and *N,N,N',N'*-tetrasubstituted vicinal diamines.

In most of these synthetic procedures, the overall conversion to the desired amines occurs in low yield, proceeds without stereochemical control,¹⁶ is often accompanied by undesired byproducts, and requires the generation of potentially hazardous in-

termediates. In addition to these limitations, the greatest disadvantage of current methods is that they do not convert readily accessible starting materials to product.

In an effort to provide a successful solution for the preparation of vicinal diamines (1), the synthetic strategy outlined in Scheme I was examined. Several attractive features of this proposed route are immediately apparent. First, this pathway should lead to the synthesis of the *N,N'*-unsubstituted vicinal diamines. Second, each step is envisioned to proceed with stereochemical control, thereby the entire sequence is stereospecific. Third, unactivated and inexpensive alkenes are employed as the initial precursors to the diamine.

The successful implementation of this approach for the synthesis of vicinal diamines (1) as well as the limitations of the method are the subjects of this paper.¹⁷

Synthesis of β -Bromoalkyl Cyanamides 5

The initial synthetic target in Scheme I is bromo cyanamide adduct 5. Two related procedures for the preparation of β -haloalkyl cyanamides have appeared.^{18,19} Ponsold and Ihn demonstrated that treatment of alkenes (2) with cyanamide (3) and *N*-bromosuccinimide (4) gave the corresponding β -bromoalkyl cyanamide (5).¹⁸ Moreover, these workers noted that in the case of cholesterol derivatives the reaction proceeded with overall trans addition to the double bond. Correspondingly, De Vries showed that alkenes could be converted to β -chloroalkyl cyanamides in the presence of cyanamide and *tert*-butyl hypochlorite.¹⁹

We have employed the method of Ponsold and Ihn¹⁸ for the synthesis of vicinal bromoalkyl cyanamides (5). Because of the central importance of this reaction in our synthetic strategy (Scheme I), we have further defined the regio- and stereochemical constraints of this transformation.

1. Results. Alkenes 2 were treated with 4 equiv of cyanamide (3) and 1.1 equiv of *N*-bromosuccinimide (NBS) (4) in methylene chloride for 3 days at room temperature to produce the desired vicinal bromo cyanamide adducts 5 (Table I). These compounds were usually of sufficient purity (>90% by NMR analysis) to be used directly for the next reaction. This finding was of importance, since significant decomposition of the product mixture often occurred during distillation. We generally observed that the stability of 5 decreased as the number of alkyl groups at the functionalized carbon atoms in the bromo cyanamide adduct was increased. In

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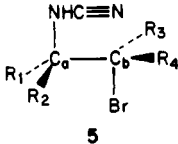
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Table II. Select Spectral Data for 5

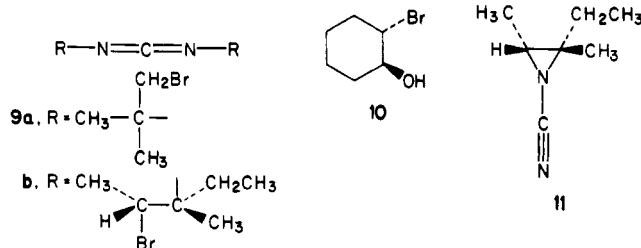


5	R ₁	R ₂	R ₃	R ₄	IR (cm ⁻¹) ^a C≡N	¹ H NMR ^b		¹³ C NMR ^{b,c}		
						C _a -H	C _b -H	Ca	Cb	C≡N
a ₁	<i>n</i> -Bu	H	H	H ^d	2220			56.7	36.2	114.9
a ₂	H	H	H	<i>n</i> -Bu ^(d)	2220			52.5	54.8	116.2
b	Me	Me	H	H	2220 ^e		3.46 (s)	55.0 (s)	42.5 (t; 152)	114.2 (s)
c	Me	H	H	Me	2220	3.37 (ddq; 4.0, 5.7, 6.6)	4.28 (dq; 4.0, 6.9)	56.4 (d; 143)	54.2 (d; 148)	115.5 (s)
d	<i>n</i> -Pr	H	H	<i>n</i> -Pr	2220	2.90–3.45 (m)	3.90–4.18 (m)	60.5 (d) ^f	60.4 (d) ^f	115.0 (s)
e	Me	H	Me	H	2220	3.38 (ddq; 4.6, 6.0, 6.6)	4.14 (dq; 4.6, 6.8)	57.3 (d; 142)	54.2 (d; 152)	115.0 (s)
f	R ^g	H	R ^g	H	2215	3.06–3.34 (m)	3.94 (ddd; 9.9, 9.9, 4.2)	60.3 (d; 139)	58.1 (d; 152)	115.0 (s)
g	Me	Et	H	Me	2230 ^e		4.18 (q; 6.9)	60.5 (s)	58.1 (d; 152)	114.8 (s)
h	Me	Me	Me	Me	2220 (KBr)			76.2 (s)	61.7 (s)	114.6 (s)

^a Infrared peak positions are recorded in cm⁻¹ vs. the 1601-cm⁻¹ band of polystyrene and taken as a thin film (NaCl) unless otherwise indicated.

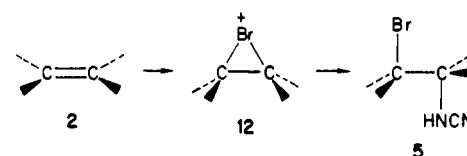
^b ¹H and ¹³C NMR spectra were taken in CDCl₃. The number in each entry is the chemical shift observed in ppm relative to Me₄Si followed by the multiplicity of the signal, followed by the coupling constant (s) in hertz. ^c Chemical shifts for carbon a and carbon b are tentative and may be reversed. See ref 1 for additional discussion. ^d The numbers cited are those obtained from the crude reaction mixture of 5a₁ and a₂. ^e The crude reaction material exhibited an additional peak at 2130 cm⁻¹. ^f An accurate determination of the coupling constant was not possible in this case because of the presence of two superimposable peaks. The value of the coupling constant is estimated to be 145 ± 6 Hz. ^g R, R = (CH₂)₄.

the reactions involving alkenes 2b and 2g, a small amount of the 2:1 adducts 9a and 9b, respectively, was produced in addition to the desired bromo cyanamide, while *trans*-2-bromocyclohexanol²⁰ (10) (10%) was formed along with 5f in the cyclohexene (2f) reaction. During the chromatographic separation of 5g and 9b, the 1:1 adduct 5g underwent conversion to aziridine 11.

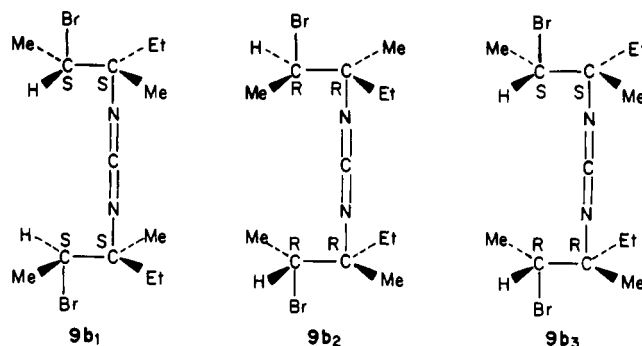


2. Spectral Properties. Select spectral (IR, ¹H, and ¹³C NMR) properties of bromo cyanamides 5 are listed in Table II.¹ Structural assignments of the 2:1 adducts 9 are tentative and are based on a series of MS, IR, and ¹H and ¹³C NMR spectral data. Chemical ionization mass spectroscopy of 9a and 9b gave a P + 1 pattern consistent with the contention that two bromine atoms were present in these compounds. The infrared spectra for 9a and 9b exhibited a strong absorption at 2130 cm⁻¹ for the carbodiimide stretching frequency.^{21,22} In the ¹H NMR spectra for both adducts (9a and 9b) no exchangeable peaks were observed. Weak signals were detected in the ¹³C NMR spectra (20 MHz) at 137.6 and 136.1 ppm for 9a and 9b, respectively, for the carbodiimide carbon.²³ Despite the inherent asymmetry of dialkyl carbodiimides,^{21,22} the simplicity of the ¹H (2 lines) and ¹³C (4 lines) NMR spectra for 9a can be rationalized by a low-energy barrier (6–9 kcal/mol) for racemization.^{21–24} Unfortunately, this rationale cannot be the sole explanation for the observed ¹³C NMR (20 and 62.5 MHz²⁵) spectra for 9b. Carbodiimide formation in this reaction should lead to the formation of the enantiomeric pair 9b₁ and 9b₂ and the meso adduct 9b₃ in an approximate 1:1

Scheme II. Addition of NBS and Cyanamide to an Alkene



ratio (see the following section for the proposed mechanism). Accordingly, 14 lines should be observed in the decoupled ¹³C NMR spectrum. We detected only 7 signals. This dilemma has not been resolved; however, we suggest that the distance between the chiral centers in these 2:1 adducts may be sufficiently large to prevent differentiation of the diastereotopic carbon atoms.



3. Discussion. The 1,2-disubstituted alkenes 2c–f gave solely the *trans* addition products 5c–f, respectively. These results are analogous to those obtained from other electrophilic addition reactions involving halogens and pseudo-halogens.^{26–30} The stereospecificity observed in these processes has been interpreted

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Table III. Summary of Ring Closure of Isoarea Salts 6 with Bases

entry no.	compound 5					base ^a (equivalents)	product ratios ^b		total yield, %		
	5	R ₁	R ₂	R ₃	R ₄		8	7			
1	a	<i>n</i> -Bu	H	H	H	Na ₂ CO ₃ (3)	a	100	a	0	95
2		H	H	H	<i>n</i> -Bu	NaOEt (2)	a	33	a	67	87
3	b	Me	Me	H	H	NEt ₃ (3)	b	100	b	0	94
4						NaOEt (2)	b	50	b	50	81
5	c	Me	H	H	Me	NEt ₃ (3)	c	100	c	0	81
6						Na ₂ CO ₃ (3)	c	90	c	10	75
7						NaOEt (2)	c	6	c	94	75
8	d	<i>n</i> -Pr	H	H	<i>n</i> -Pr	NEt ₃ (3)	d	100	d	0	90
9						Na ₂ CO ₃ (4)	d	70	d	30	80
10						NaOEt (2)	d	10	d	90	94
11	e	Me	H	Me	H	NEt ₃ (3) ^c	e		e		<i>d</i>
12						Na ₂ CO ₃ (3)	e		e		<i>d</i>
13						NaOEt (2)	e	0	e	100	62
14	f	R ^e	H	R ^e	H	NEt ₃ (3) ^c	f		f		<i>d</i>
15						Na ₂ CO ₃ (3)	f		f		<i>d</i>
16						NaOEt (2)	f		f	100	90
17	h	Me	Me	Me	Me	NEt ₃ (3) ^f	h	0	h	100	74
18						NaOEt (2)	h	0	h	100	72

^a The triethylamine-mediated reactions were conducted at reflux in ethanol (1 h). Sodium ethoxide was employed in the workup of these reactions. ^b Product ratios were calculated on the basis of the ¹H NMR spectrum. ^c Treatment of isourea salts 6e and 6f with triethylamine (18 h) at room temperature led to the formation of aziridines 7e and 7f in 62 and 84% yields, respectively. It is not known whether this reaction was completed during the initial 18 h or whether aziridine formation occurred during the basic conditions employed in the workup procedure. ^d Multiple products were formed. ^e R, R = (CH₂)₄. ^f Multiple products were observed when the reaction solution was heated to reflux (1 day).

in terms of the initial formation of a bromonium ion, followed by trans-ring opening of this cyclic species. Our results are in accord with this concept (Scheme II).

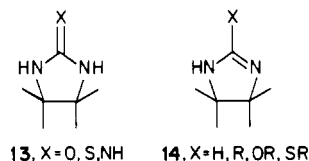
The monosubstituted alkene, 1-hexene (**2a**), yielded both the Markovnikov **5a**₁ and the anti-Markovnikov product **5a**₂ in a ratio of 2:1. Only the Markovnikov product **5b** was formed from the 1,1-disubstituted olefin, 1-methylpropene (**2b**). Similar regioselectivity has been observed for the addition of hypobromous acid (BrOH),²⁶ methyl hypobromite (BrOCH₃),^{27c} and bromoazide (BrN₃)²⁸ to unsymmetrically substituted alkenes. Although discrete carbenium ion involvement^{30,31} cannot be ruled out in the reaction of the 1,1-disubstituted alkene **2b**, the remarkably high regio- and stereospecificity observed in the *trans*-3-methyl-2-pentene (**2g**) reaction strongly suggests the formation of an unsymmetrical bromonium ion in the bromo cyanamide addition reactions to **2a,b,g**.

Structural analysis of the 2:1 adducts **9a** and **9b** obtained from the 2-methylpropene (**2b**) and *trans*-3-methyl-2-pentene (**2g**) reactions, respectively, indicates that product formation in these cases may also proceed through an unsymmetrical bromonium ion. One potential pathway for the formation of these adducts envisions reaction of the newly created β-bromoalkyl cyanamide (**5**) with a second equivalent of unsymmetrical bromonium ion to give **9**.

It is worthy to note that the regiochemistry observed for both the 1:1 and 2:1 adducts in our study is opposite to that reported by De Vries for the *tert*-butyl hypochlorite-cyanamide transformations.¹⁹ This result suggests that the *tert*-butyl hypochlorite promoted reactions may be proceeding by a free radical pathway.³²

Conversion of β-Bromoalkyl Cyanamides 5 to 2-Ethoxyimidazolidines 8

Imidazolidinone (**13**) and imidazoline (**14**) derivatives are readily prepared from vicinal diamines (**1**).³³ The converse of this reaction is also feasible.³³⁻³⁵ The stereospecific placement of a bromine and cyanamide moiety on adjacent carbon atoms should permit imidazoline and subsequent diamine formation to occur in a prescribed manner.



Encouragement for the key cyclization step (6 → 8) in Scheme I is furnished by several studies. Baker and co-workers have reported a series of intramolecular cyclization processes yielding N-substituted 2-iminoimidazolidines starting from guanidines and nitroguanidines containing a β-mesylate or tosylate group.³⁶ In a similar fashion, Beger and co-workers³⁷ have described the low

(31) Yates, K.; McDonald, R. S. *J. Am. Chem. Soc.* **1971**, *93*, 6297-6299.

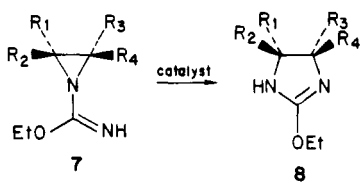
(32) Neale, R. S.; Marcus, N. L. *J. Org. Chem.* **1969**, *34*, 1808-1816.

(33) Hoffmann, K. "Imidazole and its Derivatives", Interscience Publishing Co.: New York, 1953; pp 213-242.

(34) Elderfield, R. C.; Hageman, H. A. *J. Org. Chem.* **1949**, *14*, 605-637.

(35) Flaster, H.; Kohn, H. *J. Heterocycl. Chem.* **1981**, *18*, 1425-1436 and references therein.

(36) (a) Baker, B. R.; Neilson, T. *J. Org. Chem.* **1964**, *29*, 1047-1050. (b) Baker, B. R.; Neilson, T. *Ibid.* **1964**, *29*, 1057-1062. (c) Baker, B. R.; Neilson, T. *Ibid.* **1964**, *29*, 1063-1067. (d) Baker, B. R.; Hullar, T. L. *Ibid.* **1965**, *30*, 4038-4044. (e) Baker, B. R.; Hullar, T. L. *Ibid.* **1965**, *30*, 4045-4048.

Table IV. Summary of the Conversion of Aziridines **7** to Imidazolines **8**


entry no.	7	aziridine				catalyst (equiv)	solvent	reaction conditions temp (time)	8	imidazoline 8 yield, %
		R ₁	R ₂	R ₃	R ₄					
1						NaI (15)	ethanol	reflux (2 d)	c	99
2	c	Me	H	H	Me	NaI (15)	acetone	reflux (2 d)	c	80 ^a
3						NEt ₃ (1), HCl-NEt ₃ (1), HBr-NEt ₃ (1)	ethanol	reflux (1 h)	c	74
4						NaHCO ₃ (4), NaCl (1), NaBr (1)	ethanol	r.t. (3 d) and then reflux (1 h)	c	82
5						NaBr (3)	ethanol	reflux (3 d)	b	
6						NaCl (3)	ethanol	reflux (3 d)	b	
7						NaI (3)	ethanol	reflux (4 h)	c	
8	e	Me	H	Me	H	NaI (1) ^d	DME	reflux (1 d)	e	90
9						NaI (2)	acetone	reflux (2 d)	e	63 ^a
10						NEt ₃ (1), HCl-NEt ₃ (1), HBr-NEt ₃ (1)	ethanol	reflux (1 h)	c	
11						HI-NEt ₃ (1)	ethanol	reflux (1 h)	e	80
12						NaI (1) ^e	DME	reflux (3 d)	f	87
13	f	R ^d	H	R ^d	H					
13						NaI (4)	acetone	reflux (4 d)	f	58 ^a
14	h	Me	Me	Me	Me	NaI (2)	DME	reflux (7 d)	f	

^a The aldol condensation product of acetone was also formed. ^b No reaction occurred. ^c Multiple products were formed and were not identified. ^d R, R = (CH₂)₄. ^e Use of 4 equiv of sodium iodide in this reaction led to the completion of the reaction within 4 h. ^f A series of ring-opened elimination products were obtained.⁴²

yield conversion of β -halogeno isothiouras and acetamides to vicinal diamine based substrates.³⁸

1. Results. (a) Preparation of Aziridines **7 and Imidazolines **8**.** Addition of an ethanolic solution containing 1 equiv of hydrochloric acid to an ethanolic solution of bromo cyanamide **5** gave isourea salt **6** in situ. The only adduct isolated was compound **6c**. Repeated efforts to recrystallize this hygroscopic material were unsuccessful. Characterization of adduct **6c** was accomplished by IR, ¹H NMR, and ¹³C NMR spectroscopy.

Treatment of **6** with base led to either imidazoline **8** or aziridine **7** formation. The product ratios (**8** vs. **7**) and yields (%) for this two-step, one-pot reaction are summarized in Table III. (For an expanded compilation of these base-mediated experiments, please see Supplementary Table A). Use of mild base (i.e., triethylamine, NaHCO₃) with **6a-d** yielded **8b-d**, respectively. Alternatively, treatment of **6a**, **6c-f**, and **6h** with strong bases (i.e., sodium ethoxide, NaOH) gave ethyl aziridinecarboximate **7** as the major product.

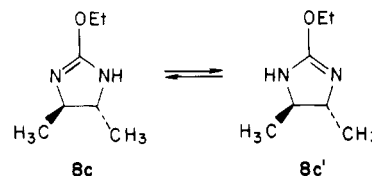
(b) Conversion of Aziridines **7 to Imidazolines **8**.** The rearrangement of aziridines **7c**, **7e**, **7f**, and **7h** to imidazolines **8c**, **8e**, **8f**, and **8h** was attempted with a number of different catalysts in various solvents. The results of these reactions are summarized in Table IV.

Stereospecific conversion of aziridine **7c** to imidazoline **8c** was accomplished with sodium iodide in ethanol or acetone³⁹ or with an ethanolic solution containing either 1 equiv each of triethylamine, triethylamine hydrochloride, and triethylamine hydrobromide (Table IV, entry 3) or 1 equiv each of sodium chloride and sodium bromide and 4 equiv of sodium bicarbonate (Table IV, entry 4). The latter two reactions (entries 3 and 4) went to completion considerably more rapidly than the sodium iodide mediated processes (entries 1 and 2).

cis-2,3-Disubstituted aziridine **7e** was converted to the corresponding imidazoline **8e**⁴¹ by treatment with either sodium iodide

(1,2-dimethoxyethane, acetone³⁹) or triethylamine hydroiodide (ethanol). Aziridine **7f** underwent a stereospecific rearrangement to **8f** with sodium iodide in 1,2-dimethoxyethane and acetone.³⁹ Unlike the other preceding rearrangements, attempted conversion of **7h** to the corresponding imidazoline **8h** failed. No detectable reaction was noted upon treatment of aziridine **7h** with sodium iodide in 1,2-dimethoxyethane at reflux for 1 day. Extension of the reflux period from 1 day to 7 days led to the formation of several ring-opened elimination products.^{1,42}

2. Spectral Properties. (a) Imidazolines **8.**¹ The proton chemical shift values for the methine hydrogens at carbons 4 and 5 in imidazolines **8** generally appeared at δ 3.20–4.00.⁴³ Of interest, the symmetrically substituted imidazolines **8c-f** exhibited significant line broadening for the carbon-4 and carbon-5 proton signal.⁴⁴ An interesting observation in the ¹³C NMR spectra of **8c** and **8d** was the appearance of a broad line for the carbon-4 and carbon-5 signal. In the case of **8c**, this line (62.7 ppm) was sharpened by the addition of trifluoroacetic acid. We have attributed this phenomenon to the existence of a tautomeric equilibrium (**8c** \rightleftharpoons **8c'**) in this system. In the absence of trifluoroacetic acid, exchange between the two tautomers is not sufficiently rapid on the NMR time scale to lead to a sharp signal for the carbon-4 and carbon-5 resonance. The addition of deu-



(40) (a) Pouchert, C. J. "The Aldrich Library of Infrared Spectra", 2nd ed.; Aldrich Chemical Co., 1978; p 224a. (b) Puchert, C. J.; Campbell, J. R. "The Aldrich Library of NMR Spectra"; Aldrich Chemical Co., 1974; Vol. 2, p 116D.

(41) Imidazoline **8e** may have been contaminated with the trans-isomer **8c** (<10%, ¹H and ¹³C NMR analyses).

(42) The details of this reaction and related processes will be the subject of a separate paper.

(43) Kohn, H.; Cravey, M. J.; Arceneaux, J. H.; Cravey, R. L.; Willcott, M. R. *J. Org. Chem.* **1977**, *42*, 941–948 and references therein.

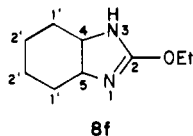
(44) (a) Jackman, L. M.; Jen, T. *J. Am. Chem. Soc.* **1975**, *97*, 2811–2818. (b) Jackman, L. M.; Sternhell, S. "Application of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry", 2nd ed.; Pergamon Press: New York, **1969**; pp 380–384.

(37) (a) Beger, J. *J. Prakt. Chem.* **1969**, *311*, 549–562. (b) Beger, J.; Schode, D.; Vogel, J. *Ibid.* **1969**, *311*, 408–419.

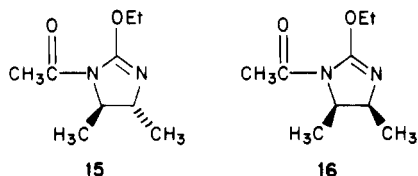
(38) Elderfield and Hageman³⁴ have observed the formation of a cyclic guanidine upon treatment of a β -bromoalkyl cyanamide with *n*-butylamine. These investigators, however, have suggested that the reaction proceeds by initial displacement of the primary bromide by *n*-butylamine followed by intramolecular cyclization to yield the cyclized adduct.

(39) The aldol product of acetone⁴⁰ was also formed in this reaction.

terium oxide to the chloroform-*d* NMR sample of **8f** led to a broadening of both the carbon-1' (28.9 ppm) and carbon-2' (21.0 ppm) signals and the appearance of discrete resonances for carbon-4 and carbon-5 (56.6, 60.8 ppm). We tentatively suggest that deuterium incorporation at nitrogen-3 (nitrogen-1) leads to a reduction in the rate of tautomeric exchange between the two different imidazoline forms.



In an effort to determine the stereochemistry of imidazolines **8c** and **8e** by NMR methods, the corresponding unsymmetrical N-acetyl derivatives **15** and **16** were prepared.⁴⁵ Both compounds exhibited vicinal coupling for the hydrogens at carbon-4 and carbon-5 as well as three-bond coupling ($^3J_{CH}$) interactions (H-C₄-C₅-CH₃, H-C₅-C₄-CH₃). The proton-proton coupling constant between the C₄-H and C₅-H hydrogens in the *cis*-adduct **16** (8.4 Hz) was larger than in the *trans*-derivative **15** (3.5 Hz). This trend is expected on the basis of the Karplus analysis of the dihedral angle between these protons and the assumption that the ring is nearly planar.⁴⁶ In the proton-coupled ¹³C NMR spectra of **15** and **16** as well as **8c** and **8e**, a larger three-bond coupling constant for the H-C₅-C₄-CH₃ interaction was observed for those cases where the dihedral angle was close to zero (compounds **8c** and **15**: $^3J_{CH}$ = 5.8–6 Hz) as compared to when it was near 120° (compounds **8e** and **16**: $^3J_{CH}$ = 2.5–4.5 Hz). This geometrical dependence of the magnitude of $^3J_{CH}$ on the dihedral angle has been previously noted.^{15a} In addition to these effects, the chemical shift for comparable types of protons at carbon-4 and carbon-5 appeared at lower field (0.4–0.5 ppm) in the *cis* adducts (i.e., **8e** and **16**) than the corresponding resonances in the *trans* compounds (i.e., **8c** and **15**). Additional information concerning the origin of these trends was inferred from the ¹³C NMR data. The resonances for carbon-4 and carbon-5 as well as the ring methyl carbon atoms appeared at higher field in the *cis* adducts (i.e., **8e** and **16**) than the corresponding signals in the *trans* compounds (i.e., **8c** and **15**). The magnitude of the upfield shift was approximately 4–8 ppm. The direction of these shifts is opposite to that previously discussed for the protons bound to these carbons. This type of inverse relationship as well as the magnitude of these shifts suggest that the values observed for the *cis* compounds result from electron density changes due to sterically induced polarization of the carbon-hydrogen bonds.⁴⁷

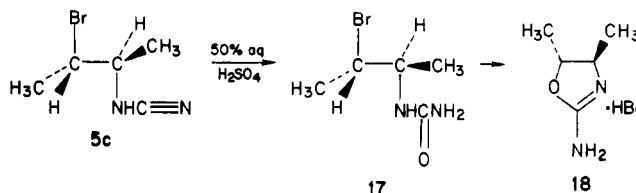


(b) Aziridines 7.¹ The chemical shift in the ¹H NMR for the ring protons in aziridines **7** typically appeared at δ 1.90–2.50.⁴⁸ Aziridines **7c–f** exhibited a single complex multiplet pattern for the ring protons; similar observations have been made as well as discussed in other aziridine systems.⁴⁹ The chemical shift for the ring protons in the *trans*-disubstituted compounds appeared at higher field (\sim 0.2 ppm) than the same protons in the *cis* adducts. A feature in the ¹³C NMR spectra which proved helpful

in the assignment of stereochemistry in **7** was discerned upon comparison of the signals for the *trans*-**7c** and *cis*-**7e** isomers. The resonances for both the ring carbons and methyl carbons attached to the ring appeared at higher field (2.5–3 ppm) in the latter adduct. A similar pattern was reported for *cis*- and *trans*-2,3-dimethylaziridines.⁵⁰ Once again, this trend may result from sterically induced polarization of the carbon-hydrogen bonds.⁴⁷

3. Discussion. (a) Preparation of Isooureas 6 from Cyanamides

5. Isooureas have been prepared by a variety of methods.^{43,51} Among these is the condensation reaction of cyanamides and alcohols with anhydrous acid.^{51b} Accordingly, vicinal bromoisoureas **6** were smoothly generated *in situ* from cyanamides **5** in ethanol in the presence of anhydrous hydrochloric acid. The importance of maintaining anhydrous conditions for the formation of isoourea **6** has been tested. Treatment of **5c** with aqueous sulfuric acid⁵² gave the bromourea **17**. Bromourea **17** is relatively unstable at room temperature. Intramolecular cyclization of this adduct gave the oxazolium salt **18**.



(b) Ring Closure of Isoourea Salts 6 with Bases and the Conversion of Aziridines 7 to Imidazolines 8. Two different products were obtained upon treatment of **6** with base: aziridines **7** and imidazolines **8**. The product ratio in these reactions was a function of the base utilized (Table III). Treatment of **6** with strong bases (2 equiv of sodium ethoxide or sodium hydroxide) led to the predominant formation of aziridines **7**, while use of milder bases such as sodium bicarbonate, sodium carbonate, or triethylamine yielded imidazolines **8** as the major product in the case of **6a–d** and multiple products in the case of **6e,f,h**.

A number of different mechanistic rationales for this product dependency on base can be considered.⁵³ One hypothesis is that all the base-mediated reactions principally proceed through the initial formation of the kinetically preferred protonated aziridine **19**. The subsequent fate of **19** is then a function of the base and solvent system employed in the reaction. In those cases where sufficient acid is present, ring opening of **19** followed by ring closure is expected to proceed to give ultimately the more thermodynamically stable adduct **8** (Scheme III).

Ample precedent exists for this hypothesis. Aziridines containing an N-acyl or comparable groups can be isomerized to the corresponding five-membered-ring compounds upon treatment with acids (i.e., HCl) or nucleophilic catalysts (i.e., I[−], Br[−], SCN[−]).⁵⁴ Since this reaction is known to proceed stereospecifically (retention of configuration) with nucleophilic catalysts, the most likely pathway involves two consecutive S_N2 reactions. In our case, protonation of aziridine **7** to give **19** may sufficiently activate ring opening by either bromide or chloride ions. Consistent with this rationale is the predominant formation of aziridine **7** from isoourea **6** with 2 equiv of sodium ethoxide or ethanolic sodium hydroxide. In these reactions, both sodium bromide and sodium chloride are

(45) This statement assumes that interconversion between the two tautomers in **8c** and **8e** is too rapid to permit the observation of different signals for the protons at carbons 4 and 5 in the ¹H NMR spectrum.

(46) Reference 44b, p 286.

(47) Grant, D. M.; Cheney, B. V. J. Am. Chem. Soc. 1967, 89, 5315–5318. Dalling, D. K.; Grant, D. M. Ibid. 1967, 89, 6612–6622. Dalling, D. K.; Grant, D. M. Ibid. 1972, 94, 5318–5324.

(48) Batterham, T. J. "NMR Spectra of Simple Heterocycles"; John Wiley and Sons, Inc.: New York, 1973; pp 135–140.

(49) (a) Reference 44b, p 366. (b) Nagel, D. L.; Woller, P. B.; Cromwell, N. H. J. Org. Chem. 1971, 36, 3911–3918.

(50) Mison, P.; Chaabouni, R.; Diab, Y.; Martino, R.; Lopez, A.; Lattes, A.; Wehrli, F. W.; Wirthlin, T. Org. Magn. Reson. 1976, 8, 79–89.

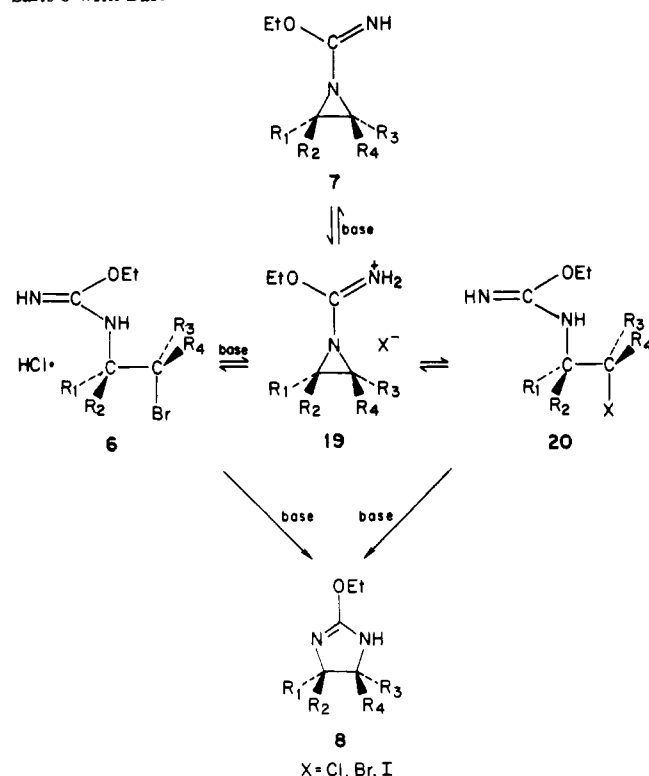
(51) (a) Patai, S. "The Chemistry of Amidines and Imidates"; John Wiley and Sons, Inc.: New York, 1975; pp 389–394. (b) Sandler, K. "Organic Chemistry"; Academic Press: New York, 1971; Vol. 2, pp 166–185.

(52) (a) Kilpatrick, M. L. J. Am. Chem. Soc. 1947, 69, 40–46. (b) Sullivan, M. J.; Kilpatrick, M. J. Ibid. 1945, 67, 1815–1823.

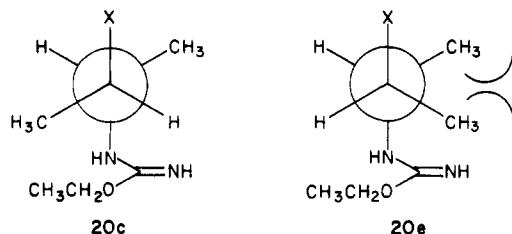
(53) Alternate explanations for the product distribution as a function of base are conceivable. One of these is that aziridine **7** formation is preceded by the initial formation of the corresponding conjugate base of the neutral isoourea adduct, while imidazoline **8** formation occurs directly from the neutral isoourea. For further discussion of this hypothesis and appropriate citations, see ref 1.

(54) (a) Hassner, A. "Small Ring Heterocycles"; John Wiley and Sons, Co.: New York, 1983; Part 1, pp 125–130. (b) Dermer, O. C.; Ham, G. R. "Ethylenimine and Other Aziridines"; Academic Press: New York, 1969; pp 283–290.

Scheme III. A Potential Pathway for the Reaction of Isourea Salts 6 with Base

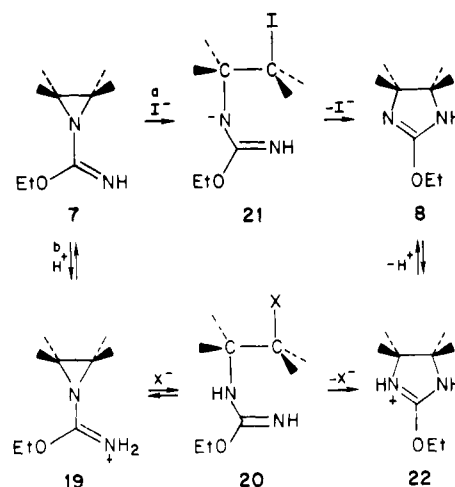


formed. Bromide and chloride ions are not particularly strong nucleophiles in ethanol.⁵⁵ Furthermore, no significant acid source is present. Both factors should minimize the subsequent interconversion of aziridine 7 to imidazoline 8. The percentage of imidazoline 8 vs. aziridine 7 successively decreased in these strongly basic reactions in proceeding from isourea salts 6a and 6b to 6c and 6d to 6e, 6f, and 6h (Table III). The significant amount of imidazoline 8 formed in the reactions of 6a and 6b under these conditions (Table III, entries 2 and 4) may be attributed to the relative ease in which these aziridines undergo ring opening and reclosure to form imidazolines 8. In both compounds, bimolecular nucleophilic attack by chloride or bromide ion should proceed at a primary carbon center. Isoureas 6e and 6f unlike the erythro derivatives 6c and 6d gave only aziridines 7e and 7f, respectively, using 2 equiv of sodium ethoxide. These observations may be explained by analysis of the conformational effects present in the transition state for the cyclization of these neutral adducts to 7 and 8 as well as the relative rates of formation of each of these cyclized compounds. A trans-coplanar arrangement of the incoming and departing groups at the transition state is considered necessary for an S_N2 reaction.⁵⁶ Cyclization of intermediate 20e (and 20f) to either aziridine 7e (and 7f) or imidazoline 8e (and 8f) should be accompanied by an unfavorable eclipsing interaction of the two methyl groups which is not present in the erythro compounds 20c (and 20d). Furthermore, cyclization proceeding



through the five-membered-ring transition state for adducts 20c-h

Scheme IV. Rearrangement of Aziridines 7 to Imidazolines 8



may be accompanied by additional steric compression of the terminal isourea nitrogen atom with the alkyl group(s) adjacent to the carbon-halogen bond. Both types of steric interactions, coupled with the entropic ease in which three-membered rings are formed as compared to the five-membered-ring systems,^{36,57} should favor formation of 7e (or 7f) vs. 8e (or 8f).⁵⁷ A related argument can be offered for the exclusive formation of 7h from isourea salt 6h. In this specific case, a further controlling factor may be the difficulty expected for nucleophilic ring opening of the fully substituted aziridine ring system.

Reduction of the amount of base introduced into the reaction led to increased amounts of imidazoline 8 formation (Table A, supplementary material). Use of only 1 equiv of sodium ethoxide should lead to the generation of either 1 equiv of hydrogen chloride or hydrogen bromide during the reaction. This acid may catalyze the slow interconversion of 7 to 8.

The ease in which isoureas 6a-d are transformed to imidazolines 8a-d with mild bases is also consistent with Scheme III. The increased acid in the reaction medium should facilitate rearrangement of intermediate 7 to 8. In the sodium bicarbonate or sodium carbonate reactions, the acid could be either sodium bicarbonate or carbonic acid. In the triethylamine mediated processes, 1 equiv each of triethylamine hydrochloride and triethylamine hydrobromide are formed which can serve as the proton source. Finally, the formation of multiple products from the reaction of isourea salts 6e and 6f and aziridine 7h from isourea 6h with mild bases may result from the adverse steric interactions encountered in the transition state for imidazoline ring closure.

Our isomerization studies (Table IV) of aziridines 7c, 7e, and 7f to the corresponding imidazolines 8c, 8e, and 8f, respectively, are also compatible with this hypothesis. Two pathways appear to exist which permit the interconversion of 7 to 8 (Scheme IV). Both proceed through two consecutive S_N2 displacement reactions and require a nucleophilic catalyst. Route a is run under neutral conditions while route b is conducted under acidic conditions. The acid-catalyzed ring expansion (i.e., pathway b) of activated aziridines to the corresponding five-membered-ring compounds (i.e., oxazolines, thiazolines, imidazolines) is well established.^{54,58} Sodium bicarbonate, triethylamine hydrochloride, triethylamine hydrobromide, and triethylamine hydroiodide can potentially serve as suitable acids in pathway b. Since the pK_a value for an isourea moiety should be approximately 9,⁵⁹ reactions 3, 4, 10, and 11 in Table IV may be acid catalyzed. Treatment of 7c with sodium iodide in ethanol (Table IV, entry 1) yielded imidazoline 8c. This

(57) For additional information concerning the formation of three- vs. five-membered ring compounds, see: Driguez, H.; Paton, J. M.; Lessard, J. *Can. J. Chem.* **1977**, *55*, 700-719.

(58) Taguchi, T.; Kojima, M. *J. Am. Chem. Soc.* **1959**, *81*, 4316-4318, 4318-4322.

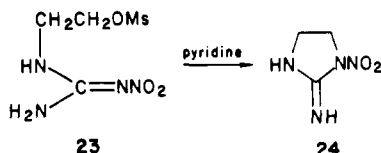
(59) Hegarty, A. F.; Bruice, T. C.; Benkovic, S. J. *J. Chem. Soc., Chem. Commun.* **1969**, 1173-74.

(55) Carey, F. A.; Sundberg, R. J. "Advanced Organic Chemistry, Part A, Structure and Mechanisms"; Plenum Press: New York, 1977; pp 208-211.
(56) Reference 55, pp 187-192.

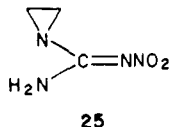
interconversion is believed to proceed by pathway a. Use of sodium bromide (Table IV, entry 5) or sodium chloride (Table IV, entry 6) in place of sodium iodide led to the recovery of the starting material. This result indicated that iodide ion is a superior nucleophile than bromide or chloride ion in ethanol.⁵⁵ Of interest, this factor can be minimized by the addition of acid (NaHCO₃, Table IV, entry 4) to the reaction medium. Under these conditions, the isomerization reaction is best explained in terms of route b in Scheme IV. Finally, the successful conversion of **7c** to **8c** by triethylamine hydrochloride, triethylamine hydrobromide, and triethylamine (Table IV, entry 3) is in agreement with our mechanistic contention that the isourea salt **6c** initially forms aziridine **7c** upon treatment with triethylamine (3 equiv) and then rearranges to imidazoline **8c**. The reaction conditions employed in this last experiment (Table IV, entry 3) mirrored those utilized in the triethylamine mediated treatment of **6c** (Table III, entry 5).

A somewhat different reactivity profile was exhibited by the cis isomers **7e** and **7f**. Treatment of **7e** with sodium iodide in ethanol led to the formation of multiple products (Table IV, entry 7). Use of an ethanolic solution of triethylamine hydrochloride, triethylamine hydrobromide, and triethylamine (Table IV, entry 10) gave multiple products as well. TLC analysis of this product mixture indicated that the product composition was similar to that obtained from the treatment of isourea salt **6e** with triethylamine (Table III, entry 11). These results suggest that alternative reaction pathways are competitive with the desired intramolecular cyclization reaction in this system due to unfavorable steric interactions in the transition state. This problem was obviated by the use of sodium iodide in acetone or 1,2-dimethoxyethane (Table IV, entries 8 and 9) or triethylamine hydroiodide in ethanol (Table IV, entry 11). Similarly, treatment of **7f** with sodium iodide in acetone or 1,2-dimethoxyethane (Table IV, entries 12 and 13) led to imidazoline formation. The success enjoyed with the iodide ion catalyzed reactions under both neutral and acidic conditions probably reflects the better leaving group ability of this moiety⁶⁰ (i.e., **20** [X = I]).

In 1964, Baker and Neilson^{36a} considered a hypothesis similar to that described in Scheme III for the cyclization of **23** to the five-membered-ring guanidine **24** in pyridine. This hypothesis



was tested by independently preparing the putative aziridine intermediate **25** and then reacting it with methanesulfonic acid. Ring expansion was not observed, and a mechanistic pathway analogous to that in Scheme III was rejected. In light of our



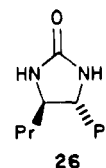
results, the value of this control reaction may be suspect since a nucleophilic catalyst was not present in the reaction medium. Indeed, Evans and co-workers⁶¹ have shown that aziridine **25** does undergo ring expansion with cyanogen bromide in benzene. Furthermore, nucleophilic acids (HBr, BrCN) successfully converted **25** to substituted imidazolines.^{61,62}

Preparation of Vicinal Diamines 1

The final step in our synthetic strategy (Scheme I) requires the conversion of imidazoline **8** to the N,N'-unsubstituted vicinal diamine **1**.

(a) **Results.** The hydrolytic cleavage of 2-ethoxyimidazoline **8** to the diamine **1** was achieved in excellent yield by heating these derivatives with an excess amount of aqueous barium hydroxide in a sealed heavy-walled tube at 120–140 °C for 1 or 2 days.³⁵ In these reactions, 10 to 11 equiv of barium hydroxide were added for each equivalent of imidazoline **8** used. The results, reaction conditions, and physical data for the diamine **1** derivatives^{63–66} are listed in Table V.

Hydrolysis of imidazoline **8d** at a lower temperature (110 °C) and a shorter reaction time (1 day) resulted in the formation of an adduct tentatively assigned as imidazolidinone **26** in 99% yield. The hydrolysis of **8d** was also accomplished with 30% sulfuric acid at reflux (18 h). Compound **1d** was obtained after workup in 39% yield as the dihydrochloride salt.



(b) **Discussion.** Treatment of imidazoline **8** with aqueous barium hydroxide led to the high-yield formation of vicinal diamine **1**. This method has been previously used for the hydrolysis of imidazolidinones.^{33,35} The formation of imidazolidinone **26** from **8d** suggested that the basic hydrolysis of imidazolines **8** proceeds through the initial formation of the corresponding imidazolidinones.

Conclusions

Unactivated alkenes **2** were successfully converted to the desired N,N'-unsubstituted vicinal diamines **1**. Each step proceeded with stereochemical control; therefore, the entire sequence (Scheme I) is stereospecific. The overall diamination reaction (alkene **2** → diamine **1**) can be envisioned as a cis-addition process. The scope of this method is wide. The only major limitation encountered was with sterically congested substrates (i.e., **2h**). Additional advantages received from this method are the development of new stereospecific synthetic routes for functionalized aziridines **7** and imidazolines **8**.

Experimental Section

Instrumental and general experimental procedures are as described previously^{15a} unless indicated otherwise. All the alkenes (**2**) employed were commercially available and were not purified prior to use. The 2-methylpropene (**2b**) (99% pure) was purchased from Matheson Co., while *trans*-2-butene (**2c**) and *cis*-2-butene (**2e**) were obtained from Union Carbide Co., Linde Division. The *cis*-2-butene (**2e**) was only available in technical grade (95%) in lecture bottle quantities and contained approximately 5% *trans*-2-butene (**2c**). The *trans*-3-methyl-2-pentene (**2g**) was purchased from Pfaltz and Bauer, Inc. Cyanamide **3** (Aldrich Co.) was also used without further purification, while the *N*-bromosuccinimide (**4**) was recrystallized once from water before it was employed.

General Procedure for the Preparation of β -Bromoalkyl Cyanamides.

Method A: Use of Volatile Alkenes. *N*-Bromosuccinimide (**4**) (25.43 g, 0.14 mol) was added to a solution of 24.00 g (0.57 mol) of cyanamide **3** in methylene chloride (250 mL) at room temperature. The resulting reaction mixture was cooled to -50 °C with a dry ice-acetone bath. The condensed alkene (**2b,c,e**) (0.13 mol) was added through a dropping funnel maintained at -78 °C with dry ice-acetone. After the addition of the alkene (**2**), the dry ice-acetone bath was removed and the reaction mixture was stirred at room temperature for 3 days. The insoluble material in the methylene chloride layer was separated, and the methylene chloride layer was washed with H₂O (5 × 200 mL), dried (Na₂SO₄), and concentrated in vacuo. The yields obtained in these reactions were based on the amount of *N*-bromosuccinimide (**4**) employed.

(63) Kempter, G.; Moser, G. *J. Prakt. Chem.* **1966**, *34*, 104–111.

(64) Minisci, F.; Galli, R.; Cecere, M. *Gazz. Chim. Ital.* **1964**, *94*, 67–90.

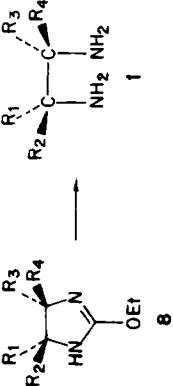
(60) Reference 55, pp 212–215.
(61) Lowe, J. U.; Oda, T. A.; Evans, R. *J. Org. Chem.* **1963**, *28*, 1496–1498.

(62) For a related example, please see: Murai, N.; Komatsu, M.; Yagii, T.; Nishihara, H.; Ohshiro, Y.; Agawa, T. *J. Org. Chem.* **1977**, *42*, 847–850.

(65) (a) Danilov, S. N.; Oglloblin, D. A. *Zh. Obshh. Khim.* **1952**, *22*, 2113–2121; *Chem. Abstr.* **1954**, *48*, 1945h. (b) Granger, R.; Techer, H. C. *R. Hebd. Seances Acad. Sci.* **1960**, *250*, 2581–2583. (c) Freifelder, M.; Hasbrouck, R. B. *J. Am. Chem. Soc.* **1960**, *82*, 696–698.

(66) Strack, E.; Schwaneberg, H. *Chem. Ber.* **1934**, *67*, 1006–1011.

Table V. Hydrolysis of Imidazolines 8



8	imidazoline 8				hydrolysis conditions	vicinal diamine 1				mp, °C		overall yield, %
	R ₁	R ₂	R ₃	R ₄		R ₁	R ₂	R ₃	R ₄	obsd	lit.	
a	<i>n</i> -Bu	H	H	H	120 °C (2 d)	<i>n</i> -Bu	H	H	H	<i>d</i>	162 ⁶³	63
b	Me	Me	H	H	120 °C (1 d)	Me	Me	H	H	292–294	292–295 ⁶⁵	47
c	Me	H	H	Me	120 °C (1 d)	Me	H	H	Me	254–256	253–254 ⁶⁶	51
d	<i>n</i> -Pr	H	H	<i>n</i> -Pr	130–140 °C (2 d)	<i>n</i> -Pr	H	H	<i>n</i> -Pr	218–220		71
e	Me	H	Me	H	120 °C (1 d)	Me	H	Me	H	324–325	325 ⁶⁶	53
f	R ^f	H	R ^f	H	120 °C (1 d)	R ^f	H	R ^f	H	310–312	312–314 ^{6c}	61

^a Melting points for the dihydrochloride salts of 1 are uncorrected. ^b Yields for the dihydrochloride salts of 1 are calculated on the basis of imidazoline 8. ^c Overall yields for the dihydrochloride salts of 1 are based on alkenes 2 except 1b,c,e. The overall yields for these last three diamines were determined on the basis of the *N*-bromosuccinimide used in the reaction. ^d The dihydrochloride salt of 1a was hygroscopic. Compound 1a was converted to the known diacetyl derivative⁶⁴ for product identification. ^e ¹³C NMR spectral analysis of the product mixture from 8e indicated that the ratio of 1e to 1c was approximately 19:1. Reprecipitation of this mixture from aqueous methanol gave the pure sulfate salt 1e, which was converted to the dihydrochloride salt of 1e for product identification. ^f R, R = (CH₂)₄.

(*erythro*-2-Bromo-1-methylpropyl)cyanamide (5c). An analytical sample was prepared by bulb-to-bulb distillation to give a colorless oil: bp 60–70 °C (0.03 torr); IR (neat, NaCl) 3200 (br s), 2220, 1445 cm⁻¹; ¹H NMR (CDCl₃) δ 1.34 (d, 3 H, *J* = 7 Hz), 1.70 (d, 3 H, *J* = 7 Hz), 3.37 (ddq, 1 H, *J* = 4, 6, 7 Hz), 4.28 (dq, 1 H, *J* = 4, 7 Hz), 5.16–5.41 (br d, 1 H, *J* = 6 Hz, exchangeable with D₂O). Selective irradiation of the signals located at δ 1.70 led to a collapse of the doublet of quartets at δ 4.28 to a doublet. ¹³C NMR (CDCl₃) 16.2 (q, *J* = 128 Hz), 22.0 (q, *J* = 129 Hz), 54.2 (d, *J* = 148 Hz), 56.4 (d, *J* = 143 Hz), 115.5 (s) ppm. Selective irradiation of the resonance located at δ 4.28 in the ¹H NMR spectrum led to a collapse of the doublet centered at 54.2 ppm in the ¹³C NMR spectrum to a singlet. MS, *m/e* (relative intensity) 178 (5), 176 (5), 137 (1), 135 (1), 109 (3), 107 (3), 97 (9), 69 (100).

Anal. Calcd for C₅H₉N₂Br: C, 33.92; H, 5.12; N, 15.82. Found: C, 34.03; H, 5.10; N, 15.71.

(*threo*-2-Bromo-1-methylpropyl)cyanamide (5e). An analytical sample was prepared by bulb-to-bulb distillation to give a colorless oil: bp 67–70 °C (0.06 torr); IR (neat, NaCl) 3190 (br s), 2220, 1445 cm⁻¹; ¹H NMR (CDCl₃) δ 1.37 (d, 3 H, *J* = 6.5 Hz), 1.76 (d, 1 H, *J* = 7 Hz), 3.38 (ddq, 1 H, *J* = 5, 6, 6.5 Hz), 4.14 (dq, 1 H, *J* = 5, 7 Hz), 4.43–4.73 (br d, 1 H, *J* = 6 Hz, exchangeable with D₂O); ¹³C NMR (CDCl₃) 18.1 (q, *J* = 128 Hz), 22.4 (q, *J* = 129 Hz), 54.2 (d, *J* = 152 Hz), 57.3 (d, *J* = 142 Hz), 115.0 (s) ppm; MS, *m/e* (relative intensity) 178 (94), 176 (100), 137 (51), 135 (53), 97 (24), 69 (25).

Anal. Calcd for C₅H₉N₂Br: C, 33.92; H, 5.12; N, 15.82. Found: C, 33.88; H, 5.22; N, 15.72.

(2-Bromo-1,1-dimethylethyl)cyanamide (5b) and (2-Bromo-1,1-dimethylethyl)carbodiimide (9a). TLC (chloroform) analysis of the crude product mixture after workup indicated the presence of two compounds (*R_f* 0.20, 0.64). ¹H and ¹³C NMR analyses showed the presence of 5b and 9a in a ratio of 4:1. The two compounds were separated by flash column chromatography (SiO₂, chloroform). The first fraction (*R_f* 0.64) contained 9a. This material was further purified by bulb-to-bulb distillation: bp 67–70 °C (0.15 torr); IR (neat, NaCl) 2130 cm⁻¹; ¹H NMR (CDCl₃) δ 1.43 (s, 12 H), 3.40 (s, 4H); ¹³C NMR (CDCl₃) 27.9 (q, *J* = 132 Hz), 44.3 (t, *J* = 152 Hz), 57.3 (s) ppm. Addition of Cr(Ac)₂ to the NMR sample led to the appearance of a signal at 137.6 ppm. MS, *m/e* (relative intensity) 299 (<1), 297 (1), 295 (<1), 233 (<1), 231 (<1), 219 (97), 217 (100), 163 (76), 161 (73), 137 (51), 135 (46); MS (CI) 315 (52), 313 (100), 311 (54).

Anal. Calcd for C₉H₁₆N₂Br₂: C, 34.64; H, 5.17; N, 8.98. Found: C, 34.63; H, 5.22; N, 9.05.

The second fraction (*R_f* 0.20) obtained from the column gave pure 5b. An analytical sample was prepared by bulb-to-bulb distillation to give a colorless oil: bp 67–70 °C (0.0005 torr); IR (neat, NaCl) 3190 (br s), 2220 cm⁻¹; ¹H NMR (CDCl₃) δ 1.41 (s, 6 H), 3.46 (s, 2 H), 6.42–6.65 (br s, 1 H); ¹³C NMR (CDCl₃) 25.5 (q, *J* = 129 Hz), 42.5 (t, *J* = 152 Hz), 55.0 (s), 114.2 (s) ppm; MS, *m/e* (relative intensity) 179 (37), 177 (36), 138 (6), 137 (54), 136 (7), 135 (50), 97 (100); mol wt 175.9953 (calcd for C₅H₉N₂Br 175.9949).

Anal. Calcd for C₅H₉N₂Br: C, 33.92; H, 5.12; N, 15.82. Found: C, 33.78; H, 5.18; N, 15.71.

General Procedure for the Preparation of β-Bromoalkyl Cyanamides. Method B: Use of Nonvolatile Alkenes. *N*-Bromosuccinimide (4) (1.1 equiv) was added to a cooled (5–10 °C) solution of the alkene 2 (1 equiv, 24–60 mmol) and cyanamide 3 (4 equiv) in methylene chloride (100–150 mL) at 5–10 °C. The resulting reaction mixture was stirred (1 h) at 5–10 °C and then stirred (3 days) at room temperature. The methylene chloride layer was washed with H₂O (6 × 150 mL), dried (Na₂SO₄), and evaporated in vacuo. The yields in these reactions were based on the amounts of the starting alkene used.

(1-(Bromomethyl)-*n*-pentyl)cyanamide (5a₁) and (2-Bromo-*n*-hexyl)cyanamide (5a₂). After workup, the product mixture was composed of 5a₁ and 5a₂ in a ratio of 2:1 (¹³C NMR analysis): IR (neat, NaCl) 3200 (br s), 2220 cm⁻¹; ¹³C NMR (CDCl₃) high intensity set—13.8, 22.2, 27.8, 32.3, 36.2, 56.7, 114.9 ppm; ¹³C NMR (CDCl₃) low intensity set—13.8, 22.0, 35.3, 52.5, 54.8, 116.2 ppm.

(*erythro*-2-Bromo-1-(*n*-propyl)-*n*-pentyl)cyanamide (5d). An analytical sample was prepared by bulb-to-bulb distillation to give a colorless oil: bp 60–70 °C (0.0005 torr); IR (neat, NaCl) 3180 (br s), 2220 cm⁻¹; ¹H NMR (CDCl₃) δ 1.00–1.20 (m, 6 H), 1.40–2.00 (m, 8 H), 2.90–3.45 (m, 1 H), 3.90–4.18 (m, 1 H), 4.70–5.10 (br s, 1 H); ¹³C NMR (CDCl₃) 12.9 (q, *J* = 129 Hz), 13.3 (q, *J* = 125 Hz), 18.9 (t, *J* = 129 Hz), 20.6 (t, *J* = 126 Hz), 32.5 (t, *J* = 127 Hz), 36.0 (t, *J* = 127 Hz), 60.4 (d, *J* = 143 Hz), 60.5 (d, *J* = 144 Hz), 115.0 (s) ppm; MS (CI) 235 (100), 233 (99); mol wt 232.0576 (calcd for C₉H₁₇N₂Br 232.0576).

(*trans*-2-Bromocyclohexyl)cyanamide (5f). General Method B was slightly modified. Six equivalents of cyanamide 3 were used, and the reaction time was extended for 6 days. After workup, a 9:1 binary mixture of 5f and 10 was obtained. Bulb-to-bulb distillation at 70–80

$^{\circ}\text{C}$ (0.0005 torr) gave **5f** as a white, waxy solid (mp 40–42 $^{\circ}\text{C}$): IR (neat, NaCl) 3150 (br s), 2215 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.25–2.50 (m, 8 H), 3.06–3.34 (m, 1 H), 3.94 (ddd, 1 H, $J = 10, 10, 4$ Hz), 4.79–5.09 (br s, 1 H). Selective irradiation of the resonance centered at δ 1.87 altered the doublet of doublets of doublets at δ 3.94 to a doublet. ^{13}C NMR (CDCl_3) 24.1 (t, $J = 129$ Hz), 26.3 (t, $J = 131$ Hz), 31.7 (t, $J = 132$ Hz), 36.7 (t, $J = 134$ Hz), 56.4 (d, $J = 153$ Hz), 60.3 (d, $J = 139$ Hz), 114.3 (s) ppm; MS, m/e (relative intensity) 204 (1), 202 (1), 123 (9), 81 (100); mol wt 202.0106 (calcd for $\text{C}_7\text{H}_{11}\text{N}_2\text{Br}$ 202.0101).

The *trans*-2-bromocyclohexanol (**10**) in the crude binary mixture was identified by comparison of the NMR spectra of the products prior to distillation to those obtained from an authentic sample of **10**:²⁰ IR (neat, NaCl) 3400 (br s), 1450 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.25–2.50 (m, 8 H), 3.09 (s, 1 H), 3.45–3.65 (m, 1 H), 3.93 (ddd, 1 H, $J = 9, 9, 4$ Hz); ^{13}C NMR (CDCl_3) 24.0, 26.5, 33.7, 36.1, 61.2, 75.0 ppm.

((**1R,2R** and **1S,2S**)-2-Bromo-1-ethyl-1-methylpropyl)cyanamide (**5g**) and (**2-Bromo-1-ethyl-1-methylpropyl**)carbodiimide (**9b**). TLC (chloroform) and spectral analysis of the crude product mixture after workup indicated the presence of two compounds (R_f 0.21, 0.69) in a ratio of 93:7. Attempted separation of the binary mixture by flash column chromatography (SiO_2 , chloroform) led to the isolation of several fractions. The first fraction contained compound **9b** (R_f 0.69). Bulb-to-bulb distillation gave the purified product: bp 88–95 $^{\circ}\text{C}$ (0.25 torr); IR (neat, NaCl) 2120 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.96 (t, 6 H, $J = 7$ Hz), 1.39 (s, 6 H), 1.60–1.94 (m, 10 H), 4.08 (q, 2 H, $J = 7$ Hz); ^{13}C NMR (CDCl_3) 8.3, 21.2, 23.3, 33.6, 57.4, 63.5, 136.1 ppm. The same ^{13}C NMR spectrum was obtained at 62.5 MHz. MS (CI) 371 (52), 369 (100), 367 (54).

The second fraction consisted of an oily material which by TLC analysis (chloroform) was composed of **5g** (R_f 0.21) and **11** (R_f 0.37). Separation of this mixture by flash column chromatography (SiO_2 , chloroform) gave **11** as the initial fraction. Compound **11** was further purified by bulb-to-bulb distillation and tentatively identified by spectral analyses: bp 45 $^{\circ}\text{C}$ (0.25 torr); IR (neat, NaCl) 2970, 2930, 2205 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.04 (t, 3 H, $J = 7$ Hz), 1.33 (s, 3 H), 1.37 (d, 3 H, $J = 6$ Hz), 1.59 (q, 2 H, $J = 7$ Hz), 2.61 (q, 1 H, $J = 6$ Hz); ^{13}C NMR (CDCl_3) 9.6, 12.0, 14.3, 31.2, 50.9, 54.3, 117.2 ppm; MS (CI) 125. The second fraction from this column chromatography consisted of a mixture of compounds **5g** and **11** in a ratio of 1:2 (^1H NMR analysis). Attempted separation of this mixture by bulb-to-bulb distillation (45–50 $^{\circ}\text{C}$ (0.25 torr)) led to the isolation of only **11**. The residue consisted of **5g**, **11**, and decomposed material.

(2-Bromo-1,1,2-trimethyl-*n*-propyl)cyanamide (**5h**). A purified sample was prepared by recrystallization of the crude reaction product from hexane: mp 109–110 $^{\circ}\text{C}$; IR (KBr) 3150 (br s), 2220 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.47 (s, 6 H), 1.85 (s, 6 H), 4.52–4.72 (br s, 1 H); ^{13}C NMR (CDCl_3) 23.9 (q, $J = 129$ Hz), 30.1 (q, $J = 129$ Hz), 61.7 (s), 76.2 (s), 114.6 (s); MS, m/e (relative intensity) 165 (<1), 163 (<1), 83 (100); MS (CI) 165 (98), 163 (100).

Anal. Calcd for $\text{C}_7\text{H}_{13}\text{N}_2\text{Br}$: C, 40.99; H, 6.39; N, 13.66. Found: C, 40.82; H, 6.26; N, 13.53.

Preparation of ((*erythro*-2-Bromo-1-methyl-*n*-propyl)amino)carboximidate (6c**). A solution containing 0.21 g (5.65 mmol) of anhydrous HCl in ethanol (5 mL) was added to a solution of 1.00 g (5.65 mmol) of **5c** in 5 mL of ethanol at 5–10 $^{\circ}\text{C}$ and then another 5 mL of ethanol was added. The resulting solution was stirred (6 h) at room temperature. The volatile components were removed in vacuo. The residue was washed with ether (100 mL) and dried in a vacuum desiccator containing P_2O_5 (3 days) to yield 1.42 g (100%) of a hygroscopic, sticky solid: IR (CHCl_3) 3300–2900 (br s), 1655, 1560 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.33 (d, 3 H, $J = 6$ Hz), 1.47 (t, 3 H, $J = 6$ Hz), 1.71 (d, 3 H, $J = 6.5$ Hz), 3.50–4.30 (m, 2 H), 4.66 (q, 2 H, $J = 6$ Hz), 8.50–9.00 (br s, 3 H); ^{13}C NMR (CDCl_3) 14.2 (q, $J = 128$ Hz), 17.1 (q, $J = 128$ Hz), 21.7 (q, $J = 129$ Hz), 52.6 (d, $J = 147$ Hz), 53.0 (d, $J = 147$ Hz), 69.5 (t, $J = 151$ Hz), 160.2 (s) ppm.**

General Procedure for the Treatment of Isoorea Salts 6 with Triethylamine. Compound **6** was generated in situ according to the procedure outlined for the preparation of **6c**, and then triethylamine (3 equiv) was added and the resulting solution was heated to reflux (1 h) unless specified differently in Table III. The reaction solution was then further basified by the addition of sodium ethoxide (2 equiv) in ethanol (10–20 mL) and evaporated in vacuo. The residue was triturated with absolute ether (100–150 mL) and the organic layer evaporated in vacuo to give the product(s) indicated in Table III. Compounds **8b–d** were purified by bulb-to-bulb distillation under vacuum.

General Procedure for the Treatment of Isoorea Salts 6 with NaHCO_3 . The preceding procedure was repeated with anhydrous NaHCO_3 (4–6 equiv, see Table A, supplementary material) in place of triethylamine. The mixture was allowed to stir at room temperature (18 h) and then in the reactions involving **6c** and **6d** heated to reflux (1 h). The insoluble

salts were filtered, and the filtrate was concentrated in vacuo. In the case of **6c**, sodium ethoxide (2 equiv) in ethanol was added to the filtrate prior to being concentrated to dryness.

General Procedure for the Treatment of Isoorea Salts 6 with Na_2CO_3 . The methodology outlined in the NaHCO_3 mediated reactions was utilized, using Na_2CO_3 (3–4 equiv, see Table III) as the base. After workup, the residue remaining after concentration under vacuum was triturated with ether (100–150 mL) and analyzed by TLC. Compounds **8a** and **7e** were purified by bulb-to-bulb distillation under vacuum, while adducts **7d** and **8d** were purified by flash column chromatography.

General Procedure for the Treatment of Isoorea Salts 6 with Sodium Ethoxide. The *O*-ethylisourea salt **6** was generated in situ according to the procedure outlined for **6c**. Ethanolic sodium ethoxide (2 equiv in 10–20 mL of ethanol) was added and the reaction mixture stirred at room temperature (18 h). (For use of 1 equiv of sodium ethoxide, see Table A, supplementary material). After removal of the insoluble salts by filtration, the filtrate was concentrated in vacuo and the residue triturated with ether (100–150 mL). The ethereal solution was concentrated in vacuo and the residue analyzed (NMR and TLC). Compounds **7a–d** and **8a–d** were purified by flash column chromatography. Compounds **7a–f** and **7h** were purified by bulb-to-bulb distillation under vacuum.

Procedure for the Treatment of Isoorea Salt 6c with NaOH. The preceding procedure was repeated with an ethanolic NaOH (2 equiv, Table A, supplementary material) solution in place of sodium ethoxide. After workup, the residue remaining after concentration under vacuum was triturated with ether (100 mL). The ethereal layer was evaporated in vacuo to yield a binary mixture of **7c** and **8c** in a 9:1 ratio, respectively.

Spectral data for all new compounds prepared by these techniques are listed below.

Ethyl 2-butyl-1-aziridinecarboximidate (7a): bp 40 $^{\circ}\text{C}$ (0.15 torr); IR (neat, NaCl) 3310 (br m), 1630 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.91 (t, 3 H, $J = 6$ Hz), 1.29 (t, 3 H, $J = 7$ Hz), 1.34–1.54 (m, 6 H), 1.87–1.97 (m, 1 H), 2.10–2.25 (m, 2 H), 4.12 (q, 2 H, $J = 7$ Hz), 4.50–4.80 (s, 1 H). Selective irradiation of the resonance located at δ 4.12 led to a collapse of the triplet at δ 1.29 to a singlet. ^{13}C NMR (CDCl_3) 14.0 (q, $J = 127$ Hz), 14.2 (q, $J = 127$ Hz), 22.4 (t, $J = 127$ Hz), 29.2 (t, $J = 125$ Hz), 32.0 (t, $J = 128$ Hz), 32.6 (t, $J = 171$ Hz), 38.9 (d, $J = 165$ Hz), 63.1 (t, $J = 147$ Hz), 167.8 (s) ppm; MS (CI) 171; mol wt 170.1422 (calcd for $\text{C}_9\text{H}_{13}\text{N}_2\text{O}$ 170.1419).

4,5-Dihydro-4-*n*-butyl-2-ethoxyimidazole (8a): bp 50 $^{\circ}\text{C}$ (0.0005 torr); IR (neat, NaCl) 3160 (br s), 1630 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.90 (t, 3 H, $J = 4$ Hz), 1.30 (t, 3 H, $J = 7$ Hz), 1.30–1.49 (m, 6 H), 3.09–3.39 (m, 1 H), 3.57–3.84 (m, 2 H), 4.25 (q, 2 H, $J = 7$ Hz), 5.45–5.75 (s, 1 H, exchangeable with D_2O); ^{13}C NMR (CDCl_3) 14.0 (q, $J = 125$ Hz), 14.6 (q, $J = 127$ Hz), 22.7 (t, $J = 127$ Hz), 28.1 (t, $J = 123$ Hz), 36.2 (t, $J = 128$ Hz), 54.2 (t, $J = 140$ Hz), 59.5 (d, $J = 143$ Hz), 64.9 (t, $J = 149$ Hz), 164.6 (s) ppm; MS, m/e (relative intensity) 170 (2), 141 (6), 113 (24), 86 (19), 85 (100); mol wt 170.1414 (calcd for $\text{C}_9\text{H}_{13}\text{N}_2\text{O}$ 170.1419).

Ethyl 2,2-dimethyl-1-aziridinecarboximidate (7b): bp 25 $^{\circ}\text{C}$ (0.10 torr); IR (neat, NaCl) 3280 (br m), 1620 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.14–1.36 (m, 9 H), 1.99 (s, 2 H), 4.15 (q, 2 H, $J = 7$ Hz), 6.02–6.26 (br s, 1 H); ^{13}C NMR (CDCl_3) 14.4 (q, $J = 127$ Hz), 22.5 (q, $J = 128$ Hz), 39.2 (t, $J = 168$ Hz), 40.3 (s), 62.9 (t, $J = 146$ Hz), 166.0 (s) ppm; MS, m/e (relative intensity) 142 (1), 127 (12), 71 (100), 70 (92); MS (CI) 143; mol wt 142.1102 (calcd for $\text{C}_7\text{H}_{14}\text{N}_2\text{O}$ 142.1106).

4,5-Dihydro-4,4-dimethyl-2-ethoxyimidazole (8b): bp 47–50 $^{\circ}\text{C}$ (0.25 torr); IR (neat, NaCl) 3180 (br s), 1620 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.03–1.33 (m, 9 H), 3.24 (s, 2 H), 4.17 (q, 2 H, $J = 7$ Hz), 5.05–5.35 (br s, 1 H); ^{13}C NMR (CDCl_3) 14.5 (q, $J = 126$ Hz), 28.9 (q, $J = 126$ Hz), 60.8 (t, $J = 140$ Hz), 61.5 (s), 64.0 (t, $J = 147$ Hz), 163.5 (s) ppm; MS, m/e (relative intensity) 142 (18), 127 (54), 99 (100), 84 (30); mol wt 142.1104 (calcd for $\text{C}_7\text{H}_{14}\text{N}_2\text{O}$ 142.1106).

Ethyl 2,3-*trans*-dimethyl-1-aziridinecarboximidate (7c): bp 20 $^{\circ}\text{C}$ (0.20 torr); IR (neat, NaCl) 3300 (br m), 1630 (s) cm^{-1} ; ^1H NMR (CDCl_3) δ 1.23 (d, 6 H, $J = 5$ Hz), 1.26 (t, 3 H, $J = 7$ Hz), 1.92–2.30 (m, 2 H), 4.15 (q, 2 H, $J = 7$ Hz), 5.55–6.05 (br s, 1 H, exchangeable with D_2O). Selective irradiation of the signals located at δ 1.23 and 1.26 led to the collapse of the quartet at δ 4.15 to a singlet and the multiplet at δ 1.92–2.30 to a singlet. Irradiation of the signals at δ 1.92–2.30 simplified the doublet at δ 1.23 to a singlet. Irradiation of the signals at δ 4.15 altered the triplet at δ 1.26 to a singlet. ^{13}C NMR (CDCl_3) 14.4 (q, $J = 127$ Hz), 15.9 (q, $J = 127$ Hz), 40.6 (d, $J = 168$ Hz), 62.7 (t, $J = 146$ Hz), 165.5 (s); MS, m/e (relative intensity) 142 (1), 71 (78), 70 (100); mol wt 142.1110 (calcd for $\text{C}_7\text{H}_{14}\text{N}_2\text{O}$ 142.1106).

4,5-Dihydro-4,5-*trans*-dimethyl-2-ethoxyimidazole (8c): bp 40 $^{\circ}\text{C}$ (0.2 torr); IR (neat, NaCl) 3200 (br s), 1630 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.20 (d, 6 H, $J = 7$ Hz), 1.28 (t, 3 H, $J = 7$ Hz), 3.24–3.62 (m, 2 H), 4.21 (q, 2 H, $J = 7$ Hz), 4.44–4.73 (br s, 1 H, exchangeable with D_2O). Successive selective irradiation of the signals at δ 4.21 and 3.24–3.62 led

to the collapse of the triplet located at δ 1.28 and the doublet located at δ 1.20 to a singlet, respectively. ^{13}C NMR (acetone- d_6 - D_2O) 14.7 (q, J = 126 Hz), 21.4 (q, J = 127 Hz; long-range coupling: d, 6 Hz), 63.6 (d, J = 140 Hz), 64.9 (t, J = 147 Hz), 164.5 (s) ppm; ^{13}C NMR (CDCl_3) 14.0, 20.8, 62.7 ($w_{1/2}$ = 20 Hz, signal sharpens upon the addition of trifluoroacetic acid), 63.6, 162.7 ppm; MS, m/e (relative intensity) 142 (26), 127 (34), 114 (29), 113 (21), 99 (78), 70 (100); mol wt 142.1110 (calcd for $\text{C}_7\text{H}_{14}\text{N}_2\text{O}$ 142.1106).

Ethyl 2,3-*trans*-di-*n*-propyl-1-aziridinecarboximidate (7d): bp 47–50 °C (0.15 torr); IR (neat, NaCl) 3300 (br m), 1635 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.96 (t, 6 H, J = 7 Hz), 1.29 (t, 3 H, J = 7 Hz), 1.16–1.76 (m, 8 H), 1.86–2.24 (m, 2 H), 4.15 (q, 2 H, J = 7 Hz), 4.85–5.35 (br s, 1 H); ^{13}C NMR (CDCl_3) 13.9 (q, J = 127 Hz), 14.3 (q, J = 127 Hz), 20.6 (t, J = 123 Hz), 33.0 (t, J = 128 Hz), 44.5 (d, J = 166 Hz), 62.8 (t, J = 146 Hz), 165.9 (s) ppm; MS (CI) 199; mol wt 198.1738 (calcd for $\text{C}_{11}\text{H}_{22}\text{N}_2\text{O}$ 198.1732).

4,5-Dihydro-4,5-*trans*-di-*n*-propyl-2-ethoxyimidazole (8d): bp 53–57 °C (0.0005 torr); IR (neat, NaCl) 3150 (br s), 1630 cm^{-1} ; ^1H NMR (acetone- d_6 - D_2O) δ 0.72–1.10 (m, 6 H), 1.24 (t, 3 H, J = 7 Hz), 1.24–1.61 (m, 8 H), 3.20–3.43 (m, 2 H), 4.17 (q, 2 H, J = 7 Hz); ^{13}C NMR (CDCl_3) 14.1 (q, J = 125 Hz), 14.5 (q, J = 127 Hz), 18.6 (t, J = 126 Hz), 38.6 (t, J = 127 Hz), 63.5 (d, J = 142 Hz), 66.9 (t, J = 152 Hz), 162.9 (s) ppm; MS, m/e (relative intensity) 198 (20), 170 (2), 169 (11), 156 (5), 155 (46), 127 (100); mol wt 198.1734 (calcd for $\text{C}_{11}\text{H}_{22}\text{N}_2\text{O}$ 198.1732).

Ethyl 2,3-*cis*-dimethylaziridinecarboximidate (7e): bp 25 °C (0.30 torr); IR (neat, NaCl) 3300 (br s), 1640 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.22 (d, 6 H, J = 5 Hz), 1.28 (t, 3 H, J = 7 Hz), 2.12–2.50 (m, 2 H), 4.11 (q, 2 H, J = 7 Hz), 4.85–5.35 (br s, 1 H). Successive irradiation of the signals at δ 2.12–2.50 and 4.11 led to the collapse of the doublet at δ 1.22 to a singlet and the triplet at δ 1.28 to a singlet, respectively. Irradiation of the signals at δ 1.22–1.28 altered the multiplet at δ 2.12–2.50 to a singlet and the quartet at δ 4.11 to a singlet. ^{13}C NMR (CDCl_3) 12.9 (q, J = 129 Hz), 14.2 (q, J = 127 Hz), 38.1 (d, J = 167 Hz), 62.9 (t, J = 146 Hz), 168.2 (s) ppm; MS (CI) 143; mol wt 142.1101 (calcd for $\text{C}_7\text{H}_{14}\text{N}_2\text{O}$ 142.1106).

Compound 7f: bp 43–47 °C (0.20 torr); IR (neat, NaCl) 3310 (br m), 1635 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.27 (t, 3 H, J = 7 Hz), 1.30–1.45 (m, 4 H), 1.65–2.03 (m, 4 H), 2.34–2.47 (m, 2 H), 4.13 (q, 2 H, J = 7 Hz), 5.75–6.00 (br s, 1 H); ^{13}C NMR (CDCl_3) 14.2 (q, J = 127 Hz), 20.0 (t, J = 129 Hz), 24.1 (t, J = 129 Hz), 37.6 (d, J = 168 Hz), 63.1 (t, J = 150 Hz), 168.6 (s) ppm; MS (CI) 169; mol wt 168.1266 (calcd for $\text{C}_9\text{H}_{16}\text{N}_2\text{O}$ 168.1263).

Ethyl 2,2,3,3-tetramethyl-1-aziridinecarboximidate (7h): bp 25–30 °C (0.15 torr); IR (neat, NaCl) 3340 (br m), 1640 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.16–1.41 (s, 15 H), 4.14 (q, 2 H, J = 7 Hz), 4.90–5.10 (s, 1 H); ^{13}C NMR (CDCl_3) 14.4 (q, J = 127 Hz), 20.3 (q, J = 127 Hz), 44.8 (s), 62.1 (t, J = 146 Hz), 163.7 (s) ppm; MS (CI) 171.

Anal. Calcd for $\text{C}_9\text{H}_{18}\text{N}_2\text{O}$: C, 63.49; H, 10.66; N, 16.46. Found: C, 63.55; H, 10.68; N, 16.39.

General Procedure for the Conversion of Aziridinecarboximidate 7 to Imidazoline 8. Aziridinecarboximidate 7 (1.4–4.1 mmol) and the catalyst were combined in the appropriate solvent. The molar ratios, solvent, temperature, and length of reaction time are indicated in Table IV. In most cases, the reactions were monitored by TLC analysis. For entries 1, 4–8, 12, and 14 the product mixture upon completion of the reaction was concentrated in vacuo and the residue triturated with ether (100 mL). The ethereal layer was then evaporated under reduced pressure to yield the products listed in Table IV. In entries 2, 9, and 13 where the aldol product of acetone was formed, the initial residue was triturated with methylene chloride (50–100 mL) and the methylene chloride layer was concentrated (~20 mL) and then extracted with 10% aqueous HCl (2 \times 10 mL). The aqueous layers were combined and washed with methylene chloride (2 \times 10 mL). The remaining aqueous layer was then made basic with Na_2CO_3 and extracted once again with methylene chloride (3 \times 20 mL). The methylene chloride layers were combined, dried (Na_2SO_4), and concentrated in vacuo to yield the products indicated in Table IV. In entries 3 and 10, sodium ethoxide (2 equiv) in ethanol was added to the reaction mixture prior to the initial concentration step, while in entry 11, sodium ethoxide (1 equiv) in ethanol was used.

Spectral data for all new compounds prepared by this technique but not previously reported in the preceding sections appear below.

4,5-Dihydro-4,5-*cis*-dimethyl-2-ethoxyimidazole (8e): bp 41 °C (0.10 torr); mp 57–59 °C; IR (neat, NaCl) 3150 (br s), 1630 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.11 (d, 6 H, J = 6 Hz), 1.28 (t, 3 H, J = 7 Hz), 3.76–4.08 (m, 2 H), 4.21 (q, 2 H, J = 7 Hz), 4.60–5.00 (s, 1 H, exchangeable with D_2O); ^{13}C NMR (CDCl_3) 14.5 (q, J = 127 Hz), 15.9 (q, J = 126 Hz), long-range coupling: d, J = 3 Hz), 58.3 (d, $w_{1/2}$ = 10 Hz, J = 142 Hz), 64.3 (t, J = 147 Hz), 164.0 (s) ppm; MS, m/e (relative intensity) 142

(8), 127 (23), 99 (52), 70 (100); mol wt 142.1103 (calcd for $\text{C}_7\text{H}_{14}\text{N}_2\text{O}$ 142.1106).

3a,4,5,6,7,7a-Hexahydro-2-ethoxybenzimidazole (8f): sublimed at 60–65 °C (0.0005 torr); mp 88–90 °C; IR (KBr) 3100 (br s), 1610 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.29 (t, 3 H, J = 7 Hz), 1.40–1.91 (m, 8 H), 3.50–3.88 (m, 2 H), 4.23 (q, 2 H, J = 7 Hz), 4.60–4.80 (s, 1 H, exchangeable with D_2O); ^{13}C NMR (CDCl_3) 14.5, 21.0, 28.9, 58.7 ($w_{1/2}$ = 30 Hz), 64.3, 165.3 ppm; ^{13}C NMR (CDCl_3 - D_2O) 14.5, 21.0 ($w_{1/2}$ = 10 Hz), 28.9 ($w_{1/2}$ = 10 Hz), 56.6 ($w_{1/2}$ = 15 Hz), 60.8 ($w_{1/2}$ = 15 Hz), 64.4, 165.3 ppm; ^{13}C NMR (acetone- d_6) 14.9 (q, J = 126 Hz), 21.8 (t, J = 127 Hz), 29.7 (t, J = 128 Hz), 59.7 (d, J = 141 Hz), 64.2 (t, J = 147 Hz), 166.0 (s) ppm; MS, m/e (relative intensity) 168 (20), 140 (25), 123 (26), 97 (100); mol wt 168.1265 (calcd for $\text{C}_9\text{H}_{16}\text{N}_2\text{O}$ 168.1263).

4,5-Dihydro-1-acetyl-4,5-*trans*-dimethyl-2-ethoxyimidazole (15). Acetic anhydride (0.43 g, 4.22 mmol) in chloroform (3 mL) was added to a solution of **8c** (0.30 g, 2.11 mmol) in chloroform (10 mL). The resulting solution was heated at reflux (0.5 h). TLC analysis (10% ethanol-chloroform) indicated the total consumption of **8c** and the formation of a new compound (R_f 0.63). The reaction solution was cooled to room temperature and washed with 5% aqueous Na_2CO_3 (3 \times 20 mL). The chloroform layer was dried (Na_2SO_4) and concentrated in vacuo to yield 330 mg (85%) of nearly pure **15**. Further purification by bulb-to-bulb distillation at 40–45 °C (0.15 torr) gave **15** as a colorless oil: IR (neat, NaCl) 2960, 1680, 1640, 1430, 1410 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.15 (d, 3 H, J = 6.5 Hz), 1.29 (d, 3 H, J = 6 Hz), 1.38 (t, 3 H, J = 7 Hz), 2.32 (s, 3 H), 3.41 (dq, 1 H, J = 3.5, 6.5 Hz), 4.00 (dq, 1 H, J = 3.5, 6 Hz), 4.34 (q, 2 H, J = 7 Hz). Selective irradiation of the signals at δ 4.34 led to a collapse of the triplet at δ 1.38 to a singlet. Irradiation of the signals at δ 4.00 altered the doublet of quartets at δ 3.41 to a quartet and the doublet at δ 1.29 to a singlet. Irradiation of the signals at δ 3.41 altered the doublet of quartets at δ 4.00 to a quartet and the doublet at δ 1.15 to a singlet. Irradiation of the signals at δ 1.15–1.38 simplified the doublet of quartets at δ 3.41 to a doublet, the doublet of quartets at δ 4.00 to a doublet, and the quartet at δ 4.34 to a singlet. ^{13}C NMR (CDCl_3) 14.3 (q, J = 127 Hz), 19.6 (q, J = 127 Hz; long-range coupling: d, J = 6 Hz), 21.9 (q, J = 127 Hz; long-range coupling: d, J = 6 Hz), 24.5 (q, J = 130 Hz), 61.5 (d, J = 146 Hz), 62.4 (d, J = 144 Hz), 66.1 (t, J = 146 Hz), 154.2 (s), 168.3 (s) ppm; MS (CI) 185; mol wt 184.1214 (calcd for $\text{C}_9\text{H}_{16}\text{N}_2\text{O}_2$ 184.1212).

4,5-Dihydro-1-acetyl-4,5-*cis*-dimethyl-2-ethoxyimidazole (16). Employing the method described for the preparation of **15**, compound **16** was synthesized with 0.17 g (1.20 mmol) of **8e** and 0.24 g (2.40 mmol) of acetic anhydride in chloroform (10 mL). After workup, 0.21 g (95%) of **16** was obtained as a colorless oil. Bulb-to-bulb distillation at 45–50 °C (0.15 torr) gave pure **16**: IR (neat, NaCl) 2980, 1670, 1630, 1430, 1400 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.15 (d, 3 H, J = 5.5 Hz), 1.23 (d, 3 H, J = 6 Hz), 1.38 (t, 3 H, J = 7 Hz), 2.29 (s, 3 H), 3.96 (dq, 1 H, J = 6, 8 Hz), 4.34 (q, 2 H, J = 7 Hz), 4.53 (dq, 1 H, J = 5.5, 8 Hz). Selective irradiation of the signals centered at δ 1.15 led to a collapse of the doublet of quartets at δ 4.53 to a doublet. Irradiation of the signal centered at δ 1.23 simplified the doublet of quartets at δ 3.96 to a doublet. Irradiation of the resonance located at δ 4.34 altered the triplet at δ 1.38 to a singlet. Irradiation of the signal at δ 3.96 led to a collapse of the doublet of quartets at δ 4.53 to a quartet and the doublet at δ 1.23 to a singlet. Irradiation of the resonance at δ 4.53 altered the doublet of quartets at δ 3.96 to a quartet and the doublet at δ 1.15 to a singlet. ^{13}C NMR (CDCl_3) 13.1 (q, J = 127 Hz; long-range coupling: d, J = 4.5 Hz), 14.4 (q, J = 127 Hz; long-range coupling: t, J = 2.5 Hz), 16.0 (q, J = 126 Hz; long-range coupling: d, J = 3 Hz), 24.3 (q, J = 130 Hz), 57.4 (d, J = 140 Hz), 58.3 (d, J = 145 Hz), 66.0 (t, J = 148 Hz), 154.8 (s), 167.4 (s) ppm. Selective irradiation of the signal located at δ 1.23 in the ^1H NMR spectrum led to a collapse of the quartet at 16.0 ppm in the proton coupled ^{13}C NMR spectrum to a singlet. Irradiation of the resonance centered at δ 3.96 in the ^1H NMR spectrum altered the doublet at 57.4 ppm in the proton coupled ^{13}C NMR spectrum to a singlet. MS, m/e (relative intensity) 184 (6), 169 (19), 156 (32), 141 (22), 127 (47), 112 (33), 99 (81), 70 (100); MS (CI) 185; mol wt 184.1215 (calcd for $\text{C}_9\text{H}_{16}\text{N}_2\text{O}_2$ 184.1212).

Synthesis of (erythro-2-Bromo-1-methylpropyl)urea (17). Cyanamide **5c** (1.00 g, 5.65 mmol) was dissolved in ether (1 mL) and cooled in an ice bath. To this solution, chilled 50% (v/v) aqueous H_2SO_4 (1 mL) was added dropwise. The stirred reaction mixture was allowed to warm to room temperature and then to remain at room temperature (1 h). The reaction mixture was poured onto crushed ice (5 g), and the precipitate was filtered and washed with cold H_2O . The white solid was dried in a vacuum desiccator containing P_2O_5 and then recrystallized from methylene chloride to yield 0.43 g (39%) of **17**: mp 86–87 °C. The aqueous filtrate was extracted with methylene chloride (3 \times 30 mL) and the organic layers were combined, dried (Na_2SO_4), and evaporated in vacuo.

Recrystallization of the residue from methylene chloride gave 0.23 g (20%) of urea **17**: mp 86–87 °C. The overall yield was 59%. IR (KBr) 3400, 3340, 1655, 1600, 1530 cm^{-1} ; ^1H NMR (acetone- d_6) δ 1.14 (d, 3 H, $J = 7$ Hz), 1.62 (d, 3 H, $J = 7$ Hz), 3.50–4.00 (m, 1 H), 4.37 (dq, 1 H, $J = 3, 7$ Hz), 4.80–5.30 (br s, 2 H), 5.40–6.22 (br s, 1 H). After 1 day, the spectrum was completely transformed to the following set: δ 1.45 (d, 3 H, $J = 6.5$ Hz), 1.60 (d, 3 H, $J = 6.5$ Hz), 4.06 (quintet, 1 H, $J = 6.5$ Hz), 4.81 (quintet, 1 H, $J = 6.5$ Hz), 8.43–9.26 (br s, 2 H), 9.47–10.10 (br s, 1 H); ^{13}C NMR (CD_3OD -acetone- d_6) 16.4, 23.2, 51.7, 58.3, 157.0 ppm; MS, m/e (relative intensity) 196 (2), 194 (2), 138 (5), 136 (5), 109 (3), 107 (3), 87 (100).

Anal. Calcd for $\text{C}_5\text{H}_{11}\text{N}_2\text{BrO}$: C, 30.78; H, 5.68; N, 14.36. Found: C, 30.61; H, 5.75; N, 14.23.

Conversion of (erythro-2-bromo-1-methylpropyl)urea (17) to 4,5-Di-hydro-4,5-trans-dimethyl-2-aminooxazolinium Bromide (18). The interconversion of the NMR sample of urea **17** to oxazolinium salt **18** was verified by the isolation of the neutral oxazoline. Accordingly, urea **17** (0.50 g, 2.56 mmol) was dissolved in acetone (30 mL) at room temperature and set aside for 3 days. The solution was evaporated in vacuo and the residue dissolved in 10% aqueous Na_2CO_3 (20 mL). The aqueous solution was continuously extracted with methylene chloride (3 days) and then the methylene chloride layer was dried (Na_2SO_4) and concentrated under reduced pressure to give 0.26 g (89%) of neutral oxazoline. Bulb-to-bulb distillation at 65–70 °C (0.70 torr) gave the pure product. IR (neat, NaCl) 3450–3130 (br s), 1685, 1420, 1385 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.16 (d, 3 H, $J = 6.5$ Hz), 1.32 (d, 3 H, $J = 6.5$ Hz), 3.55 (quintet, 1 H, $J = 6.5$ Hz), 4.11 (quintet, 1 H, $J = 6.5$ Hz), 4.70 (s, 2 H). Selective irradiation of the signals located at δ 1.16 and 1.32 led to the collapse of the quintet at δ 3.55 to a doublet and the quintet at δ 4.11 to a doublet. ^{13}C NMR (CDCl_3) 19.7 (q, $J = 127$ Hz; long-range coupling: d, $J = 6$ Hz), 21.3 (q, $J = 126$ Hz; long-range coupling: d, $J = 5.5$ Hz), 65.9 (d, $J = 136$ Hz), 83.6 (d, $J = 149$ Hz), 160.3 (s) ppm; MS, m/e (relative intensity) 114 (20), 99 (100), 84 (36), 70 (22), 69 (24); mol wt 114.0796 (calcd for $\text{C}_5\text{H}_{10}\text{N}_2\text{O}$ 114.0793).

Further confirmation of the formation of the neutral oxazoline was accomplished by the synthesis of the corresponding picrate salt. The oxazoline adduct (0.39 g, 3.42 mmol) was dissolved in ethanol (10 mL), and an ethanolic solution saturated with picric acid was added dropwise until precipitation was complete. The precipitate was collected by filtration and recrystallized from ethanol to yield 1.05 g (89%) of the picrate salt of **18**: mp 192–195 °C; IR (KBr) 3370, 3180, 1705, 1620, 1575, 1530 cm^{-1} ; ^1H NMR ($\text{Me}_2\text{SO}-d_6$) δ 1.25 (d, 3 H, $J = 6.5$ Hz), 1.40 (d, 3 H, $J = 6.5$ Hz), 3.80 (quintet, 1 H, $J = 6.5$ Hz), 4.68 (quintet, 1 H, $J = 6.5$ Hz), 8.66 (s, 2 H), 8.66–9.00 (br s, 2 H), 9.17–9.50 (br s, 1 H).

Anal. Calcd for $\text{C}_{11}\text{H}_{13}\text{N}_5\text{O}_8$: C, 38.49; H, 3.82; N, 20.41. Found: C, 38.51; H, 3.80; N, 20.37.

dl-2,3-Diaminobutane (1c). Compound **8c** (0.20 g, 1.41 mmol) was placed in a heavy glass-walled tube (170 \times 12 mm) and then $\text{Ba}(\text{OH})_2$ (4.30 g, 27.9 mmol) and H_2O (8.6 mL) were added. The reaction mixture was frozen in dry ice and the tube sealed with a torch and heated in an oil bath at 120 °C (18 h). The tube was opened, and the contents were transferred to a 250-mL Erlenmeyer flask with the aid of 50 mL of H_2O . CO_2 gas was bubbled into the reaction mixture until the pH was 7. After removal of the insoluble salts by filtration with the aid of a Celite pad, the pH of the filtrate was acidified (Congo red) with 1 N aqueous H_2SO_4 . The insoluble salts were filtered with the aid of a Celite pad, and the filtrate was concentrated in vacuo to give a white solid. The product was reprecipitated from H_2O (2 mL) by the addition of methanol (50 mL) to give 250 mg (96%) of the sulfate salt of **1c** (mp >320 °C): ^1H NMR (D_2O , external Me_4Si) δ 1.91 (d, 3 H, $J = 6$ Hz), 4.08–4.48 (m, 1 H); ^{13}C NMR (D_2O , external Me_4Si) 14.1, 50.0 ppm.

In order to confirm the formation of diamine **1c**, the sulfate salt was converted to the dihydrochloride adduct. The sulfate salt of **1c** (250 mg, 1.34 mmol) was dissolved in H_2O (50 mL). The pH of the solution was adjusted to 14 with 30% aqueous NaOH (1 mL) and distilled until the distillation flask was almost dry. The distillate was acidified with concentrated aqueous HCl to pH 1 and then evaporated in vacuo to give a white solid. The product was reprecipitated from methanol (5 mL) by the addition of ether (50 mL). The white solid was dried in a vacuum desiccator overnight to give 220 mg (99%) of the dihydrochloride of **1c**: mp 254–256 °C (lit.⁶⁶ mp 253–254 °C); IR (KBr) 3200–2700 (br s), 1600, 1550, 1490, 1470 cm^{-1} ; ^1H NMR (D_2O , external Me_4Si) δ 1.91 (d, 3 H, $J = 6$ Hz), 4.10–4.50 (m, 1 H); ^{13}C NMR (D_2O , external Me_4Si) 13.7, 49.9 ppm (lit.⁶⁷ 14.24, 49.98 ppm).

1,2-Diamino-2-methylpropane (1b). The procedure used for the preparation of **1c** was repeated beginning with imidazoline **8b** (0.40 g, 2.82 mmol), $\text{Ba}(\text{OH})_2$ (5.00 g, 29.2 mmol), and H_2O (10 mL). After

workup, reprecipitation of the residue in H_2O (2 mL) by the addition of methanol (50 mL) gave 0.53 g (99%) of the sulfate salt of diamine **1b**: mp 298–300 °C dec; ^1H NMR (D_2O , external Me_4Si) δ 2.14 (s, 6 H), 3.85 (s, 2 H). Confirmation of the synthesis of the desired diamine **1b** was made by the conversion of the sulfate salt to the corresponding dihydrochloride salt⁶⁷ with the procedure outlined for **1c**. The product was reprecipitated from ethanol-ether and then dried in a vacuum desiccator (18 h) to yield 0.35 g (99%) of the dihydrochloride salt of **1b**: mp 292–294 °C (lit.⁶⁵ mp 292–295 °C); IR (KBr) 3200–2600 (br s), 2030, 1560, 1510, 1455, 1400, 1380 cm^{-1} ; ^1H NMR (D_2O , external Me_4Si) δ 2.06 (s, 6 H), 3.88 (s, 2 H); ^{13}C NMR (D_2O , external Me_4Si) 24.3, 47.7, 54.2 ppm.

meso-2,3-Diaminobutane (1e). The procedure used for the preparation of **1c** was repeated beginning with 0.40 g (2.82 mmol) of imidazoline **8e** (contaminated with trans-isomer **8c**, $\leq 10\%$ by ^1H NMR analysis), 5.00 g (29.2 mmol) of $\text{Ba}(\text{OH})_2$, and H_2O (10 mL). After workup, 0.53 g (99%) of the residue was obtained. ^{13}C NMR analysis indicated that the residue contained the sulfate salts of **1e** and **1c** in a ratio of $\sim 19:1$. Addition of methanol (50 mL) to a solution of the above residue in H_2O (2 mL) selectively precipitated the sulfate salt of **1e** (0.46 g, 88%): mp >320 °C; ^1H NMR (D_2O , external Me_4Si) δ 1.94 (d, 3 H, $J = 6$ Hz), 3.98–4.38 (m, 1 H); ^{13}C NMR (D_2O , external Me_4Si) 15.5, 50.8 ppm.

Confirmation of the formation of **1e** was accomplished by conversion of the sulfate salt of **1e** to the dihydrochloride salt⁶⁹ with the procedure outlined for **1c**. The product was reprecipitated from methanol (5 mL) by the addition of ether (100 mL) and then dried in a vacuum desiccator (18 h) to give 0.39 g (98%) of the dihydrochloride salt of **1e**: mp 324–325 °C (lit.⁶⁶ mp 325 °C); IR (KBr) 3200–2600 (br s), 1600, 1500, 1450, 1410 cm^{-1} ; ^1H NMR (D_2O , external Me_4Si) δ 2.04 (d, 3 H, $J = 6.5$ Hz), 4.12–4.52 (m, 1 H); ^{13}C NMR (D_2O , external Me_4Si) 16.2, 51.3 ppm (lit.⁶⁷ 15.98, 50.98 ppm).

dl-4,5-Diaminooctane (1d). Imidazoline **8d** (0.30 g, 1.52 mmol), $\text{Ba}(\text{OH})_2$ (2.59 g, 15.2 mmol), and H_2O (6 mL) were placed in a thick-walled glass tube (170 \times 12 mm) according to the procedure for the preparation of **1c**. The tube was sealed with a torch, heated in an oil bath (130–140 °C) for 2 days, and opened, and the contents were transferred to a 250-mL Erlenmeyer flask with the aid of H_2O (30 mL). The resulting mixture was extracted with ether (3 \times 60 mL). The organic layers were combined, dried (Na_2SO_4), and then made strongly acidic with 10% ethanolic HCl . The solution was evaporated to dryness in vacuo to give 0.26 g (79%) of the dihydrochloride salt of **1d**. The product was reprecipitated from methanol (3 mL) by the addition of ether (50 mL) to give 0.25 g (76%) of the dihydrochloride salt of **1d** as a white solid: mp 218–220 °C; IR (KBr) 3200–2700 (br s), 1580, 1500, 1480, 1450, 1375 cm^{-1} ; ^1H NMR (CD_3OD) δ 1.03 (t, 6 H, $J = 6$ Hz), 1.34–1.86 (m, 8 H), 3.54–3.84 (m, 2 H); ^{13}C NMR (CD_3OD) 14.0, 19.9, 30.4, 53.6 ppm.

Anal. Calcd for $\text{C}_8\text{H}_{22}\text{N}_2\text{Cl}_2$: C, 44.24; H, 10.02; N, 12.90. Found: C, 44.32; H, 10.18; N, 12.92.

trans-4,5-Di-n-propyl-2-imidazolidinone (26). Imidazoline **8d** (0.40 g, 2.02 mmol), $\text{Ba}(\text{OH})_2$ (3.45 g, 20.2 mmol), and H_2O (7 mL) were placed in a thick-walled glass tube (170 \times 12 mm) and sealed with a torch. The tube was heated in an oil bath (110–115 °C) for 1 day and opened. The contents were transferred to a 250-mL round-bottomed flask with the aid of H_2O (30 mL) and ether (30 mL). The mixture was continuously extracted with ether for 24 h. The organic layer was dried (Na_2SO_4), acidified (pH 1) with 10% ethanolic HCl , and concentrated to dryness in vacuo to yield 0.34 g (99%) of the tentatively proposed structure **26**. Compound **26** was sublimed at 105–108 °C (0.0005 torr): mp 113–115 °C; IR (KBr) 3200 (br s), 2960, 2920, 2860, 1705, 1460 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.90–1.10 (m, 6 H), 1.32–1.56 (m, 8 H), 3.19–3.43 (m, 2 H), 5.93–6.03 (br s, 2 H); ^{13}C NMR (CDCl_3) 14.0, 18.9, 38.6, 58.6, 163.8 ppm; MS, m/e (relative intensity) 170 (6), 127 (100), 84 (9).

cis-1,2-Diaminocyclohexane (1f). With use of the method described for the preparation of **1d**, compound **1f** was synthesized beginning with imidazoline **8f** (0.30 g, 1.79 mmol), $\text{Ba}(\text{OH})_2$ (3.05 g, 17.9 mmol), and H_2O (6 mL). The mixture was heated for 1 day with an oil bath maintained at 120–130 °C. The reaction mixture was continuously extracted (2 days) with ether. The ethereal layer was dried (Na_2SO_4), acidified (pH 1) with 10% ethanolic HCl , and evaporated to dryness in vacuo to give 0.32 g (96%) of the dihydrochloride salt of **1f**: mp 310–312 °C (lit.⁶⁶ mp 312–314 °C); IR (KBr) 3200–2700 (br s), 1580, 1550, 1510 cm^{-1} ; ^1H NMR (D_2O , external Me_4Si) δ 2.00–2.70 (m, 8 H), 4.40–4.70 (m, 2 H); ^{13}C NMR (D_2O , external Me_4Si) 21.4, 27.0, 51.2 ppm.

1,2-Diaminohexane (1a). With use of the method described for the preparation of **1d**, diamine **1a** was synthesized beginning with imidazoline **8a** (0.47 g, 2.76 mmol), $\text{Ba}(\text{OH})_2$ (5.00 g, 29.2 mmol), and H_2O (10 mL). The contents were heated for 2 days with an oil bath maintained at 120 °C. After workup, 0.46 g (88%) of the hygroscopic dihydro-

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chloride salt⁶³ of **1a** was obtained: ¹H NMR (D₂O, external Me₄Si) δ 1.37–1.57 (m, 3 H), 1.80–2.10 (m, 4 H), 2.16–2.46 (m, 2 H), 3.94 (d, 2 H, *J* = 5.5 Hz), 4.07–4.37 (m, 1 H), ¹³C NMR (D₂O, external Me₄Si) 14.6, 23.0, 27.5, 31.0, 42.3, 50.9 ppm.

Formation of diamine **1a** was confirmed by the preparation of the corresponding diacetyl derivative.⁶⁷ The dihydrochloride salt of **1a** (0.25 g, 1.34 mmol) was dissolved in methanol (2 mL) and made basic with a methanolic solution of sodium methoxide (0.07 g [3.04 mmol] of Na in 3 mL of methanol). To this mixture ether (50 mL) was added, and the insoluble material was removed by filtration. The filtrate was evaporated in vacuo, and the residue was triturated with ether (50 mL). Concentration of the ethereal solution gave 0.12 g (77%) of **1a**. Diamine **1a** was dissolved in pyridine (2 mL), acetic anhydride (0.32 g, 3.10 mmol) was added, and the resulting mixture was stirred (0.5 h) at room temperature. Benzene (50 mL) was then added and the reaction mixture evaporated in vacuo to give 0.19 g of material. Recrystallization of the residue from benzene yielded 0.16 g (77%) of the diacetamide: mp 147–148 °C (lit.⁶⁴ mp 151 °C); IR (KBr) 3300, 1655, 1560 cm⁻¹; ¹H NMR (CDCl₃) δ 0.89 (t, 3 H, *J* = 5 Hz), 1.34–1.46 (m, 6 H), 1.97 (s, 3 H), 1.98 (s, 3 H), 3.13–3.43 (m, 2 H), 3.78–4.08 (m, 1 H), 6.18–6.38 (br s, 1 H), 6.54–6.84 (br s, 1 H); ¹³C NMR (CDCl₃) 13.9, 22.5, 23.1, 23.4, 28.1, 32.4, 44.8, 50.2, 171.3 ppm.

Acid Hydrolysis of 4,5-Dihydro-4,5-*trans*-di-*n*-propyl-2-ethoxy-imidazole (8d). Imidazoline **8d** (0.51 g, 2.58 mmol) was dissolved in 30% aqueous H₂SO₄ and then heated at reflux (18 h). The reaction was made basic (pH 14) with 20% aqueous NaOH and extracted with ether (3 × 60 mL). The organic layers were combined, dried (Na₂SO₄), made acidic (pH 1) with 10% ethanolic HCl, and concentrated to dryness in vacuo to give 0.22 g (39%) of the dihydrochloride salt of **1d**. Recrystallization of the residue from methanol (2 mL) by the addition of ether (50 mL) gave 0.17 g (30%) of the dihydrochloride of **1d** as a white solid: mp

218–220 °C. The product was identified by IR and ¹H NMR spectroscopy.

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Registry No. (±)-**1a**, 95647-75-9; (±)-**1a**·HCl, 95647-76-0; (±)-**1a** (diacetamide), 95648-07-0; **1b**·H₂SO₄, 95647-77-1; **1b**·2HCl, 15444-85-6; (±)-**1c**·H₂SO₄, 95647-78-2; (±)-**1c**·2HCl, 66427-25-6; (±)-**1d**·2HCl, 85782-34-9; *meso*-**1e**·H₂SO₄, 95647-79-3; *meso*-**1e**·2HCl, 28971-67-7; *meso*-**1f**·2HCl, 10027-80-2; **2a**, 592-41-6; **2b**, 115-11-7; **2c**, 624-64-6; **2d**, 14850-23-8; **2e**, 590-18-1; **2f**, 110-83-8; **2g**, 922-62-3; **2h**, 563-79-1; **3**, 420-04-2; **4**, 128-08-5; (±)-**5a**₁, 95647-80-6; (±)-**5a**₂, 95647-81-7; **5b**, 90304-06-6; (±)-**5c**, 85782-20-3; (±)-**5d**, 85782-24-7; (±)-**5e**, 85782-21-4; (±)-**5f**, 85782-23-6; (±)-**5g**, 95647-82-8; **5h**, 95647-83-9; (±)-**6a**, 95647-84-0; **6b**, 95647-85-1; (±)-**6c**, 95647-86-2; (±)-**6d**, 95647-87-3; (±)-**6e**, 95647-88-4; (±)-**6f**, 95647-89-5; (±)-**7a**, 95647-90-8; **7b**, 95647-91-9; **7c**, 95647-92-0; (±)-**7d**, 95673-89-5; *meso*-**7e**, 85782-30-5; **7f**, 85782-31-6; **7h**, 95647-93-1; (±)-**8a**, 95647-94-2; **8b**, 95647-95-3; (±)-**8c**, 85782-25-8; (±)-**8d**, 85782-29-2; (±)-**8e**, 95673-90-8; (±)-**8f**, 95647-96-4; **9a**, 95647-97-5; (±)-**9b**, 95647-98-6; (±)-**10**, 60933-67-7; (±)-**11**, 95647-99-7; (±)-**15**, 95648-00-3; (±)-**16**, 95648-01-4; (±)-**17**, 95648-02-5; (±)-**18**, 95648-03-6; (±)-**18**-PICRATE, 95648-05-8; (±)-**26**, 95648-06-9.

Supplementary Material Available: An expanded list (Table A) of the reaction of isourea salts **6** with bases is reported herein (1 page). Ordering information is given on any current masthead page.

Total Syntheses of Rivularins D₁ and D₃

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Abstract: Two of the recently discovered metabolites of *Rivularia firma* Womersley, (+)-3',5,5'-tribromo-7'-methoxy-3,4'-bi-1*H*-indole (rivularin D₁) and (+)-2,3',5,5'-tetrabromo-7'-methoxy-3,4'-bi-1*H*-indole (rivularin D₃), were synthesized in racemic form. 2-Methoxy-1-naphthalenamine, prepared by nitration of 2-methoxynaphthalene and reduction of the resulting 2-methoxy-1-nitronaphthalene, gave 5,8-dihydro-2-methoxy-1-naphthalenamine upon Birch reduction. Subsequent bromination, *N*-tosylation, ozonolysis, and acid-catalyzed cyclization furnished 5-bromo-7-methoxy-1-[(4-methylphenyl)sulfonyl]-1*H*-indol-4-acetaldehyde, which was converted to 5-bromo-4-(5-bromo-1*H*-indol-3-yl)-7-methoxy-1-[(4-methylphenyl)sulfonyl]-1*H*-indole with (4-bromophenyl)hydrazine. Hydrolytic detosylation and a bromination with pyridinium bromide perbromide gave (±)-rivularin D₁. A further bromination with *N*-bromosuccinimide led to (±)-rivularin D₃.

Two indole nuclei, which are connected directly to each other by bridging only two positions, can form 28 constitutional isomers. The historical indigo, the oldest known organic dye, can be regarded as a member of this class of compounds. It consists of two oxindole moieties linked to each other by a double bond, as in the most celebrated member, 2-(1,3-dihydro-3-oxo-2*H*-indol-2-ylidene)-1,2-dihydro-3*H*-indol-3-one, also known as indigotin. In addition to the 2,2'-internuclear connection of the indigotins there are the indirubins with 2,3'- and the isoindirubins with 3,3'-linkages.¹ The variety of these dyes is further enhanced by a number of substituents in the benzenoid portions. Whereas the dyes derived from herbal precursors appear to be devoid of substituents, those from the animal kingdom are likely to contain bromine and occasionally methoxy groups as well. Tyrian Purple, for instance, is 6,6'-dibromoindigo and was derived by the ancients from several species of mollusks of the genus *Murex*, whereas the 5,5'-7,7'-tetrabromo-6,6'-dimethoxyindigo is the most highly

substituted indigotin described to date and was discovered, among other congeners, in the acorn worm *Ptychodera flava*.^{2a-c}

Lacking the ene-1,4-dione moiety of the indigo dyes, biindoles with single-bond internuclear connections are colorless and have only recently come to light. A 7,7'-bi-1*H*-indole system is found in 11,11'-dihydroxy-12,12'-biconaridine, an alkaloid isolated from the plant *Bonafoisia tetrastachya* (family *Apocynaceae*),^{3a} 1,3'- and 3,3'-systems are present in the gliotoxin-related antibiotics chaetomin and the chaetocin family,^{3b} and the rivularins, metabolites of the marine blue-green alga *Rivularia firma* Womersley, represent biindoles featuring 1,3'-, 1,4'-, 3,3'-, and 3,4'-intramolecular linkages. In contrast to the indigo dyes derived from plants, all rivularins contain anywhere from three to six bromine atoms and some exhibit an additional methoxy group.⁴

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