Electrophilic Cyclization and Thermal Rearrangement of Allylic 1,1-Dimethylisoureas

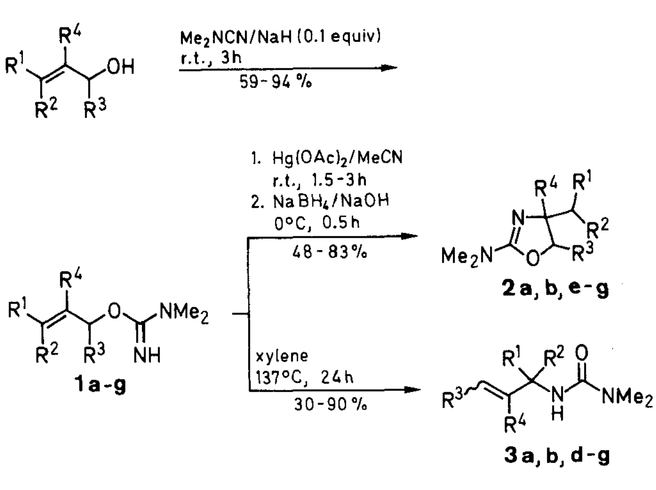
Robert M. Giuliano, Tien T. Duong, Ted W. Deisenroth, Wayne G. McMahon, Walter J. Boyko
Department of Chemistry, Villanova University, Villanova, PA 19085, USA

A series of substituted 2-allyl-1,1-dimethylisoureas (allyl *N*,*N*-dimethylcarbamimidates) was prepared by the reaction of the corresponding allylic alcohols with dimethylcyanamide in the presence of sodium hydride. Treatment of the isoureas with mercuric acetate in acetonitrile, followed by reduction with sodium borohydride, afforded substituted 4,5-dihydrooxazoles. Thermal rearrangement of the 1,1-dimethylisoureas occurred in refluxing xylene to give trisubstituted ureas.

Electrophilic cyclization and thermal rearrangement reactions of allylic imidates and the related isoureas (allyl carbamimidates) are useful methods for the addition of nitrogen functionality to olefinic bonds, providing access to vicinal amino alcohols or allylic amines, alternatively. Both procedures have been developed for imidates derived from trichloroacetonitrile,[1] and the thermal rearrangement reaction has been described for allylic and propargylic isoureas prepared from *N*-cyanopyrrolidine.[2] Applications of these two methods to the synthesis of compounds that contain amino alcohol[3] and other nitrogen functionalities[4] have been described in the literature; however, very few examples of the use of other nitriles in either context have been reported.[5] During the course of our studies of branched-chain carbohydrate synthesis, we discovered that isoureas[6] derived from dimethylcyanamide were suitable for the conversion of allylic alcohols to vicinal amino alcohols in carbohydrate systems by the electrophilic cyclization -hydrolysis sequence.[7] Since these results were reported, dimethylcyanamide has been used as a reagent for the synthesis of additional carbohydrate amino alcohols in our own[8] as well as other[9] laboratories, but limited information regarding the scope and limitations of the cyclization reaction is available from these few cases.

Examples of this transformation have not been reported for acyclic 1,1-dimethylisoureas **1a**–**e**. The thermal rearrangement of 2-allyl-1,1-dimethylisoureas, although established for their pyrrolidine analogs, has also not been reported. In an effort to expand the synthetic utility of these substrates, we have now demonstrated that the electrophilic cyclization of **1** occurs readily in the presence of mercuric acetate in acetonitrile to give 4,5-dihydrooxazoles **2**, while the thermal rearrangement of **1** in refluxing xylene gives trisubstituted ureas **3** (Scheme A).

The allylic isoureas **1a**–**g** were prepared by stirring equimolar quantities of the corresponding allylic alcohols and dimethylcyanamide in the presence of sodium hydride (0.1 molar equivalents) at room temperature. The reaction is slightly exothermic. Isourea formation was complete within three hours, and the products were isolated in the yields indicated by an extractive workup. The isoureas decomposed on standing for extended periods at room temperature, and difficulties were encountered in obtaining satisfactory microanalyses. No other products were detected in the reaction, as evidenced by the NMR spectra, nor was any significant amount of unreacted allylic alcohol observed. The isoureas obtained were suitable for the electrophilic cyclization and thermal rearrangement reactions without further purification.



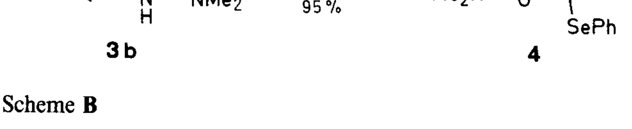
1-3	R^1	R^2	R^3	R^4
a	H	H	Me	H
b	H	H	Pr	H
c	H	H	Ph	H
d	Ph	H	H	H
e	Pr	H	H	H
f	H	$-(CH_2)_3-$		H
g	H	H	$-(CH_2)_4-$	

Scheme A

The electrophilic cyclization of the 1,1-dimethylisoureas was attempted with mercuric acetate, mercuric trifluoroacetate, or mercuric nitrate in both acetonitrile and tetrahydrofuran. In some cases, an equimolar mixture of mercuric acetate and mercuric trifluoroacetate was used. Demercuration was carried out in the same operation with sodium borohydride, except when the course of the cyclization reaction was monitored by NMR. Best results were obtained for the cyclization reaction with mercuric acetate in acetonitrile. In our previous work, cyclizations were carried out with mercuric trifluoroacetate based on the assumption that the more nucleophilic acetate anion might give rise to other products in the mercuration step. Contrary to this expectation, products resulting from trapping of the intermediate mercurical with acetate, or other side products, were not observed. The use of acetonitrile, rather than tetrahydrofuran, gave more reproducible yields of 4,5-dihydrooxazoles. Oxazole formation was detected by NMR within 0.5 h and the cyclization was usually complete within 3 h, except for the isoureas **1c** and **1d** which remained essentially unchanged in the presence of the mercuric salts. Isourea **1a** gave a 1.7:1 ratio of *cis* to *trans* 2-dimethylamino-4,5-dimethyl-4,5-dihydrooxazoles, while the cyclization of **1b** was non-stereoselective. In the cases of **1a** and **1b**, the formation of mercurio-4,5-dihyrooxazoles was monitored by ^{1}H-NMR, and, in separate runs, products were isolated after demercuration. In the ^{1}H-NMR spectrum of the initial cyclization product (mercurial), the H-5 resonance of the *trans* isomer and the H-4 resonance of the *cis* isomer overlapped. Complete assignments of the ^{1}H-NMR spectra of both isomers of **1a** were made by 2-D COSY analysis and NOE difference spectroscopy. The value of $J_{4,5}$ for the *cis* and *trans* isomers of **1a** were 8.2 and 7.1 Hz, respectively, while the values observed for the mercuriooxazoles were 7.6 and 6.1 Hz. The ratio of *cis* to *trans* isomers, observed initially while starting material was still present, remains constant throughout the reaction. In no case was any change in the initial isomer ratio observed, even after stirring isoureas **1a** and **1b** for prolonged periods (up to several days) in the presence of the mercuric salt, or after reduction with sodium borohydride. These results suggest that equilibration of reaction intermediates occurs neither under the conditions of cyclization nor during reduction, as has been suggested for other ring-forming reactions involving mercuric salts.[10] Our results for isoureas **1a** and **1b** differ from those reported for the mercuric ion-initiated cyclization of structurally related acylaminomethyl ethers,[11] which underwent cyclization to form *trans* oxazolidines stereoselectively. The selectivity observed was thought to result from kinetic control, and is consistent with other recent examples of amidomercuration.[12] In cyclic allylic 1,1-dimethylisoureas (**1f** and **1g**), a single diastereomer was produced during cyclization, as expected.

Cleavage of the 2-dimethylamino-4,5-dihydrooxazoles was attempted by several hydrolytic and reductive methods. Metal hydride reducing agents ($LiAlH_4$, $NaBH_4$, $LiEt_3BH$, DIBAL-H) either failed to react or gave complex mixtures of products. Hydrolysis with aqueous pyridine and *p*-toluenesulfonic acid, the method used for 2-trichloromethyl-dihydrooxazoles[3,13] was also unsuccessful. Basic hydrolysis of the dihydroxazoles to give vicinal amino alcohols was achieved with aqueous barium hydroxide, a reagent used by Kohn for the hydrolysis of imidazolidinones.[14] The application of this method to the hydrolysis of carbohydrate-derived dihydrooxazoles, was reported previously from our laboratory.[8] In a recent synthesis of the antibiotic lincomycin, hydrolysis of a 2-dimethylamino-4,5-dihydrooxazole was carried out with potassium hydroxide in ethylene glycol/ethanol.[9]

Thermal rearrangement of the 2-allyl-1,1-dimethylisoureas results in the transposition of oxygen and nitrogen functionality. This process, a [3,3]-sigmatropic rearrangement, was described in detail for the conversion of allylic trichloroacetimidates to the allylic amides by Overman, who also reported the thermal rearrangement of allylic and propargylic isoureas derived from *N*-cyanopyrrolidine.[1,2] In the course of our work on the electrophilic cyclization of allylic isoureas derived from dimethylcyanamide, we found that rearrangement of the 2-allyl-1,1-dimethylisoureas to trisubstituted ureas could be effected in refluxing xylene. The ureas prepared by this procedure are shown in table 3. Isoureas **1a** and **1b**, which are derived from secondary alcohols, gave *E*-allylic ureas, consistent with results reported by Overman for trichloroacetimidates. Isourea **1c** decomposed under the reaction conditions. The conversion of the allylic ureas to the corresponding amines was attempted by several reductive ($LiAlH_4$, $LiEt_3BH$, Ca/NH_3,[15] $NaBH_4$/pyridine[16]) and hydrolytic procedures. In most cases, unreacted starting material was recovered. The electrophilic cyclization of the allylic ureas was also investigated. This process generates an amino alcohol with different regiochemistry than that obtained by cyclization of the allylic isourea from which the urea is derived. Cyclization of the ureas in the presence of mercuric salts or iodine was not observed. Recently, Salazar described the cyclization of allylic ureas and isoureas using phenylselenenyl chloride in the presence of silica gel.[17] When 1-(2-hexenyl)-2,2-dimethylurea (**3b**) was subjected to these conditions, 2-dimethylamino-5-[1-phenylseleno)butanyl]-4,5-dihydrooxazole (**4**) was obtained in quantitative yield. Application of this method to the other trisubstituted ureas in this study remains to be demonstrated.



3b **4**

Scheme **B**

The electrophilic cyclization and thermal rearrangement reactions of 2-allyl-1,1-dimethylisoureas have now been investigated in a variety of cyclic and acyclic systems.

Table 1. 2-Allyl-1,1-dimethylisoureas **1** Prepared

Product	Time (h)	Yield (%)	Molecular Formula[a]	IR (film) ν(cm^{-1})	^{1}H-NMR ($CDCl_3$/TMS) δ, J(Hz)	^{13}C-NMR ($CDCl_3$) δ
1a	1.5	68	$C_7H_{14}N_2O$ (142.2)	3354 1628	1.35 (d, 3H, J = 6.38, CH_3), 2.88 (s, 6H, NMe_2), 4.73 (br s, 1H, NH), 5.12 (dt, 1H, J = 1.39, HC=), 5.24 (m, 2H, J = 5.3, 6.4, 2HC=), 5.98 (dq, 1H, J = 10.6, 17.5)	20.5, 37.1, 72.5, 114.6, 139.0, 160.5
1b	3	81	$C_9H_{18}N_2O$ (170.3)	3313 1627	0.93 (t, 3H, CH_3), 1.30–1.72 (m, 2H, CH_2), 2.88 (s, 6H, NMe_2), 4.60 (br s, 1H, NH), 5.13 (m, 1H, HC=), 5.19 (q, 1H, J = 5.8, 6.0, CH), 5.28 (m, 1H, HC=), 5.84 (m, 1H, HC=)	13.7, 18.1, 36.7, 36.9, 76.0, 115.1, 137.6, 160.4
1c	2	73	$C_{12}H_{16}N_2O$ (204.3)	3395 1651	2.89 (s, 6H, NMe_2), 5.20 (m, 1H, HC=), 5.29 (m, 1H, J = 6.0, PhCH), 5.39 (t, 1H, J = 1.4, 11, HC=), 6.06 (m, 1H, J = 5.0, 11.1, HC=), 7.30 (m, 5H, PhH)	40.5, 74.6, 114.9, 126.2, 127.5, 128.4, 140.1, 142.5, 160.5
1d	3	94	$C_{12}H_{16}N_2O$ (204.3)	3368 1623	2.90 (s, 6H, NMe_2), 4.77 (d, 2H, J = 5.8, CH_2), 6.36 (dt, 1H, J = 5.9, 16.0, HC=), 6.66 (d, 1H, J = 16.0, HC=), 7.48–7.17 (m, 5H, PhH)	36.6, 66.3, 124.0, 125.9, 127.2, 127.9, 131.9, 135.9, 160.3
1e	4	82	$C_9H_{18}N_2O$ (170.3)	3357 1624	0.92 (t, 3H, CH_3), 1.41 (m, 2H, CH_2), 2.05 (m, 4H, CH_2), 2.89 (s, 6H, NMe_2), 5.70 (m, 2H, 2HC=)	13.3, 21.8, 34.0, 36.8, 66.8, 124.7, 134.3, 160.4
1f	4	59	$C_9H_{16}N_2O$ (168.3)	3358 1626	2.17–2.50 (m, 6H, CH_2), 2.89 (s, 6H, NMe_2), 5.16 (br s, 1H, NH), 5.57–5.96 (m, 3H, OCH, 2HC=)	18.5, 24.4, 28.0, 36.5, 68.6, 126.3, 130.8, 160.1
1g	4	73	$C_{10}H_{18}N_2O$ (182.3)	3371 1623	1.26–2.45 (m, 8H, CH_2), 2.85 (s, 6H, NMe_2), 3.95 (br s, 1H, NH), 4.05 (m, 1H, OCH), 4.74 (m, 1H, HC=), 4.90 (m, 1H, HC=)	23.2, 27.5, 33.4, 33.5, 37.0, 71.2, 104.8, 147.5, 160.3

[a] Satisfactory HRMS obtained: m/z ±0.0017 ($M^+ + 1$).

Table 2. 2-Dimethylamino-4,5-dihydrooxazoles **2** Prepared

Product	Yield (%)	*cis/trans*	Molecular Formula	IR (film) ν(cm^{-1})	^{1}H-NMR ($CDCl_3$/TMS) δ, J(Hz)	^{13}C-NMR ($CDCl_3$) δ
2a	50	1.7 : 1	$C_7H_{14}N_2O$ (142.2)	1657	(*cis* isomer) 1.10 (d, 3H, J = 6.8, CH_3), 1.24 (d, 3H, J = 6.6, CH_3), 2.88 (s, 6H, NMe_2), 4.03 (m, 1H, J = 8.2, CH), 4.67 (m, 1H, CH) (*trans* isomer) 1.20 (d, 3H, J = 6.5, CH_3), 1.34 (d, 3H, J = 6.2, CH_3), 2.88 (s, 6H, NMe_2), 3.58 (m, 1H, J = 7.1, CH), 4.08 (m, 1H, CH)	(*cis* isomer) 14.6, 16.0, 37.8, 58.9, 81.0, 160.7, (*trans* isomer) 19.4, 20.8, 37.7, 64.7, 84.9, 160.7
2b	78	1 : 1	$C_9H_{18}N_2O$ (170.3)	1661	(*cis* isomer) 0.94 (t, 3H, CH_3), 1.09 (d, 3H, J = 6.8, CH_3), 1.42 (m, 2H, CH_2), 1.57 (m, 2H, CH_2), 2.89 (s, 6H, NMe_2), 4.04 (m, 1H, $J_{4,5}$ = 8.8, H-4), 4.50 (m, 1H, H-5) (*trans* isomer) 0.98 (t, 3H, CH_3), 1.20 (d, 3H, J = 6.5, CH_3), 1.48 (m, 2H, CH_2), 1.64 (m, 2H, CH_2), 2.89 (s, 6H, NMe_2), 3.67 (m, 1H, $J_{4,5}$ = 8.3, H-4), 4.07 (m, 1H, H-5)	(*cis* isomer) 13.8, 18.6, 22.2, 36.6, 60.9, 83.5, 161.0, (*trans* isomer) 16.6, 19.8, 31.3, 37.3, 65.0, 87.5, 161.3
2e	48		$C_9H_{18}N_2O$ (170.3)	1666	0.90 (t, 3H, CH_3), 1.2–2.0 (m, 6H, CH_2), 2.91 (s, 6H, NMe_2), 3.85 (dd, 1H, H-5), 3.94 (m, 1H, $J_{4,5}$ = 7.6, $J_{4,5'}$ = 7.1, H-4), 4.34 (dd, 1H, H-5)	13.8, 22.5, 27.8, 36.4, 37.4, 64.4, 73.2, 161.2
2f	53	1 : 0	$C_9H_{16}N_2O$ (168.3)	1647	1.2–2.1 (m, 8H, CH_2), 2.90 (s, 6H, NMe_2), 3.79 (q, 1H, $J_{4,5}$ = 7.2, H-4), 4.48 (m, 1H, H-5)	19.5, 20.0, 26.4, 29.1, 37.3, 61.2, 79.2, 162.2
2g	83	1 : 0	$C_{10}H_{18}N_2O$ (182.3)	1650	1.1–2.3 (m, 8H, CH_2), 1.32 (d, 3H, CH_3), 3.00 (s, 6H, NMe_2), 4.20 (t, 1H, H-5)	18.9, 19.8, 25.3, 25.5, 35.2, 37.8, 62.9, 86.1, 160.6

[a] Satisfactory HRMS obtained: m/z ±0.0020 ($M^+ + 1$).

Cyclization of the isoureas in the presence of mercuric acetate in acetonitrile, followed by reduction with sodium borohydride gives substituted 2-dimethylamino-4,5-dihydrooxazoles. The thermal rearrangement of the 2-allyl-1,1-dimethylisoureas **1** gives trisubstituted allylic ureas. Regioisomeric dihydrooxazoles can be obtained from the ureas by selenium-promoted cyclization, as demonstrated for one of the allylic ureas. Further development of this methodology is in progress.

Melting points were determined on a Thomas-Hoover apparatus and they are uncorrected. IR spectra were recorded on an Analect FX-6160 spectrophotometer. Only the strongest and structurally most significant peaks are reported. ^{1}H-NMR spectra and ^{13}C-NMR spectra were recorded on a Varian XL-200 spectrometer at 200 and 50.3 MHz, respectively. Chemical shifts were recorded relative to TMS for ^{1}H resonances and $CDCl_3$ (δ = 76.9) for ^{13}C resonances. NOE difference spectroscopy was performed in CD_3CN without degassing. Selective multiplet excitation was achieved using Varian's DOCYCL for decoupler-offset cycling, with a 40 ms. tau and an 8 s saturation time. All 2D-NMR experiments were performed in the magnitude mode using pseudo-Gaussian spin-echo filtration in t_1 and t_2. Generally, COSY and HETCOR spectra were obtained using 512^2 matrix sizes with 156 increments in t_1. Mass spectra were recorded at the University of Pennsylvania on a VG-7070H spectrometer, under CI conditions with ether ammonia or isobutane. Me_2NCN was purchased from Aldrich Chemical Co. and used without further purification.

2-Allyl-1,1-dimethylisoureas 1; General Procedure:

A solution of the corresponding allylic alcohol (25.0 mmol) and Me_2NCN (1.75 g, 25.0 mmol) is stirred under N_2 at r.t.. NaH (100 mg of a 60% oil dispersion, 2.5 mmol) is added in portions and the resulting mixture is stirred for 3 h. CH_2Cl_2 (30 mL) is added and the mixture is washed with H_2O (3 × 30 mL). The organic phase is washed with sat. NaCl solution (30 mL), dried ($MgSO_4$), and evaporated to give **1** as a yellow oil.

Table 3. Trisubstituted Ureas **3** Prepared

Product	Yield (%)	Molecular Formula	IR (film) ν(cm^{-1})	^{1}H-NMR ($CDCl_3$/TMS) δ, J(Hz)	^{13}C-NMR ($CDCl_3$) δ
(*E*)-**3a**	71	$C_7H_{14}N_2O$[a] (142.2)	1634	1.67 (m, 3H, CH_3), 2.89 (s, 6H, NMe_2), 3.81 (t, 2H, CH_2), 4.31 (br s, 1H, NH), 5.47 (m, 1H, HC=), 5.61 (m, 1H, J = 14.8, HC=)	17.5, 36.0, 42.7, 127.2, 128.3, 158.1
(*E*)-**3b**	90	$C_9H_{18}N_2O$[b] (170.3)	1637	0.89 (t, 3H, CH_3), 1.41 (m, 2H, CH_2), 2.01 (m, 2H, CH_2), 2.90 (s, 6H, NMe_2), 3.80 (t, 2H, CH_2), 4.32 (br s, 1H, NH), 5.42–5.50 (m, 1H, J = 5.7, HC=), 5.53–5.68 (m, 1H, J = 15.4, 6.1, HC=)	13.4, 22.0, 34.0, 35.9, 42.7, 127.1, 132.2, 158.1
3d	42	$C_{12}H_{16}N_2O$[b] (204.3)	1633	2.85 (s, 6H, NMe_2), 4.58 (bs, 1H, NH), 5.09–5.22 (m, 2H, HC=), 5.46 (m, 1H, CH), 6.0 (m, 1H, HC=)	35.9, 56.2, 115.0, 126.9, 128.3, 138.5, 141.6, 157.2
3e	60	$C_9H_{18}N_2O$[a] (170.3)	1645	0.92 (t, 3H, CH_3), 1.21–1.70 (m, 4H, CH_2), 2.91 (s, 6H, NMe_2), 4.37 (m, 1H, J = 5.4, HC–C=), 5.19 (m, 2H, HC=), 5.74 (m, 1H, HC=)	13.7, 18.8, 36.0, 37.4, 52.2, 113.7, 139.8, 157.6
3f	30	$C_9H_{16}N_2O$[a] (168.3)	1631	1.25–2.18 (m, 6H, CH_2), 2.90 (s, 6H, NMe_2), 4.00 (br s, 1H, NH), 4.09–5.00 (m, 1H, HC=), 5.57–5.98 (m, 2H, HC=, HCN–)	19.6, 24.8, 30.1, 36.0, 70.4, 128.8, 130.1, 157.6
3g	53	$C_{10}H_{18}N_2O$[a] (182.3)	1638	0.80–2.32 (m, 8H, CH_2), 2.85 (s, 6H, NMe_2), 2.90 (m, 2H, CH_2), 4.78 (m, 1H, HC=)	22.9, 26.4, 36.4, 45.5, 120.0, 134.8, 157.8

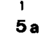
[a] Satisfactory microanalysis obtained: C ±0.40, H ±0.30.

[b] Satisfactory HRMS obtained: m/z ±0.0020 (M^+ + 1).

Table 4. NMR Data for the Mercurio-4,5-dihydrooxazole **5a**[a] Prepared from **1a**

Compound	^{1}H-NMR (CD_3CN) δ, J(Hz)	^{13}C-NMR (CD_3CN) δ
5a *cis/trans*-mixture	(*cis* isomer) 1.39 (d, 3H, J = 6.6, CH_3), 1.86 (s, 3H, CH_3CO), 1.87 (dd, 1H, J = 12.0, 9.4, H-7), 2.05 (dd, 1H, J = 12.0, 5.7, H-7'), 3.01 (3, 6H, NMe_2), 4.45 (m, 1H, $J_{4,5}$ = 7.6, H-4), 4.92 (m, 1H, H-5) (*trans* isomer) 1.38 (d, 3H, J = 6.2, CH_3), 1.76 (dd, 1H, J = 11.6, 7.7, H-7), 1.80 (dd, 1H, J = 11.6, 5.2, H-7'), 1.86 (s, 3H, CH_3CO), 2.98 (s, 6H, NMe_2), 4.02 (m, 1H, $J_{4,5}$ = 6.1, H-4), 4.41 (m, 1H, H-5)	(*cis* isomer) 14.4 (CH_3), 23.7 (CH_3CO), 24.5 (CH_2), 38.4 (NMe_2), 63.0 (C-4), 87.7 (C-5), 162.8 (C-2), 176.5 (C=O) (*trans* isomer) 19.6 (CH_3), 23.7 (CH_3CO), 30.3 (CH_2), 38.3 (NMe_2), 68.5 (C-4), 83.9 (C-5), 162.3 (C-2), 176.5 (C=O)

[a] Protons assigned accordingly to the numbering:



5a

2-Dimethylamino-4,5-dihydrooxazoles 2; General Procedure:
A mixture of the allylic isourea **1** (2.9 mmol), anhydrous MeCN (3.0 mL), and mercuric acetate (0.92 g, 2.9 mmol) is stirred at r.t. under N_2 for 3 h. The mixture is cooled to 0 °C in a ice bath and made basic by the addition of 3 N NaOH (1 mL). A 3 N solution of $NaBH_4$ in NaOH (0.5 mL) is added slowly and the reaction is stirred for 0.5 h. The deposited mercury is removed by centrifugation, and the supernatant is decanted and evaporated to an oil. The crude product is dissolved in CH_2Cl_2 (25 mL) and the solution is washed with H_2O (3 x 25 mL) and sat. aq NaCl solution (25 mL), dried ($MgSO_4$), and evaporated to give **2** as a pale yellow oil.

Trisubstituted Ureas 3; General Procedure:
A solution of the allylic isourea **2** (5.9 mmol) in xylene (30 mL) is boiled and stirred under reflux (137 °C) for 24 h. Solvent is evaporated and the crude product is dissolved in CH_2Cl_2 (50 mL) and the solution is washed with H_2O (3 x 25 mL) and sat. aq NaCl (25 mL), dried ($MgSO_4$), and evaporated to give **3**. Urea **3a** is obtained as a crystalline solid; ureas **3b–g** as yellow oils. For further purification, the urea is dissolved in CH_2Cl_2 and filtered through a pad of silica gel in a scintered glass funnel. Analytically pure products are obtained by flash chromatography using EtOAc as the eluant.

NMR Studies of 4,5-Dihydrooxazole Formation; Typical Procedure:
A solution of the isourea **1a** (0.100 g, 0.7 mmol) and mercuric acetate (0.233 g, 0.7 mmol) in CD_3CN (1.0 mL of 100.0 atom % D, Aldrich) was prepared in an NMR tube and ^1H spectra were recorded at 22 °C at the following intervals: 15 min, 45 min, 2 h, 3 h, 26 h, and 97 h. NMR data are shown in Table 4 for the mercuriooxazole derivative **5a** prepared from **1a**.

Cyclization of Urea 3b with Phenylselenenyl Chloride:
A mixture of urea **3b** (0.175 g, 1.03 mmol), phenylselenenyl chloride (0.306 g, 1.65 mmol), and silica gel 60 (2.00 g) in $CHCl_3$ (35 mL) is stirred at r.t. under N_2 for 68 h. Sat. aq Na_2CO_3 (20 mL) is added to the mixture which is then extracted with CH_2Cl_2 (3 x 60 mL). The combined organic extracts are washed with H_2O (2 x 60 mL) and sat. aq NaCl (60 mL), dried ($MgSO_4$), and evaporated under reduced pressure to give 0.29 g (95 %) of **4** as a thick syrup.

HRMS: (m/z), $C_{13}H_{18}SeN_2O$, calc.: 299.0662 ($M^+ + 1$); found: 299.0606 ($M^+ + 1$)

^1H-NMR ($CDCl_3$/TMS): $\delta = 1.46$ (d, 3 H, CH_3), 2.84 (s, 6 H, NMe_2), 3.29 (m, 1 H, $J = 7$ Hz, $\underline{H}CCH_3$), 3.61 (m, 1 H, $J = 6.9$, 10.1 Hz, H-4), 3.89 (m, 1 H, $J = 8.82$, 6.9 Hz, H-4'), 4.57 (m, 1 H, $J = 8.8$, 5.4 Hz, H-5).

^{13}C-NMR ($CDCl_3$/TMS): $\delta = 17.9$, 37.3, 42.7, 57.4, 83.8, 127.9, 128.9, 129.0, 135.6, 161.7.

The authors thank Research Corporation, the National Institutes of Health, and Villanova University of financial support of this research.

Received: 9 April 1990; revised: 18 July 1990

(1) Cardillo, G.; Orena, M. *Tetrahedron* **1990**, *46*, 3321.
Cardillo, G.; Orena, M. Sandri, S. *J. Chem. Soc., Chem. Commun.* **1983**, 1489.
Overman, L. *Acc. Chem. Res.* **1980**, *13*, 218.
Overman, L. *J. Am. Chem. Soc.* **1976**, *98*, 2901.

(2) Overman, L.; Tsuboi, S.; Roos, J.P.; Taylor, G.F. *J. Am. Chem. Soc.* **1980**, *102*, 747.
Tsuboi, S.; Stromquist, P.; Overman, L. *Tetrahedron Lett.* **1976**, 1145.

(3) Fraser-Reid, B.; Pauls, H.W. *J. Org. Chem.* **1983**, *48*, 1392.
Bognini, A.; Cardillo, G.; Orena, M.; Sandri, S.; Tomasini, C. *Tetrahedron* **1983**, *39*, 3801.

(4) Overman, L. *Tetrahedron Lett.* **1975**, 1149.

(5) Lauer, W.M.; Benton, C.S. *J. Org. Chem.* **1959**, *24*, 804.
Hussein, F.A.; Kazandji, S.Y. *J. Indian. Chem. Soc.* **1966**, *43*, 663.

(6) Sandler, S.R.; Karo, W. *Organic Functional Group Preparations*, Vol. 3, Academic Press, New York, NY. 1972, pp. 268–320, Vol. 2, 1971, pp. 166–185.

(7) Giuliano, R.M.; Deisenroth, T.W.; Frank, W.C. *J. Org. Chem.* **1986**, *51*, 2304.

(8) Giuliano, R.M.; Deisenroth, T.W. *Carbohydr. Res.* **1986**, *158*, 249.

(9) Knapp, S.; Kukkola, P. *J. Org. Chem.* **1990**, *55*, 1632.

(10) Bartlett, P.A., in: *Asymmetric Synthesis*, Vol 3, Morrison, J.D., (ed.), Academic Press, Orlando, 1984, pp. 411–454.

(11) Harding, K.E.; Stephens, R.; Hollingsworth, D.R. *Tetrahedron Lett.* **1984**, *25*, 4631.

(12) Harding, K.E.; Marman, T.H.; Nam, D. *Tetrahedron Lett.* **1988**, *29*, 1627;
Takacs, J.M.; Helle, M.A.; Yang, L. *Tetrahedron Lett.* **1989**, *30*, 1770.

(13) Gent, P.A.; Gigg, R. *J. Chem. Soc., Perkin Trans. 1* **1972**, 2748.

(14) Jung, S.-H.; Kohn, H. *J. Am. Chem. Soc.* **1985**, *107*, 2481.

(15) Mills, J.S.; Ringold, H.J.; Djerassi, C. *J. Am. Chem. Soc* **1958**, *80*, 6118.

(16) Kikugawa, Y.; Yamada, S. *Tetrahedron Lett.* **1969**, 699.

(17) Betancor, C.; Leon, E.; Prange, T.; Salazar, J.; Suarez, E *J. Chem. Soc., Chem. Commun.* **1989**, 450.
Freire, R.; Leon, E.I.; Salazar, J.A.; Suarez, E. *J. Chem. Soc. Chem. Commun.* **1989**, 452.