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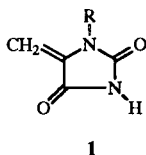
2-Propynamides react with aryl isocyanates in the presence of triethylamine to give 5-methylene-2,4-imidazolidinediones **5** in good yields. If the propynamide contains a terminal trimethylsilyl group, *Z*-trimethylsilylidenehydantoin (**7**) is produced.

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In recent publications we have reported the preparation of 2-propynamides [1] and the generation and reaction of dianions derived from them [2]. In this paper we wish to describe further chemistry associated with 2-propynamides targeted at the synthesis of molecules with potential biological interest.

The formation of the 3-isothiazolone nucleus has been accomplished by reaction of propiolamides with hydrogen thiocyanate [3,4]. Since the chemistry of acetylenic amides has not been thoroughly explored, we undertook an investigation into the formation of heterocyclic systems utilizing these amides as building blocks.

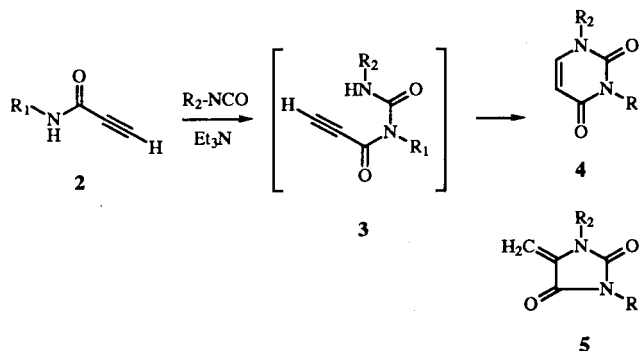
It has been reported that 5-methylene-2,4-imidazolidinediones **1** exhibit a variety of pharmacological profiles including fungicidal, herbicidal, and bacteriocidal activities [5,6].



It was rationalized that these compounds may be easily synthesized by the reaction of 2-propynamides with isocyanates (Scheme 1). In the presence of an organic base, initial reaction should be at the amido functionality to produce intermediate **3**. Cyclization with the acetylene might then occur either at the terminal carbon to produce uracil **4** or at the internal carbon to give the 5-methylenehydantoin **5**. Both modes of cyclization are favored according to Baldwin's Rules [7]. A 6-*Endo*-Dig ring closure would produce **4** whereas a 5-*Exo*-Dig closure would give **5**.

When equimolar quantities of *N*-benzyl-2-propynamide (**2**,  $R_1 = \text{CH}_2\text{C}_6\text{H}_5$ ), phenyl isocyanate, and triethylamine [8] are stirred at room temperature for 18 hours, a single cyclic adduct forms in 82% yield. In the  $^1\text{H}$ -nmr spectrum the olefinic protons are seen as two sets of doublets at  $\delta$  5.45 and 4.85 with coupling constants of 2 Hz each. The magnitude of the *J* value is indicative of geminal-type

Scheme 1

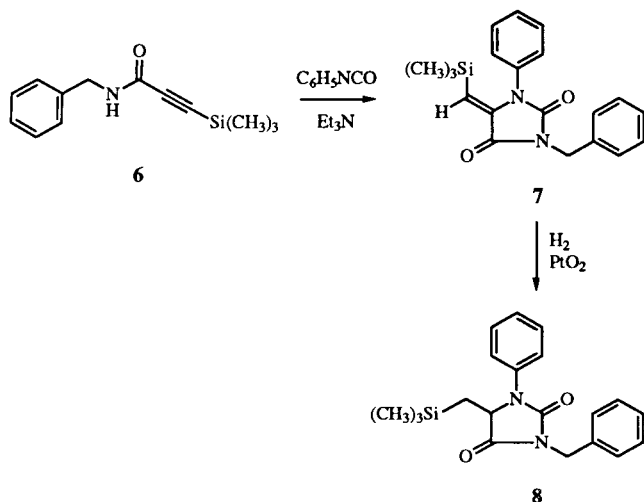


coupling which supports structure **5**. Typical coupling constants for uracil derivatives **4** range from 7.5-8.0 Hz [9] and proton shifts are further downfield than that observed for **5**. Final proof for structure **5** was provided by analysis of the  $^{13}\text{C}$ -nmr spectrum. The carbonyl groups at position 4 and 2 were observed at  $\delta$  162.2 and 155.0 respectively while the carbon at position 5 in the hydantoin nucleus fell at  $\delta$  137.1 and the methylene carbon at  $\delta$  96.0. The coupled spectrum showed the signal at  $\delta$  96.0 as a triplet. Splitting of this type would be expected for an exomethylene functionality whereas a uracil derivative should produce two doublets.

The formation of **5** appears to be general with the use of aryl isocyanates, however, when alkyl isocyanates are used, the reaction takes a different course. The increased basicity of the nitrogen bearing the alkyl group causes intermolecular interactions to occur resulting in the formation of polymers.

For example, the reaction of equimolar amounts of *N*-benzyl-2-propynamide (**2a**,  $R_1 = \text{CH}_2\text{C}_6\text{H}_5$ ), methyl isocyanate, and triethylamine in tetrahydrofuran at room temperature for 24 hours resulted in the formation of a glasslike polymer (53% yield) whose molecular weight was determined to be 1080. A similar reaction with *N*-methyl-2-propynamide (**2b**,  $R = \text{CH}_3$ ) and methyl isocyanate produced a crystalline polymer (79% yield) while **2a** and ethyl isocyanatoacetate afforded a flexible plastic-like polymer (35% yield), probably due to the crosslink-

Scheme 2

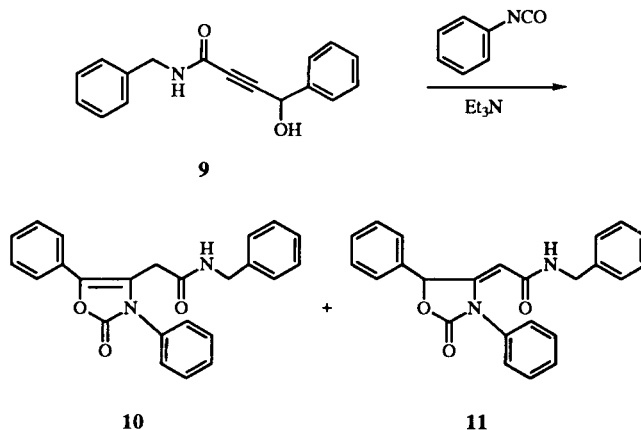


ing effect of the ester group. Molecular weights for the last two polymers were not determined due to their insolubility in appropriate solvents.

The scope of the reaction between 2-propynamides and aryl isocyanates was extended to include propynamides which were substituted at the terminal carbon of the acetylene. Our initial investigations were performed with the silicon-substituted propynamide **6** which was easily prepared by reaction of the lithium dianion of **2a** with chlorotrimethylsilane [2]. When **6** was allowed to react with stoichiometric amounts of phenyl isocyanate and triethylamine, the silyl-substituted hydantoin **7** was isolated in 68% yield (Scheme 2).

The stereochemistry of the olefin was determined to be

Scheme 3



the *Z*-isomer as shown. In the  $^1\text{H}$ -nmr spectrum the position of the trimethylsilyl protons, which are observed at  $-0.3$  ppm, is consistent with the proposed structure because the methyl groups would be forced into the shielding cone of the adjacent phenyl group thereby causing these protons to appear upfield from tetramethylsilane. Catalytic hydrogenation of **7** in the presence of platinum oxide cleanly reduced the double bond and **8** was isolated in nearly quantitative yield.

The reaction was further extended to include alcohols such as **9** where a possible competitive reaction of the isocyanate with either the hydroxyl or amido function may occur. When the reaction of **9** and phenyl isocyanate was carried out as in the previously described examples, two products **10** and **11** were formed (Scheme 3). The struc-

Table 1  
Reaction of Propiolamide **2** with Isocyanates

No.	$\text{R}_2$	$\text{R}_1$	Yield, %	Mp, $^\circ\text{C}$	Formula	Analysis		
						%C	Calcd. (Found) %H	%N
<b>5a</b>			82	64-67	$\text{C}_{17}\text{H}_{14}\text{N}_2\text{O}_2$	73.4 (73.2)	5.1 (5.5)	10.1 (10.0)
<b>5b</b>		$\text{CH}_3$	67	153-156	$\text{C}_{11}\text{H}_{10}\text{N}_2\text{O}_2$	65.3 (65.3)	5.0 (5.0)	13.9 (13.8)
<b>5c</b>			55	[a]	$\text{C}_{16}\text{H}_{12}\text{N}_2\text{O}_2$	72.7 (72.6)	4.6 (4.3)	10.6 (10.1) [b]
<b>5d</b>			60	80-83	$\text{C}_{18}\text{H}_{13}\text{F}_3\text{N}_2\text{O}_2$	62.4 (62.8)	3.8 (3.9)	8.1 (7.9)
<b>5e</b>		$\text{CH}_3$	40	[c]	$\text{C}_{12}\text{H}_9\text{F}_3\text{N}_2\text{O}_2$	53.3 (53.2)	3.4 (3.6)	10.4 (10.1)
<b>5f</b>			70	[d]	$\text{C}_{17}\text{H}_{13}\text{ClN}_2\text{O}_2$	no analysis [e]		
<b>5g</b>			71	[c]	$\text{C}_{18}\text{H}_{16}\text{N}_2\text{O}_3$	70.2 (69.9)	5.2 (5.1)	9.1 (8.9)

[a] Glass-like material. [b] Reanalysis of nitrogen did not improve the value. [c] A viscous, rubbery oil. [d] A tacky foam. [e] Ir (chloroform): 1780, 1730, 1665  $\text{cm}^{-1}$ ,  $^1\text{H}$ -nmr (deuteriochloroform):  $\delta$  7.6-7.0 (m, 9H), 5.45 (d,  $J = 2$  Hz, 1H), 4.8 (d,  $J = 2$  Hz, 1H), 4.75 (s, 2H); ms: (70 eV)  $m/z$  312 ( $\text{M}^+$ ).

ture of the major product **10** was determined by the following evidence: The carbonyl region of the ir spectrum closely resembles that of a 2-oxazolinone [10]. In the  $^1\text{H}$ -nmr spectrum, signals are observed at  $\delta$  4.3 (doublet, benzylic methylene) and  $\delta$  3.35 (singlet,  $\text{CH}_2\text{C}=\text{O}$ ) which is consistent with the proposed structure. Additional corroboration is supplied by its  $^{13}\text{C}$ -nmr spectrum (see Table 2). Analysis of the coupled spectrum reveals that carbons numbered 8 and 9 appear as triplets with coupling constants of approximately 130 Hz which confirms the hybridization of these carbons.

The fact that an N-H absorption is observed at  $3310\text{ cm}^{-1}$  in the ir spectrum and the benzyl methylene protons exist as a doublet (which collapses to a singlet upon deuterium exchange) in the  $^1\text{H}$ -nmr spectrum indicates that the isocyanate preferentially reacts with the hydroxyl group of **9** rather than the amide.

The minor product isolated from the mixture is assumed to be **11** based on chemical precedent for the formation of 4-methylene-2-oxazolidinones in reactions of ethynyl alcohols with aryl isocyanates [10,11,13-15]. The carbonyl region of its ir spectrum closely resembles that of 4-methylene-2-oxazolidinones [11,12] and in the  $^1\text{H}$ -nmr spectrum three doublets are observed. The signal at  $\delta$  3.85 suggests that the integrity of the  $\text{NHCH}_2\text{C}_6\text{H}_5$  remains intact and that initial reaction had taken place on oxygen. The remaining two doublets at  $\delta$  6.0 and 4.9 compare favorably with shifts reported for 4-methylene-2-oxazolidinone analogs [13].

The  $^{13}\text{C}$ -nmr data (Table 2) also support structure **11** due to the highfield shift of the enamine-type carbon at 97.0 ppm. In addition, the protonated carbons numbered 6 and 9 exist, as expected, as doublets ( $J = 160\text{ Hz}$ ) in the coupled spectrum.

The observance of **11** as the minor product in the reac-

tion mixture suggest that **11** probably was the initially formed product and that subsequent isomerization to **10** occurred. Assuming, after initial reaction of the isocyanate with the hydroxyl group of **9**, cyclization with the acetylene occurred with *trans*-addition of hydrogen (analogous to **7**) the stereochemistry of the olefin in **11** would be the *Z*-isomer as shown.

Table 3

 $^1\text{H}$ -NMR Spectral Data for 5-Methylene-2,4-imidazolidinediones **5**

No.	$^1\text{H}$ -NMR Spectrum (ppm, deuteriochloroform)
<b>5a</b>	7.50-7.05 (m, 10H), 5.45 (d, 1H), 4.85 (d, 1H), 4.79 (s, 2H)
<b>5b</b>	7.50-7.10 (m, 5H), 5.38 (d, 1H), 4.77 (d, 1H), 3.10 (s, 3H)
<b>5c</b>	7.59-7.28 (m, 10H), 5.53 (d, 1H), 4.88 (d, 1H)
<b>5d</b>	7.75-7.20 (m, 9H), 5.55 (d, 1H), 4.90 (d, 1H), 4.80 (s, 2H)
<b>5e</b>	7.78-7.40 (m, 4H), 5.54 (d, 1H), 4.86 (d, 1H), 3.23 (s, 3H)
<b>5f</b>	7.58-7.28 (m, 9H), 5.53 (d, 1H), 4.81 (d, 1H), 4.76 (s, 2H)
<b>5g</b>	7.53-6.82 (m, 9H), 5.40 (d, 1H), 4.73 (s, 2H), 4.72 (d, 1H), 3.80 (s, 3H)

## EXPERIMENTAL

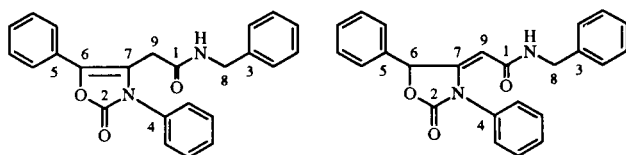
Melting points were determined on a Thomas-Hoover Unimelt apparatus and are uncorrected. The infrared spectra were recorded on an Analect FX-6200 spectrometer. Absorption frequencies are quoted in reciprocal centimeters. Nuclear magnetic resonance spectra were recorded on Jeol FX-90Q and Jeol FX-200 spectrometers using tetramethylsilane as an internal reference. Chemical shifts are quoted in parts per million (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet). The carbon-13 magnetic resonance spectra were obtained in the Fourier transform mode on a Jeol FX-200 spectrometer operating at carbon resonance frequencies of 50.1 MHz. Sample concentrations were approximately 0.1M in deuterated solvent and were placed in 5 mm (od) sample tubes. Acquisition parameters used were: 220 ppm spectral width, a pulse width corresponding to a  $45^\circ$  pulse angle (3 msec), 1.8 second pulse repetition time, and 16K time-domain points. The mass spectra were determined on an LKB 9000 or Finnegan 4600 spectrometers either in EI or CI modes. Molecular weight determination for polymers were performed by vapor pressure techniques on a Mechrolab 301A osmometer and the values are  $\pm 5\%$ .

Unless otherwise stated, all solutions of organic compounds were washed with saturated sodium chloride solution then were dried over sodium sulfate. No attempt has been made to optimize the yields of the described reactions.

General Procedure for the Preparation of 5-Methylene-2,4-imidazolidinediones **5** (Table 1).

To a solution of 0.025 mole of the 2-propynamide **1** and 0.025 mole of the appropriate isocyanate in 40 ml of dry tetrahydrofuran was added 2.5 g (0.025 mole) of triethylamine. In some cases, cooling may be necessary since the initial reaction is fairly exothermic. The mixture was then stirred at room temperature for 18 hours. The solvent was removed under reduced pressure and the residue was chromatographed on a column of

Table 2

 $^{13}\text{C}$ -Nmr Shift Data for Compounds **10** and **11**

Carbon No.	<b>10</b>	<b>11</b>
1	167.4	162.6
2	153.6	155.6
3	138.4	139.4*
4	137.1	137.3*
5	133.1*	136.4*
6	127.1*	79.8
7	118.1*	144.7
8	43.4	41.9
9	31.3	97.0

silica gel using chloroform to elute the product **5**. Solid products were usually crystallized from ether/pentane.

### 3-Benzyl-1-phenyl-5-trimethylsilylidenehydantoin (**7**).

A mixture of 2.7 g (0.0116 mole) of **6** [1], 1.4 g (0.012 mole) of phenyl isocyanate, and 1.5 g (0.0148 mole) of triethylamine in 50 ml of dry tetrahydrofuran was stirred at room temperature for 18 hours. The solvent was removed under reduced pressure and the residue was chromatographed on a column of silica gel using chloroform to elute the product, 2.8 g (68%) of **7**. An analytical sample was crystallized from methylene chloride/ether, mp 157-159°; ir (potassium bromide): 1765, 1710, 1625 cm<sup>-1</sup>; <sup>1</sup>H-nmr (deuteriochloroform): δ 7.6-7.2 (m, 10H), 5.9 (s, 1H), 4.75 (s, 2H), -0.3 (s, 9H); ms: (70 eV) m/z 350 (M<sup>+</sup>).

*Anal.* Calcd. for C<sub>20</sub>H<sub>22</sub>N<sub>2</sub>O<sub>2</sub>Si: C, 68.5; H, 6.3; N, 8.0. Found: C, 68.4; H, 6.6; N, 8.1.

### 3-Benzyl-1-phenyl-5-trimethylsilylmethylhydantoin (**8**).

A solution of 0.75 g (2.14 mmoles) of **7** in 50 ml of ethyl acetate was hydrogenated at 3.5 atm over 0.15 g of platinum oxide. After 24 hours the uptake of hydrogen ceased and the catalyst was filtered from the reaction mixture. The solvent was removed under reduced pressure to yield pure **8**, 0.75 g (99%). An analytical sample was crystallized from ether/pentane, mp 140-142°; ir (chloroform): 1770, 1710 cm<sup>-1</sup>; <sup>1</sup>H-nmr (deuteriochloroform): δ 7.6-7.1 (m, 10H), 4.7 (s, 2H), 4.65 (m, 1H), 1.15 (m, 2H), -0.05 (s, 9H).

*Anal.* Calcd. for C<sub>20</sub>H<sub>24</sub>N<sub>2</sub>O<sub>2</sub>Si: C, 68.1; H, 6.9; N, 7.9. Found: C, 67.8; H, 7.1; N, 7.9.

### 2,3-Dihydro-2-oxo-3,5-diphenyl-*N*-(phenylmethyl)-5-oxazoleacetamide (**10**).

A mixture of 4.6 g (0.017 mole) of **9** [1], 2.1 g (0.0176 mole) of phenyl isocyanate, and 1.7 g (0.0168 mole) of triethylamine in 80 ml of dry tetrahydrofuran was stirred at room temperature for 18 hours. The solvent was removed under reduced pressure and the resulting solid was crystallized from methylene chloride/ether to give 2.1 g (31%) of **10**, mp 205-207°; ir (potassium bromide): 3310, 1750, 1640 cm<sup>-1</sup>; <sup>1</sup>H-nmr (deuteriochloroform): δ 7.65-6.95 (m, 15H), 6.3 (m, 1H, NH), 4.3 (d, J = 6 Hz, 2H), 3.35 (s, 2H); ms: (70 eV) m/z 384 (M<sup>+</sup>).

*Anal.* Calcd. for C<sub>24</sub>H<sub>20</sub>N<sub>2</sub>O<sub>3</sub>: C, 75.0; H, 5.3; N, 7.3. Found: C, 75.4; H, 5.6; N, 6.9.

### *N*-(Phenylmethyl)-2-(2-oxo-3,5-diphenyloxazolidin-4-ylidene)acetamide (**11**).

The second fraction obtained from the crystallization of **10** furnished 0.4 g (6%) of **11**, mp 204-205°; ir (chloroform): 3430, 1785, 1680, 1650 cm<sup>-1</sup>; <sup>1</sup>H-nmr (deuteriochloroform): δ 7.7-6.9 (m, 15H), 6.0 (d, J = 1.8 Hz, 1H), 5.3 (m, 1H), 4.9 (d, J = 1.8 Hz, 1H), 3.85 (d, J = 6 Hz, 2H); ms: (70 eV) m/z 384 (M<sup>+</sup>).

*Anal.* Calcd. for C<sub>24</sub>H<sub>20</sub>N<sub>2</sub>O<sub>3</sub>: C, 75.0; H, 5.3; N, 7.3. Found: C, 75.3; H, 5.7; N, 7.3.

The mother liquor from the crystallization still contained appreciable amounts of **10** and **11**.

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