Base-Catalyzed Cyclization of *N*-Propargylamides to Oxazoles

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The base-catalyzed cyclization of some *N*-propargylamides to oxazoles has been studied in the presence of sodium hydride and potassium carbonate. The α-arylsubstituted propargylamides **1c-d** (Ar = *p*-$OMeC_6H_4$ (**1c**), C_6H_5 (**1d**), and *p*-$O_2NC_6H_4$ (**1e**)) cyclized with markedly higher rates (**1e** > **1d** > **1c**) than the unsubstituted and α-methyl substituted propargylamides **1a** and **1b**. A ^1H nmr spectroscopic experiment demonstrated the presence of an allenic intermediate in the potassium carbonate-catalyzed ring closure of **1e**. The observed rank order of reactivities correlates well with the acidities of the respective propargylic hydrogens of the amides and with the ability of the ring closed intermediates to stabilize an oxazole anion. The results demonstrate that the base-catalyzed formation of oxazoles from propargylamides may proceed *via* an allenic intermediate.

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Introduction.

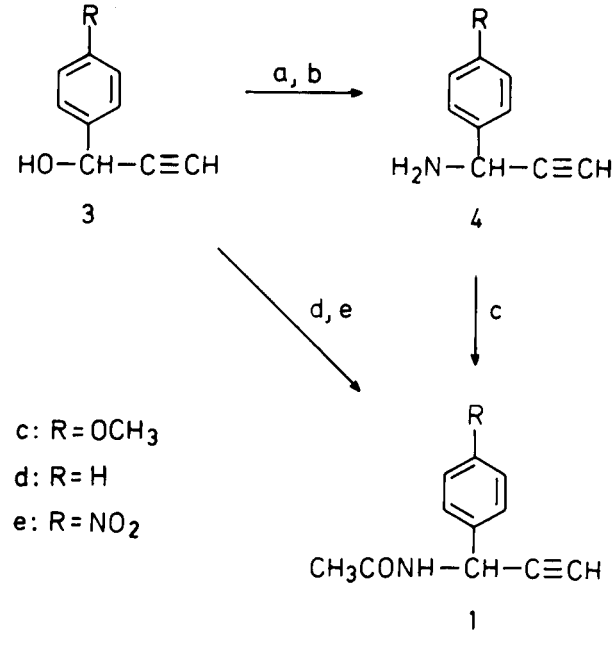
In connection with a pharmacologically oriented investigation of oxotremorine analogues [1], we wanted to *N*-methylate *N*-(1-phenyl-2-propynyl)acetamide (**1d**) by use of standard conditions (sodium hydride, iodomethane, tetrahydrofuran, 20°). Under these conditions, *N*-propargylacetamide (**1a**) and *N*-(3-butyn-2-yl)acetamide (**1b**) are converted to the *N*-methylated propargylamides in almost quantitative yields. However, the only product observed from the reaction of **1d** was 2,5-dimethyl-4-phenyloxazole (**2d**). Acid and metal catalyzed cyclization of *N*-propargylamides are well investigated processes [2,3]. In contrast, only a few examples of the corresponding base-catalyzed reactions have been reported [3-5]. Therefore, we have investigated the base-catalyzed formation of oxazoles **2a-f** from *N*-propargylamides **1a-f** in some detail (Table 1).

Results and Discussion.

The *N*-propargylamides were prepared by two different routes (Scheme I). Acylation of propargyl amines **4c** and **4d** gave **1c** and **1d**, respectively. The amines were obtained from the corresponding mesylates by treatment with sodium amide in liquid ammonia. The low yields obtained were probably due to the instability of the mesylates [6,7]. Attempts to prepare **1e** by the same route failed; no desired product was isolated from the reaction between the preformed mesylate (or the chloride) and sodium amide. However, **1e** was readily obtained from **3e** by a Ritter reaction in acetonitrile by use of concentrated sulfuric acid as the dehydrating agent; heating under reflux for two hours resulted in 30% yield of **1e** (Scheme I). Similarly, and in 83% yield, **1d** was obtained from **3d** by this route. However, the methoxy substituted derivative **3c** produced no desired product when subjected to Ritter conditions.

Base induced cyclizations of amides **1a-f** were performed in the presence of 0.3-0.4 equivalents of sodium

Scheme I[a]

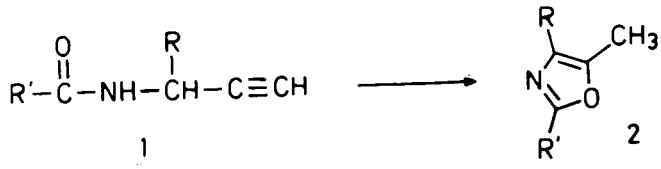


[a] reagents: (a) $MsCl/Et_3N$; (b) $NaNH_2/NH_3(l)$; (c) CH_3COCl, pyridine; (d) CH_3CN/H_2SO_4; (e) H_2O

hydride in tetrahydrofuran (Method A, Table I) or in the presence of powdered potassium carbonate (10 equivalents) in acetonitrile (Method B, Table I). With the exception of **2a** and **2b**, the oxazoles were isolated in fair to good yields; the former compounds are volatile and co-distilled with the reaction solvent. The rate of cyclization of the α-aryl substituted *N*-propargylamides **1c-e** was much faster than that of **1a** and **1b** (Table I). The *p*-nitro deriva-

Table I

Base-Catalyzed Cyclizations of *N*-Propargylamides to Oxazoles



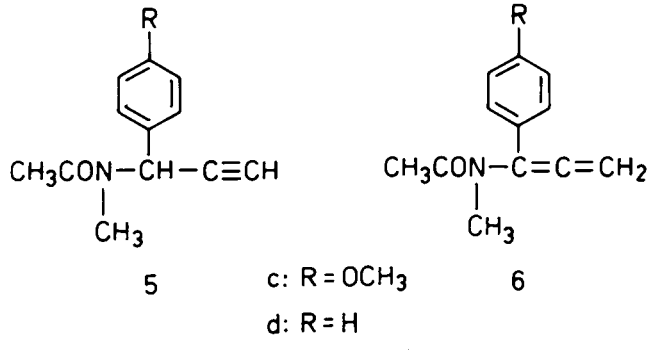
1 2

Run	Substrate	R	R¹	Method [a]	Reaction conditions °C, hours		Product	Conversion (GC) [b]	Isolated yield, %
1.	**1a** [c]	H	CH_3	A	70	10	**2a** [d]	87	5 [e]
2.				A	20	168	**2a**	12	—
3.	**1b** [f]	CH_3	CH_3	A	70	126	**2b** [g]	58	16 [h]
4.	**1c**	*p*OMePh	CH_3	A	−21	1.2	**2c**	19	—
				A	−21	3.4	**2c**	87	—
				A	−21	5.8	**2c**	>98	—
5.				A	20	0.25	**2c**	[i]	54
6.				B	20	490	**2c**	76	—
7.	**1d**	Ph	CH_3	A	−21	0.2	**2d**	9	—
				A	−21	0.8	**2d**	90	—
				A	−21	1.2	**2d**	>98	—
8.				A	20	<0.25	**2d**	[i]	93
9.				B	20	168	**2d**	>98	—
10.	**1e**	*p*-NO_2Ph	CH_3	A	−21	0.3	**2e**	36 [j,k]	—
				A	−21	0.75	**2e**	>98 [j]	—
11.				A	20	<0.1	**2e**	[i]	78
12.				B	20	<0.3	**2e**	[i,j]	95
13.	**1f**	Ph	CF_3	A	20	20	**2f**	>98	78
14.				B	20	168	**2f**	>98	97

[a] A: Sodium hydride (0.3 euivalents) in THF; B: powdered potassium carbonate (10 equivalents) in acetonitrile; for details, see Experimental. [b] Determined by gc and expressed as (**2**/**2** + **1**) × 100. [c] Previously reported [22]. [d] Previously reported [23]. [e] Isolated by fractional distillation; **2a** co-distills with the THF. [f] Previously reported [24]. [g] Previously reported [20b-d]. [h] Isolated by fractional distillation. [i] Complete conversion according to tlc. [j] Conversion determined by ^1H nmr. [k] No allenic intermediate was observed in a ^1H nmr spectrum of a quenched aliquot.

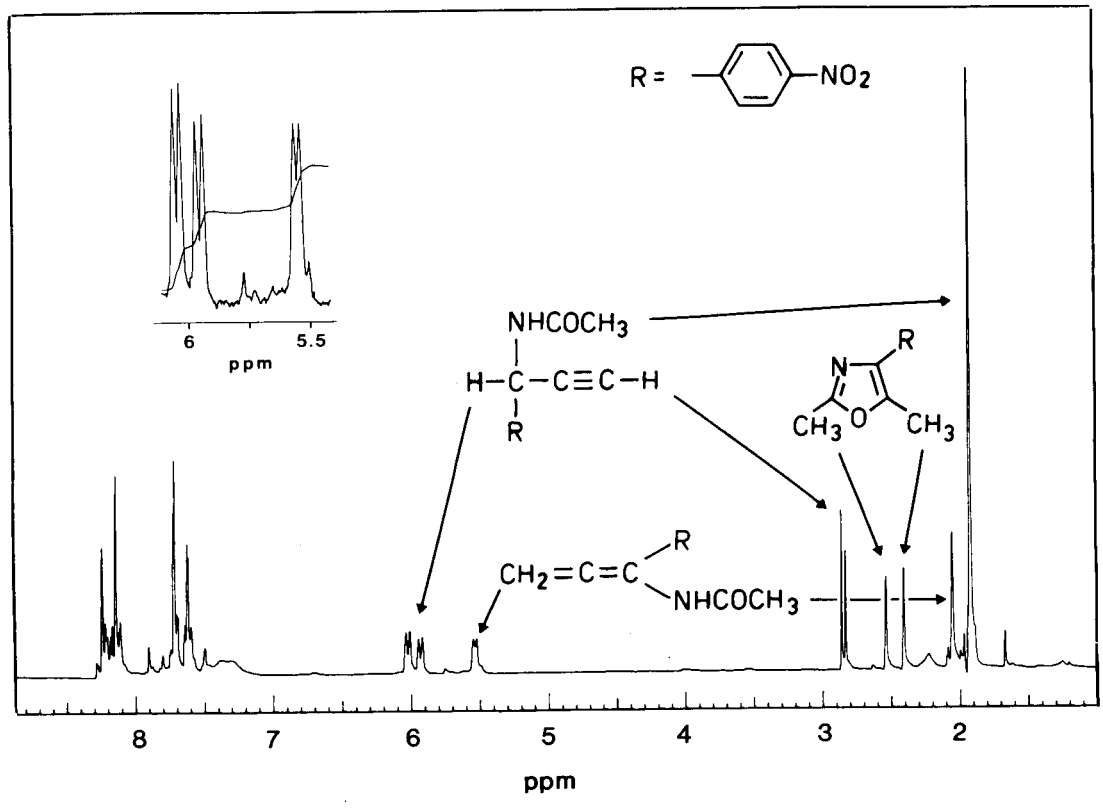
tive **1e** cyclized very fast, even when the rather weak base potassium carbonate was used as catalyst. In contrast, the cyclization of *p*-methoxy derivatie **1c** was fairly slow, even in the presence of sodium hydride. The trifluoroacetamide **1f** cyclized much slower in the presence of sodium hydride than the other phenyl substituted derivatives. This is consistent with the low basicity of the trifluoroacetamide anion and the decreased nucleophilicity of the trifluoroacetamide oxygen.

In identically performed competition experiments, **1c-e** were allowed to react with an excess of iodomethane (four equivalents) and equimolar amounts of sodium hydride in tetrahydrofuran at slowly increasing temperature (−78° → 15°). Methylation of **1c** and **1d** (or of allenic isomers thereof) successfully competed with ring closure under these conditions. However, neither *N*-methylated allene nor *N*-methylated acetylene was formed from **1e**. Thus, the base-catalyzed cyclization of **1e** appears to be very fast. Control experiments showed that the *N*-methylated allene **6d** may arise from isomerization of the *N*-methylated acetylene **5d** under the conditions used. Thus, the observed acetylene/allene ratios probably do reflect the relative ability of the compounds to stabilize a benzylic carbanion.



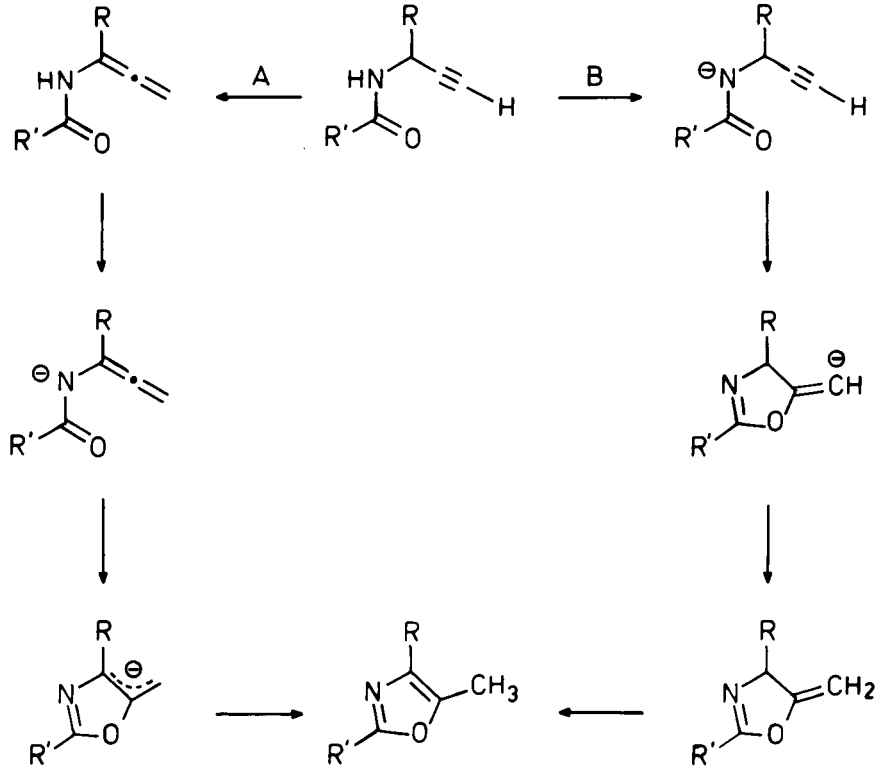
5 c: R = OCH_3 6

d: R = H



^{1}H nmr spectrum of reaction mixture in acetonitrile-d_4 (1.8 hour after the addition of potassium carbonate) containing starting material (**1e**), allenic intermediate, and product (**2e**).

Scheme II



The cyclization of compound **1e** was also studied by ^1H nmr spectroscopy of an acetonitrile-d_3 solution to which a catalytic amount of potassium carbonate had been added (Figure 1). As the reaction proceeded, a doublet (J = 2 Hz) appeared at δ 5.5 ppm. This doublet collapsed to a singlet after addition of deuterium oxide and was assigned to the allene formed by isomerization of **1e**. Thus, although we have not been able to isolate an allenic intermediate, its presence is strongly supported by this nmr-experiment. After two hours, the intensity of the doublet due to the allenic protons started to decrease and the two singlets due to the methyl groups of **2e** increased in intensity. In addition, some unassigned multiplets of minor intensity appeared in the olefinic region. The cyclization of **1e** was almost complete after four hours. We could not detect an allenic intermediate when sujbecting **1d** and **1f** to similar ^1H nmr experiments.

Two mechanisms that would account for the base-catalyzed formation of oxazoles from the propargylic amides are depicted in Scheme II. In mechanism A, the acetylenes rearrange to allenes and the central allenic carbon is attacked by the nucleophilic amide oxygen. In mechanism B, an acetylenic carbon is the electrophilic species. Mechanism B normally operates in base-catalyzed cyclizations of acetylenic derivatives [8]. However, in the present investigation the following observations support mechanism A (see also [9]); (a) the observed rank order of reactivities correlates well with the expected acidities of propargylic hydrogens of the amides and thus with their tendency to undergo a base-catalyzed isomerization to allenes, (b) similarly, the rank order of reactivities agrees well with the ability of the putative ring closed intermediates to stabilize an oxazole anion, and (c) a ^1H nmr experiment demonstrated the presence of an allenic intermediate in the conversion of **1e** to **2e**.

Table II

Competition Experiments [a]

Substrate	Products, yield, % [b,c] Ring Closure	*N*-Methylation
1c	**2c**, 9 (4)	**5c**, 31 and **6c**, 60 [d]
1d	**2d**, 50 (38)	**6d**, 50 (50)
1e	**2e**, 100 (91)	

[a] Compounds **1c-e** were allowed to react with methyl iodide (four equivalents and sodium hydride (one equivalent) at slowly increasing temperature (−78° → 15°); for details, see Experimental. [b] Determined by GC- and ^1H nmr analyses. [c] Isolated yields are given in parenthesis. [d] Isolated as an inseparable mixture of **5c** and **6c** in a 45:55 ratio.

EXPERIMENTAL

Melting points (uncorrected) were determined in open glass capillaries on a Thomas-Hoover apparatus. Chemicals and solvents were used as received, except for tetrahydrofuran, which was distilled from sodium metal in the presence of benzophenone under dry nitrogen. The ^1H, ^{19}F and ^{13}C nmr spectra were recorded on a JEOL FX 90Q spectrometer at 89.55, 84.3 and 22.5 MHz, respectively. Samples were dissolved in deuteriochloroform unless otherwise stated. The ^1H and ^{13}C nmr spectra were referenced to internal tetramethylsilane. The ^{19}F nmr spectra were referenced to internal fluorotrichloromethane. The ir spectra were recorded on a Perkin-Elmer 157G spectrophotometer. The mass spectra were obtained on a LKB 9000 spectrometer (EI, 70 eV, direct insertion). All spectra were in accordance with the assigned structures [10,11]. Capillary-GC analyses were performed on a Carlo-Erba 6000 equipped with a flame-ionization detector (FID-40) and a Milton Roy CI-10B integrator, by use of a SE 52 column. The carrier gas was He (2 ml/minute). E. Merck silica gel 60 F (230-400 mesh) was used for flash chromatography [12]. Thin-layer chromatography (tlc) was carried out on aluminium sheets precoated with silica gel 60 F_{254} (0.2 mm), E. Merck. Elemental analyses were performed by Mikro Kemi AB, Uppsala, Sweden.

1-(4-Nitrophenyl)-2-propynyl-1-ol (**3e**).

n-Buthyllithium (145 ml, 1.2 *M* in hexane, 174 mmoles) was added to tetrahydrofuran (800 ml) kept at −78° under nitrogen and a rapid flow of acetylene was passed through the solution. After three hours, a solution of *p*-nitrobenzaldehyde (25.5 g, 170 mmoles) in tetrahydrofuran (300 ml) was added dropwise to the lithium acetylide solution. The reaction mixture was stirred for five hours at −78° and the reaction temperature was allowed to rise to −40°. The reaction was quenched [13] by dropwise addition of glacial acetic acid (12.5 g, 210 mmoles) in ether (100 ml). The mixture was concentrated and ether (800 ml) was added. The ether solution was washed with 0.5 *M* hydrochloric acid (5 × 200 ml), dried (magnesium sulfate), filtered, and concentrated to give an oil. Flash chromatography on silica using ether/hexane 1:1 as eluant gave 25.0 g (84%) of **3e** which was pure according to ^1H nmr. An analytical sample of **3e** was prepared by recrystallization from ether/hexane, mp 55-56°; tlc R_f 0.31 (ether/hexane 1:1); ir (potassium bromide): 3280, 3250 (broad), 2105, 1605, 1595, 1565, 1345 cm^{-1}; ^1H nmr: δ 8.35-7.65 (m, 4H, ArH's), 5.58 (d, J = 2.2 Hz, 1H, H-1), 2.74 (d, J = 2.2 Hz, 1H, H-3), 2.64-2.36 (br, 1H, OH); ^{13}C nmr: δ 147.6, 146.9, 127.4, 123.7 (Ar C's), 82.3 (C2), 75.9 (C3), 63.2 (C1); ms: m/z (ion, relative intensity) 177 (M^+, 6), 160 (45), 53 (100).

Anal. Calcd. for $C_9H_7NO_3$: C, 61.0; H, 4.0; N, 7.9. Found: C, 61.2; H, 3.9; N, 7.9.

1-Phenyl-2-propynylamine (**4d**).

A freshly prepared solution of 1-phenyl-2-propynyl methanesulfonate [15] in ether (135 ml) [prepared from 1-phenyl-2-propyn-1-ol (**3d**, 12.73 g, 96 mmoles), methanesulfonyl chloride (11.03 g, 96 mmoles) and triethylamine (9.75 g, 96 mmoles) in ether kept at −78° under nitrogen] was filtered directly into a preformed suspension of sodium amide [16] [prepared from sodium (2.2 g, 96 mmoles)] in liquid ammonia (800 ml) kept at −40°. The reaction was quenched after another five hours by addition of solid ammonium chloride (5 g). Ether was added, and the ammonia was allowed to evaporate overnight. Hydrochloric acid (1 *M*, 450 ml) was added to the residue and the mixture was extracted with ether. The water layer was alkalinized with 5 *M* aqueous sodium hydroxide to *p*H 11-12 and extracted with ether. The combined organic layers were dried (potassium carbonate), filtered, and concentrated. The resulting oil was distilled to give 5.2 g (41%) of **4d**, bp 49-53.5° (0.35-0.5 mm of Hg) [lit [17] bp 51-61° (0.008 Torr)]; ^1H nmr data were consistent with those reported previously [17]; ^{13}C nmr: δ 141.5, 128.6, 127.8, 126.6, (Ar C's), 85.9 (Cl), 72.3 (C3), 47.3 (Cl).

Alternatively, **4d** could be obtained in 73% yield after acid hydrolysis (3.5 *M* hydrochloric acid) of **1d** at 90° for five hours followed by work up.

1-(4-Methoxyphenyl)-2-propynylamine (**4c**).

Compound **4c** was prepared from **3c** [18] (15 g, 93 mmoles) by the above procedure. Distillation of the crude product gave 1.6 g (11%) of **4c**, bp 96-100° (0.4-0.7 mm of Hg); ir (film): 3370, 3290, 1610, 1510, 1250 cm^{-1}; ^1H nmr: δ 7.50-6.80 (m, 4H, ArH's), 4.72 (d, J = 2.4 Hz, 1H, H-1),

3.77 (s, 3H, OMe), 2.50 (d, J = 2.2 Hz, 1H, H-3), 1.77 (s, 2H, NH_2); ^{13}C nmr: δ 159.1, 133.9, 127.8, 113.9, 86.4 (C2), 72.1 (C3), 55.2 (OMe), 46.6 (C1); ms: m/z (ion, relative intensity) 161 (M^+, 69), 130 (100). An analytical sample was prepared as the oxalate salt (double salt) by recrystallization from methanol-water, mp 189° dec.

Anal. Calcd. for $C_{22}H_{24}N_2O_6$: C, 64.1; H, 5.9; N, 6.8. Found: C, 63.9; H, 5.8; N, 6.8.

N-[1-(4-Methoxyphenyl)-2-propynyl]acetamide (**1c**).

A solution of acetyl chloride (0.69 g, 8.8 mmoles) in ether (75 ml) was added to a stirred solution of **4c** (1.25 g, 7.7 mmoles) and pyridine (0.61 g, 7.7 mmoles) in ether (100 ml) kept under nitrogen at 0°. The ice-bath was removed and the mixture was stirred for three hours. The mixture was filtered and concentrated to give the crude amide which was purified by flash chromatography using ether as eluant to give 1.32 g (84%) of pure **1c**, mp 126-128°; tlc R_f 0.45 (ether); ir (potassium bromide): 3290, 3270, 2110, 1640, 1510 cm^{-1}; ^1H nmr: δ 7.50-6.75 (m, 4H, ArH's), 6.48 (br m, 1H, NH), 5.92 (dd, J = 2.4 Hz, J = 8.2 Hz, H-1), 3.78 (s, 3H, OMe), 2.47 (d, J = 2.4 Hz, 1H, H-3), 1.97 (s, 3H, CH_3CO); ^{13}C nmr: δ 169.0 (C=O), 159.4, 130.5, 128.3, 114.0 (ArC's), 82.0 (C2), 72.7 (C3), 55.3 (OMe), 43.9 (C1), 23.0 (CH_3CO); ms: m/z (ion, relative intensity) 203 (M^+, 33), 160 (M^+ -CH_3CO, 20), 44 (100).

Anal. Calcd. for $C_{12}H_{13}NO_2$: C, 70.9; H, 6.5; N, 6.9. Found: C, 71.2; H, 6.4; N, 6.8.

N-(1-Phenyl-2-propynyl)acetamide (**1d**).

Compound **1d** was prepared from **4d** (3.1 g, 23 mmoles) in a quantitative yield by the above procedure. The analytical sample was recrystallized from ether, mp 82.5-84°; tlc R_f 0.55 (silicagel, ether); ir (potassium bromide): 3295, 1645, 1530 cm^{-1}; ^1H nmr: δ 7.40 (m, 5H, ArH's), 6.85-6.54 (br m, 1H, NH), 5.97 (dd, J = 2.3 Hz, J = 8.9 Hz, H-1), 2.46 (d, J = 2.3 Hz, H-3), 1.95 (s, 3H, CH_3CO); ^{13}C nmr: δ 169.2 (C=O), 138.3, 128.7, 128.1, 127.0 (Ar C's), 81.8 (C2), 72.9 (C3), 44.4 (C1), 23.0 (CH_3CO); ms: m/z (ion, relative intensity) 173 (M^+, 60), 130 (M^+ -CH_3CO, 100), 43 (54).

Anal. Calcd. for $C_{11}H_{11}NO$: C, 76.3; H, 6.4; N, 8.1. Found: C, 76.3; H, 6.2; N, 8.1.

Alternative Preparation of **1d**.

A solution of 96% sulfuric acid (43.5 g, 444 mmoles) in acetonitrile (90 ml) was added dropwise to a stirred mixture of **3d** (11.73 g, 89 mmoles) and anhydrous sodium sulfate (12.6 g, 89 mmoles) in acetonitrile (140 ml) at −25°. The temperature was allowed to reach room temperature and the mixture was stirred for 48 hours. The mixture was concentrated and poured on ice. The organic layer was extracted with ether and dichloromethane. The combined organic layers were dried (magnesium sulfate), filtered, and concentrated. Flash chromatography by use of ether/light petroleum 1:1, followed by ether, as eluants afforded 12.8 g (83%) of pure **1d**. In addition, a small amount (4.4%) of cinnamic aldehyde was isolated.

N-[1-(4-Nitrophenyl)-2-propynyl]acetamide (**1e**).

A mixture of **3e** (2.5 g, 14 mmoles), anhydrous sodium sulfate (7.0 g, 49 mmoles) and 96% sulfuric acid (5.0 g, 49 mmoles) in acetonitrile (25 ml) was heated to reflux for one and a half hour. Ether and water were added. The aqueous layer was extracted with dichloromethane. The combined organic layers were dried (magnesium sulfate), filtered and concentrated. The residue was subjected to flash chromatography with ether/light petroleum 1:1 as eluant, affording 920 mg (30%) of **1e**, mp 138-139.5°; tlc R_f 0.5 (ether); ir (potassium bromide): 3260, 2110, 1640, 1520, 1345 cm^{-1}; ^1H nmr (methanol-d_6): δ 8.31-7.65 (m, 4H, ArH's), 6.01 (d, J = 2.4 Hz, 1 H, H-1), 3.05 (d, J = 2.4 Hz, H-3), 1.99 (s, 3H, CH_3CO); ^{13}C nmr (methanol-d_4): δ 169.3 (C=O), 147.6, 145.5, 128.0, 123.9 (Ar C's), 80.3 (C2), 74.4 (C3), 44.0 (C1), 23.0 (CH_3CO); ms: m/z (ion, relative intensity) 218 (M^+, 28), 43 (CH_3CO, 100).

Anal. Calcd. for $C_{11}H_{10}N_2O_3$: C, 60.6; H, 4.6; N, 12.8. Found: C, 60.5; H, 4.6; N, 12.9.

Also isolated from the above reaction was a diastereomeric mixture (1:1) of di[1-(*p*-nitrophenyl)propargyl]ether, yield 280 mg (6%); tlc R_f 0.45 (ether/hexane 1:1); spectroscopic data of the mixture; ir (potassium bromide): 3290, 2110, 1600, 1515, 1340 cm^{-1}; ^1H nmr: δ 8.33-7.64 (m, 8 H, ArH's), 5.81 and 5.41 (d's, J = 1.8 Hz and 2.2 Hz, respectively, 2H, H-1), 2.85 and 2.78 (d's, J = 2.2 Hz, 2H, H-3); ^{13}C nmr: δ 148.1 and 148.0, 144.0 and 143.9, 128.5 and 128.3, 123.9 and 123.7, 79.6 and 79.1, 78.3 and 78.0, 68.6 and 68.3.

N-(1-Phenyl-2-propynyl)trifluoroacetamide (**1f**).

A mixture of **4d** (1.5 g, 11 mmoles), pyridine (0.89 g, 11 mmoles) and trifluoroacetic anhydride (2.57 g, 12 mmoles) was stirred for two hours at 0°. The mixture was filtered and concentrated and the crude product was purified by flash chromatography using ehter/light petroleum 1:1 as eluant to give 2.4 g (92%) of **1f**, mp 94.5-95.5°; tlc R_f 0.65 (ether/light petroleum 1:1); ir (potassium bromide): 3300, 1700, 1545 cm^{-1}; ^1H nmr: δ 7.45 (m, 5H, ArH's), 7.05-6.53 (br m, 1 H, NH), 5.98 (dd, J = 2.4 Hz, J = 8.4 Hz, 1H, H-1), 2.60 (d, J = 2.4 Hz, 1H, H-3); ^{19}F nmr: δ −76.22; ^{13}C nmr: δ 156.2 (q, J_{CF} = 38 Hz, C=O), 136.2, 127.1, 127.0, 115.7 (q, J_{CF} = 288 Hz, CF_3), 79.5 (C2), 74.7 (C3), 45.4 (C1); ms: m/z (ion, relative intensity) 227 (M^+, 5).

Anal. Calcd. for $C_{11}H_8F_3NO$: C, 58.1; H, 3.6; N, 6.2. Found: C, 58.3; H, 3.3; N, 6.2.

General Procedure for the Sodium Hydride Catalyzed Cyclizations of *N*-Propargylamides (Method A, Table I).

Sodium hydride (4 mg, 0.17 mmole) was added to a solution of the appropriate *N*-propargylamide (0.66 mmole) in dry tetrahydrofuran (5.5 ml) kept under nitrogen. The reaction temperature is given in Table I. The progress of the reaction was followed by transfer of aliquots to vials containing glacial acetic acid (0.25 ml) in ether (3.5-5 ml) followed by analysis by use of capillary gc. Analysis (gc) of the reactions of **1e** was not possible since the product **2e** and the starting material had identical gc properties [19]. Therefore, these reactions were monitored by ^1H nmr spectroscopy. Throughout, tlc analyses were performed on the quenched aliquots. In preparative runs, in which the scale was 2-5 times larger, the workup procedure consisted of addition of ether (50-75 ml) to the reaction mixture followed by filtration, concentation and flash chromatography.

General Procedure for the Potassium Carbonate Catalyzed Cyclizations of *N*-Propargylamines (Method B, Table I).

A mixture of the propargylic amide (0.06 mmole) in acetonitrile (3 ml) and powdered anhydrous potassium carbonate (0.72 mmole) was stirred at room temperature. Aliquots were analyzed directly by gc or ^1H nmr spectroscopy, and tlc. For preparative purposes, the cyclizations were performed in 20-100 times larger scale. Products were isolated by flash chromatography after filtration and concentration of the reaction mixtures.

2,5-Dimethyl-4-phenyloxazole (**2d**).

This compound has been prepared previously [20]; tlc R_f 0.3 (chloroform); ir (film): 1600 cm^{-1}; ^1H nmr: δ 7.5 (m, 5H, ArH's), 2.45 and 2.43 (s's, 6H, Me's); ^{13}C nmr (methanol-d_6): δ 161.1 (C1), 145.0 (C5), 135.0, 133.0, 129.6, 128.3, 127.6, 13.4 (C1-Me), 11.6 (C5-Me). Mass spectral data of **2d** were in agreement with those previously reported [21].

2,5-Dimethyl-4-(4-methoxyphenyl)oxazole (**2c**).

This compound had mp 30-32°; tlc R_f 0.25 (ether/hexane 1:1); ir (potassium bromide): 1595, 1510, 1245 cm^{-1}; ^1H nmr: δ 7.65-6.85 (m, 4H, ArH's), 3.81 (s, OMe), 2.44 (s, 6H, Me's); ^{13}C nmr: δ 158.5, 158.4, 141.9, 133.6, 127.4, 113.6, 54.8 (OMe), 13.4 (C1-Me), 11.2 (C5-Me); ms: m/z (ion, relative intensity) 203 (M^+, 100), 134 (90).

Anal. Calcd. for $C_{12}H_{13}NO_2$: C, 70.9; H, 6.5; N, 6.9. Found: C, 71.1; H, 6.5; N, 6.7.

2,5-Dimethyl-4-(4-nitrophenyl)oxazole (**2e**).

This comopund had mp 144-145° (ether-acetone); tlc R_f 0.5 (ether/hexane 1:1); ir (potassium bromide): 1605, 1510, 1345, 1330 cm^{-1}; ^1H nmr: δ 8.30-7.70 (m, 4H, ArH's), 2.57 and 2.49 (s's, 6H, Me's); ^{13}C nmr: δ 159.8

(C2), 146.5, 145.9, 138.9, 132.7, 126.7, 124.0, 13.7 (C2-Me), 12.2 (C5-Me); ms: m/z (ion, relative intensity) 218 (M^+, 100).

Anal. Calcd. for $C_{11}H_{10}N_2O_3$: C, 60.6; H, 4.6; N, 12.8. Found: C, 60.5; H, 4.5; N, 12.9.

2-Trifluoromethyl-5-methyl-4-phenyloxazole (**2f**).

An analytical sample was obtained after distillation, bp 106° (7-8 mm of Hg); tlc R_f 0.76 (ether/light petroleum 1:3); ir (film): 1585 cm^{-1}; ^1H nmr (acetonitrile-d_6): δ 7.80-7.25 (m, 5H, ArH's), 2.61 (unresolved q, J_{HF} = 0.7 Hz, 3H, Me); ^{19}F nmr (acetonitrile-d_6): δ −65.4 (q, J_{FH} = 0.7 Hz); ^{13}C nmr: δ 146.7, 136.0, 130.5, 128.7, 128.1, 126.8, 116.6 (q, J_{CF} = 270 Hz, CF_3), 11.7 (C5-Me); ms: m/z (ion, relative intensity) 227 (M^+, 96).

Anal. Calcd. for $C_{11}H_8F_3NO \cdot \frac{1}{2} H_2O$: C, 55.9; H, 3.8; N, 5.9. Found: C, 56.3; H, 3.4; N, 5.8.

Competition Experiments (Table II).

Sodium hydride (14 mg, 0.58 mmole) followed by iodomethane (0.28 g, 2 moles) were added to solutions of each of the *N*-propargylamides **1c-e** (0.58 mmole) in tetrahydrofuran (4 ml) kept at −78° under nitrogen. The reaction temperature was allowed to rise slowly to 15° during a period of 19 hours. The product distribution (see Table II) was determined by capillary gc and ^1H nmr spectroscopy of the crude reaction mixtures. Ether (50 ml to each) was added, the precipitate formed was filtered off, and products were isolated by use of flash chromatography.

N-Methyl-*N*-(1-phenyl-1,2-propadienyl)acetamide (**6d**).

Compound **6d** was isolated in 50% yield after flash chromatography, using ether/hexane (1:1) as eluant, from the competition experiment with **1d**; tlc R_f 0.45 (ether); ir (film): 1940, 1660 cm^{-1}; ^1H nmr: δ 7.34 (m, 5 H, ArH's), 5.45 (s, 2H, $=CH_2$), 3.12 (s, 3H, N-Me), 2.05 (s, 3H, CH_3CO); ^{13}C nmr: δ 207.9 (C2), 171.5 (C=O), 132.3, 128.8, 127.9, 125.0 (Ar C's), 114.9 (C1), 83.2 (C3), 34.7 (N-Me), 21.6 (CH_3CO).

Anal. Calcd. for $C_{12}H_{13}NO$: C, 77.0; H, 7.0; N, 7.5. Found: C, 76.8; H, 7.2; N, 7.4.

N-Methyl-[1-(4-methoxyphenyl)-2-propynyl]acetamide (**5c**) and *N*-Methyl-[1-(4-methoxyphenyl)-1,2-propadienyl]acetamide (**6c**).

The competition experiment of **1c** gave at 45:55 mixture of **5c** and **6c** (65 mg, 51%) after flash chromatography using ether/hexane 1:1 as eluant. This mixture could not be separated chromatographically. However, the following characteristics were obtained from the mixture of **5c** and **6c**, tlc R_f 0.44 (ether); ir (film): 3290, 3210, 1940 (vw), 1650, 1605, 1510 cm^{-1}; ^1H nmr: δ 7.48-6.80 (m, 8H, Ar H's), 5.42 (s, 2H, $=CH_2$; **6c**), 3.82 and 3.80 (s's, 6H, OMe's), 3.11 (s, 3H, N-Me; **6c**), 2.82 (s, 3H, N-Me; **5c**), 2.51 (d, J = 2.6 Hz, H-3; **5c**), 2.13 and 2.05 (s's, 2·CH_3CO); ^{13}C nmr: δ 207.4 (=C=), 171.5 and 170.2, (C=O's), 83.2 (=CH_2), 80.0 (*C*=CH), 74.2 (C=*C*H), 55.3 and 55.2 (OMe's), 47.6 (benzylic CH), 21.9 and 21.7 (2·CH_3CO).

N-Methyl-*N*-(1-phenyl-2-propynyl)trifluoroacetamide (**7**).

A mixture of iodomethane (4.4 g, 31 mmoles), powdered anhydrous potassium carbonate (13.0 g, 94 mmoles) and **1f** (2.1 g, 9.2 mmoles) in acetonitrile (50 ml) under nitrogen was stirred for 12 hours at room temperature. Filtration and concentration followed by distillation afforded 2.1 g (85%) of **7**, bp 72-74° (0.4-0.5 mm of Hg); tlc R_f 0.7 (ether/light petroleum 1:3); ir (film): 3290, 2120, 1690 cm^{-1}; ^1H nmr: δ (ratio *E*/*Z* = 15:85), 7.65-7.30 (m, 5H, ArH's), 6.76 (d, J = 2.4 Hz, *Z*-H-1), 6.03 (d, J = 2.2 Hz, *E*-H-1), 2.96 (q, J_{HF} = 1.6 Hz, *Z*-N-Me), 2.81 (unressolved m, *E*-N-Me), 2.71 (d, J = 2.4 Hz, *E*-H-3), 2.64 (d, J = 2.4 Hz, *Z*-H-3); ^{19}F nmr: δ −68.2 (unresolved m, *E*-N-Me), −70.2 (q, J_{FH} = 1.6 Hz, *Z*-N-Me); ^{13}C nmr: δ 157.1 (q, J_{CF} = 36 Hz, C=O), 134.4, 128.9,-127.5, 127.2 (Ar C's), 116.4 (q, J_{CF} = 287 Hz, CF_3), 77.8 (C2), 76.3 (*E*-C3), 76.0 (*Z*-C3), 52.8 (m, *E*-C1), 50.5 (*Z*-C1), 30.0 (*E*-N-Me), 29.9 (q, J_{CF} = 3.5 Hz, *Z*-N-Me).

Anal. Calcd. for $C_{12}H_{10}F_3NO$: C, 59.8; H, 4.2; N, 5.8. Found: C, 59.5; H, 4.1; N, 6.0.

N-Methyl-*N*-(1-phenyl-2-propynyl)acetamide (**5d**).

Sodium borohydride (1.5 g, 40 mmoles) was added to a stirred solution of **7** (1.19 g, 4.93 mmoles) in dry ethanol (85 ml) under nitrogen at room temperature. The deacylation was complete after 35 minutes. The reaction mixture was diluted with water and 1 *M* hydrochloric acid was added dropwise. The ethanol was evaporated, more water was added and the mixture was alkalinized with solid sodium bicarbonate to *p*H 8.5. Dichloromethane was added and the organic layer was dried (potassium carbonate), filtered, and concentrated to give 0.7 g (97%) of crude *N*-Methyl-1-phenyl-2-propyn-1-ylamine (**8**).

A solution of acetyl chloride (0.47 g, 4.8 mmoles) in ether (25 ml) was added dropwise to a stirred solution of crude **8** (0.7 g, 4.8 mmoles) and pyridine (0.38 g, 4.8 mmoles) in ether (40 ml) kept at 0° under nitrogen. The stirring was continued for 75 minutes and 1 *M* hydrochloric acid and ether were added to the reaction mixture. The organic layer was washed with saturated aqueous sodium carbonate, dried (sodium sulfate), filtered, and concentrated. The resulting oil was distilled to give 0.74 g (82%) of **5d**, bp 108-110° (0.35-0.45 mm of Hg); tlc R_f 0.6 (ether); ir (film): 3290, 3230, 2110, 1650 cm^{-1}; ^1H nmr: δ (*E*/*Z* ratio = 1.5) 7.56-7.24 (m, 5H, Ar's), 6.91 (d, J = 2.4 Hz, *Z*-H-1), 5.85 (d, J = 2.2 Hz, *E*-H-1), 2.82 (s, *Z*-N-Me), 2.75 (s, *E*-N-Me), 2.68 (d, J = 2.4 Hz, *E*-H-3), 2.55 (d, J = 2.6 Hz, *Z*-H-3), 2.30 (s, *E*-CH_3CO), 2.15 (s, *Z*-CH_3CO); ^{13}C nmr: δ 168.7 (C=O), 134.8, 126.8, 126.4, 125.7 (Ar C's), 78.0 (C2), 74.1 (*E*-C3), 72.9 (*Z*-C3), 52.3 (*E*-C1), 46.5 (*E*-C1), 29.5 (*Z*-N-Me), 27.3 (*E*-N-Me), 20.2 (*Z*-CH_3CO), 20.0 (*E*-CH_3CO).

Anal. Calcd. for $C_{12}H_{13}NO$: C, 77.0; H, 7.0; N, 7.5. Found: C, 76.7; H, 7.2; N, 7.5.

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