Acetylenic Amides. 2 [1]. The Generation and Reactions of Dianions Derived From 2-Propynamides

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The dianion of N-benzyl-2-propynamide can be generated by the treatment of **4** with two equivalents of LDA at -65° or ethylmagnesium bromide at -20°. The trilithio species **6** is readily formed using 3 equivalents of LDA. Reaction of **5** with aldehydes or ketones produce hydroxypropynamides **9** in good yields. Silation of **5a** with chlorotrimethylsilane produces N-benzyl-3-trimethylsilyl-2-propynamide (**13**) in high yield. Reduction of **9** furnishes either fully saturated amides **15** or partially reduced *cis*-olefins **16** or **18**. Compounds **16**, on heating, rearrange to 4-ketoamides **17**. Carboxylation of **5a** with carbon dioxide produces 3-benzyl-2,4-dioxo-5-oxazidinylacetic acid (**11**). Warming **11** in dimethyl sulfoxide results in the loss of carbon dioxide and the formation of N-benzylpyruvamide (**21**).

Recently we have described the preparation of a variety of 2-propynamides **3** [1]. The two basic routes employed were the reaction of activated esters of propiolic acid **1a,b** with amines to furnish **3** directly or by the reaction of lithiotrimethylsilylacetylene with isocyanates followed by fluoride catalyzed protodesilation of intermediate **2** to give **3**. In this manner, large quantities of 2-propynamides were able to be prepared for various chemical investigations.
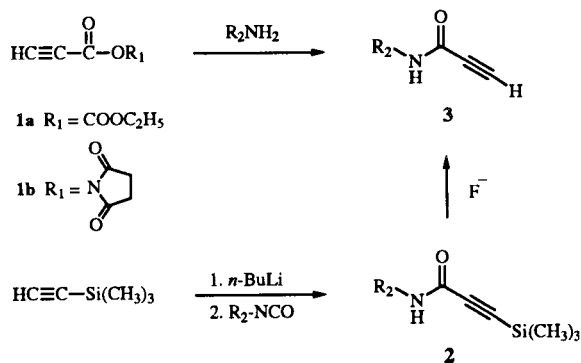
Within the past three decades, the use of polymetallated organic molecules has gained prominence in the construction of complex organic entities. Dianions of such functional groups as ketones, β-ketoesters, carboxylic acids, carboxamides, imides, sulfonamides, sulfones, nitriles, oximes, ylides, hydrazones, azines, alcohols, thiols, ethers, and amines have been described and their reactions with a variety of electrophiles has been well documented [2].

Although a plethora of substrates have been converted to their polymetallated derivatives, it appeared to us that dianions of 2-propynamides have not been explored, probably due to the relative inaccessibility of these compounds. In this report we will describe the generation of the dilithio species of one such derivative, namely N-benzyl-2-propynamide (**4**), and investigate its reactions with various electrophiles.

Generation of Dianions.

Our initial experiments employed the two simplest amides in the series, 2-propynamide (**3**, R = H) and N-methyl-2-propynamide (**3**, R = CH$_3$) [3]. The treatment of either of these amides with two equivalents of lithium diisopropylamide (LDA) or ethylmagnesium bromide in tetrahydrofuran at -20° gave a thick white precipitate. In either case, when benzaldehyde was added to the mixture, only the starting amides were isolated. Even the addition of hexamethylphosphoramide (HMPA) up to 10% by volume of the solvent did not facilitate the reaction and the amide again was recovered unchanged.

At this stage it was not clear whether dianion formation indeed had occurred or whether subsequent reaction with the aldehyde was at fault. Consequently, deuteration experiments were conducted in order to determine if the acetylenic proton had been abstracted. When N-methyl-2-propynamide was treated with two equivalents of LDA, a white precipitate formed as described previously. After quenching with deuterium chloride, analysis of the ^{1}H-nmr spectrum (DMSO-d$_6$) indicated that the intensity of the acetylene proton at δ 4.0 was diminished by one-half with respect to the N-CH$_3$ group (δ 2.7), suggesting that 50% dianion formation had occurred. Extending the reaction time fourfold did not increase the amount of deprotonation.

From these results it was postulated that the white precipitate was the monoanion of N-methyl-2-propynamide and, due to its insolubility, the formation of the dianion was greatly hampered. However, it is not clear why no adduct with benzaldehyde was isolated even though half of the dianion was present.

We speculated that a propynamide which would form a more soluble mono- and dianion was required and this increased solubility should favor subsequent reactions. The amide chosen was N-benzyl-2-propynamide (**4**) which can be readily synthesized in large quantities [1].
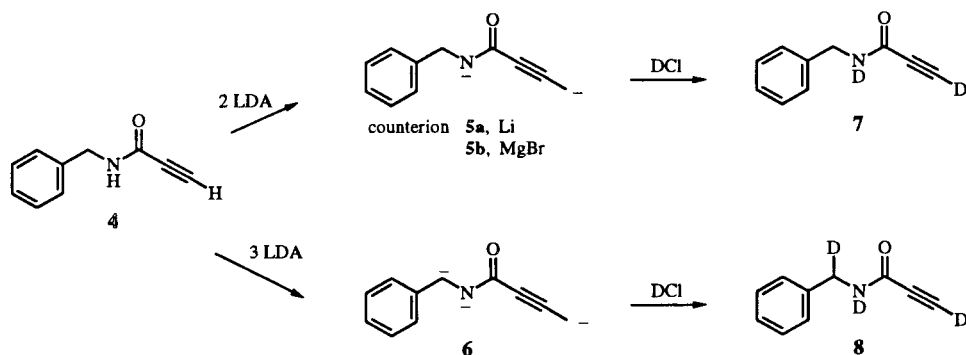
When **4** was deprotonated with two equivalents of LDA [4] in tetrahydrofuran, a brownish-red solution formed. After one hour, the presumed dianion **5a** was quenched with deuterium chloride. The ^{1}H-nmr spectrum of **7** revealed that the acetylenic proton formerly at δ 2.8 was completely exchanged with deterium and the N-benzyl methylene doublet at δ 4.4 (J = 6 Hz) collapsed to a sharp singlet. This observation suggests that **5a** indeed was formed.

The thermal stability of **5a** was investigated by quenching the solution of the dianion with hydrochloric acid at various temperatures and comparing the nmr spectrum of the regenerated **4** with an authentic sample. These tests indicated that **5a** was thermally stable up to -20°. The dianion was also somewhat stable at 0° but after one hour some decomposition was noticed.

The Grignard dianion **5b** may also be generated by the treatment of **4** with two equivalents of ethylmagnesium bromide, however, this species is not soluble in tetrahydrofuran and precipitates from solution. After one, hour, quenching the suspension with deuterium chloride gives a product whose nmr spectrum is identical with that of the LDA-generated dianion, indicating that the mixture contained the di-Grignard species and not the precipitated monoanion as previously described for N-methyl-2-propynamide.

The thermal stability of **5b** is higher than that of **5a**. No change in the nmr spectrum of regenerated **4** is observed even at room temperature. Higher temperatures were not investigated.

It is interesting to note that the brownish-red color of the LDA-generated dianion **5a** is actually due to small quantities of trianion **6**. When dianion generation is carried out by inverse addition (adding the base to **4**) using 95% of the theoretical quantity of LDA, a yellow solution results. The addition of a slight excess of LDA to the reaction causes the color of the solution to change to brownish-red.

The generation of the trianion **6** can readily be accomplished by the treatment of **4** with three equivalents of LDA in tetrahydrofuran for 1 hour at -20°. The resultant deep reddish-brown solution, after quenching with deu-

terium chloride, furnishes the trideuteriopropynamide **8** whose nmr spectrum exhibits a singlet at δ 4.4. Comparison of this signal with the aromatic region indicates a ratio of 1:5 which is consistent with structure **8**.
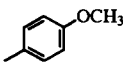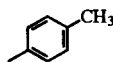
Reactions of Dianions.

Being assured that the dianion **5** could be generated readily, we undertook an investigation into the possible chemistry surrounding such an entity. The first candidates chosen to react with **5** were carbonyl-containing compounds such as aldehydes or ketones. The reaction of benzaldehyde with **5a** at -20° was complete within 30 minutes, and N-benzyl-4-hydroxy-4-phenyl-2-butynamide (**9a**) was formed in 78% yield.

Dianion **5a** also reacts with ketones under analogous conditions but reaction times generally are longer (e.g. **9f** requires 3.5 hours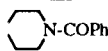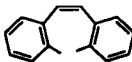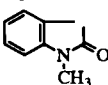). In two cases the reaction of the di-Grignard dianion **5b** was investigated. When **5b** was allowed to react with benzaldehyde at room temperature, **9a** was isolated in 63% yield after a reaction time of 90 minutes, whereas reaction with benzophenone produced **9f** also in 63% yield but only after a reaction time of 4 days. The reaction of **5** with a variety of aldehydes and ketones are summarized in Table 1.
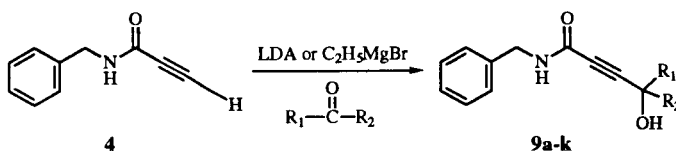
Dianion **5a** reacts readily with carbon dioxide at -20° over a period of 20 minutes to initially give a green precipitate which slowly dissolves and subsequently forms a yellow solution. After work-up, an acid-containing product was isolated in 29% yield. The yield can be increased to 58% by allowing the solution of **5a** to stir under an atmosphere of carbon dioxide for 48 hours. at room temperature. An analogous reaction of **5b** with carbon dioxide resulted in extensive decomposition; no identifiable products were isolated.

Table 1

Reaction of Dianion **5** with Carbonyl-containing Compounds

No.	R_1	R_2	Yield, %	Mp,°C	Formula	Analysis Calcd./Found		
						%C	%H	%N
9a	H	(phenyl)	78 63 [a]	70-74 [b]	$C_{17}H_{15}NO_2$	77 0 76.8	5.7 5.7	5.3 5.1
9b	H	(4-Cl-phenyl)	60	111-113	$C_{17}H_{14}ClNO_2$	68.1 68.1	4.7 5.0	4 7 4.7
9c	H	(4-OCH₃-phenyl)	85	90-93 lb]	$C_{18}H_{17}NO_3$	73.2 73.2	5.8 6.1	4.7 4.8
9d	H	(4-CH₃-phenyl)	49	72-75 [b]	$C_{18}H_{17}NO_2$	77.4 77.1	6.1 6.1	5.0 4.8
9e	H	(furyl)	63	oil	$C_{15}H_{13}NO_3$			
9f	(phenyl)	(phenyl)	67 63 [a]	155-158 [c]	$C_{23}H_{19}NO_2$	80.9 80.8	5.6 5.9	4.1 4.2
9g	H	$CH_3(CH_2)_3-$	48	oil	$C_{15}H_{19}NO_2$			
9h	(cyclohexyl)		27	oil	$C_{16}H_{19}NO_2$			
9i	(N-COPh piperidyl)		31	100-105	$C_{22}H_{22}N_2O_3$	72.9 72.6	6.1 6.4	7.7 7.9
9j	(dibenzo olefin)		48	159-161 [c]	$C_{25}H_{19}NO_2$	82.2 81.9	5.3 5.7	3.8 3.9
9k	(N-CH₃ indolinone)		52	227-230 [d]	$C_{19}H_{16}N_2O_3$	71.2 71.6	5.0 5.4	8.8 8.7

[a] Derived from the di-Grignard dianion. [b] Crystallized from ether/pentane. [c] Crystallized from methylene chloride/ether. [d] Crystallized from tetrahydrofuran.

Elemental and mass spectral analysis indicate that two equivalents of carbon dioxide are incorporated into the product. The ir spectrum shows a clear absence of an acetylenic absorption, which suggests a further reaction with the triple bond. Cyclization of the *N*-carboxy anion in intermediate **10** could, in principle, take place at either end of the acetylene to furnish the oxazolidine-2,4-dione **11** or the oxazine-2,4-dione **12**.
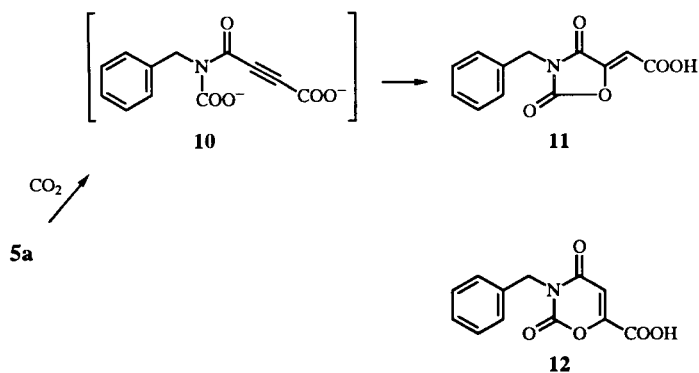
The ir spectrum of the cyclic adduct exhibits four absorptions in the carbonyl region (1850, 1750, 1705, and 1680 cm^{-1}). The absorptions at 1850 and 1750 cm^{-1} are characteristic of the 2- and 4-C=O vibrations in an oxazolidine-2,4-dione [5]. The carbonyl frequencies in **12** would be expected to fall at lower wavenumbers. The absorptions at 1705 and 1680 cm^{-1} are assigned to the acid carbonyl and C=C stretching vibrations respectively.

Being confident of the formation of the five-membered ring, the question of the isomeric relationship of the carboxylic acid remains to be resolved. Chemically, the Z-isomer should preferentially be produced if the cyclization of **10** follows the rule of *trans*-nucleophilic addition [6-8]. In the ^{1}H-nmr spectrum, the olefinic proton appears as a sharp singlet at δ 6.0 suggesting that only a single isomer is present. Analysis of the ^{13}C-nmr spectrum, whose shifts are shown in Figure 1, provides some insight into the olefin geometry. The coupled spectrum indicates that the value of the long range CH coupling of the olefinic proton to the carbonyl carbon in the 4-position of the ring is rather small (J = 4.4 Hz). A coupling constant of this magnitude suggests a *cis*- relationship of the proton to the carbonyl therefore supporting the structure of the Z-isomer as shown. The E-isomer would be expected to exhibit a larger J value [9].

The silation of **5a** can readily be achieved in high yield by treatment with chlorotrimethylsilane. In this manner, *N*-benzyl-3-trimethylsilyl-2-propynamide (**13**) is produced
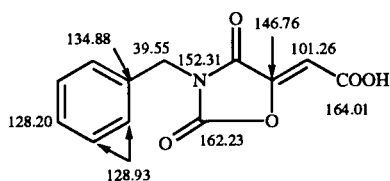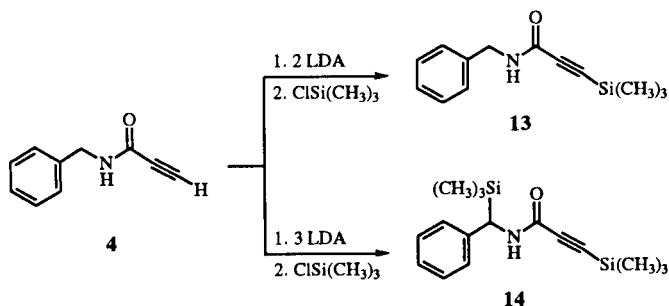
Figure 1.

in 87% yield. Analogous treatment of trianion **6** with an excess of chlorotrimethylsilane furnishes crude **14** in 95% yield. Gas chromatography indicates that the material is 90-95% pure. Attempts to purify **14** by column chromatography results in a significantly lower yield probably due to the relatively labile benzylic trimethylsilyl functionality.

Catalytic hydrogenation of **9a** and **9f** in the presence of platinum oxide at one atmosphere affords **15a** and **15b** in 50% and 89% yields respectively. Partial reduction of the acetylene to the *cis*-olefin **16a-d** can be readily accomplished with yields in excess of 90% by use of palladium-on-calcium carbonate as the catalyst. These compounds are rather unstable and slowly decompose on standing at room temperature. Appreciable degradation occurs even after 24 hours. An analogous reduction of **9j** furnishes **18** in 67% yield and this compound appears to be stable.

If intermediates **16a-d**, immediately after isolation, are refluxed in toluene for periods of 3-18 hours (see Table 2), rearranged products **17a-d** are produced. The formation of **17** may arise as a result of a 1,5-sigmatropic rearrangement as shown below.
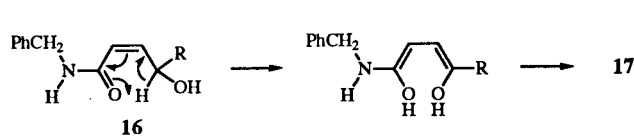
Saturation of the acetylene moiety of silyl adduct **13** can be accomplished either partially [10] by catalytic hydrogenation over palladium-on-calcium carbonate to give **19** (54% yield) or fully with platinum oxide at 3.5 atmospheres to afford **20** in 68% yield.

Chemistry of Adducts.

Since the adducts derived from the reactions of the dianions with various electrophiles represent potentially interesting intermediates, some further chemistry was performed with these compounds.
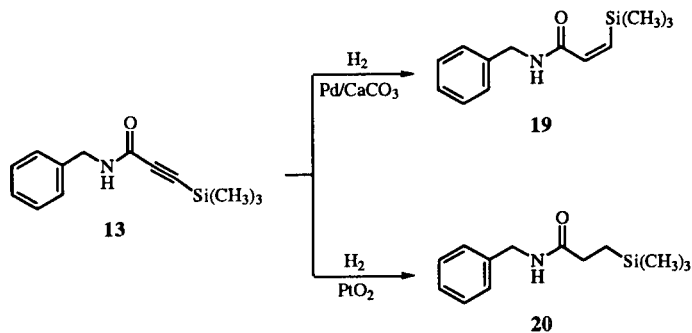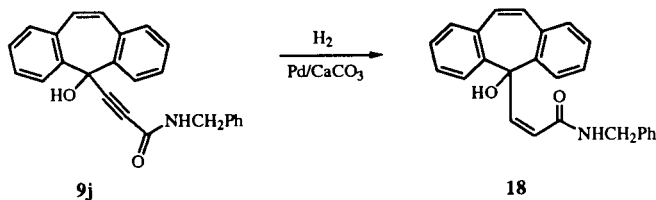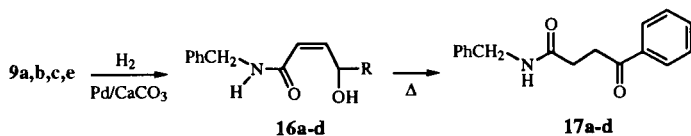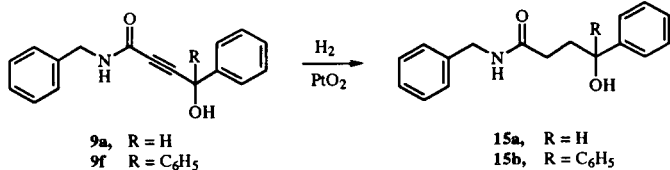
During the course of ^{13}C-nmr spectral analysis of **11** it was observed that the sample, after a period of several days in solution (DMSO-d_6), slowly began to change and new carbon signals began to appear in the ^{13}C-nmr spectrum. Within two weeks, virtually none of **11** remained. Heating the sample hastened the process and gas evolution (presumably carbon dioxide) occurred.

To investigate this transformation, a sample of **11** was heated in moist DMSO for 3 days at 60° at which point the reaction appeared complete. The [1]H-nmr spectrum reveals three main signals; a broad singlet at δ 7.3 (6H including one exchangeable), a doublet at δ 4.4 (2H), and a singlet at δ 2.45 (3H). The ^{13}C-nmr spectrum (see
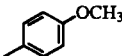
Table 2

Rearrangement of **16** to 4-ketoamides **17**

No.	R	Starting Material	Reaction time, hours	Yield, %	Mp,°C	Formula	Analysis Calcd. (Found)		
							%C	%H	%N
17a	(phenyl)	9a	3	95	107-109	$C_{17}H_{17}NO_2$	76.4	6.4	5.2
							76.6	6.3	5.1
17b	(4-Cl-aryl)	9b	6	83	132-135	$C_{17}H_{16}ClNO_2$	67.7	5.4	4.6
							67.3	5.8	4.4
17c	(4-OCH$_3$-aryl)	9c	18	72	111-113	$C_{18}H_{19}NO_3$	72.7	6.5	4.7
							72.3	6.1	4.7
17d	(furyl)	9e	7	48	106-109	$C_{15}H_{15}NO_3$	70.0	5.9	5.4
							70.4	5.7	5.4

Table 3

1H-NMRSpectral Data for Hydroxy Propiolamides **9**

No.	1H-NMR Spectrum (ppm)
9a	7.55-6.85 (m, 11H), 5.40 (s, 1H), 4.72 (s, broad, 1H), 4.19 (d, J = 5 Hz, 2 H)
9b	7.40-7.03 (m, 9H), 6.71 (m, 1H), 5.42 (m, 1H), 4.73 (m, 1H), 4.31 (d, J = 5 Hz, 2H)
9c	7.40 (m, 6H), 7.04 (q, 4H), 5.40 (d, J = 4 Hz, 1H), 4.89 (d, 1H), 4.28 (d, J = 5 Hz, 2H), 3.68 (s, 3H)
9d	7.43-7.00 (m, 9H), 6.71 (m, 1H), 5.43 (d, broad, 1H), 4.56 (d, broad, 1H), 4.33 (d, J = 5 Hz, 2H), 2.30 (s, 3H)
9e	7.32-7.15 (m, 7H), 6.43-6.10 (m, 2H), 5.48 (s, broad, 1H), 5.09 (s, broad, 1H), 4.29 (d, 2H)
9f	9.35 (m, 1H), 7.75-7.04 (m, 16H), 4.38 (d, J = 5 Hz, 2H)
9g	7.36 (s, 5H), 7.01 (m, 1H), 4.56-4.20 (m, 2H), 4.40 (d, J = 5 Hz, 2H), 1.83-0.72 (m, 9H)
9h	7.31 (s, 5H), 6.99 (m, 1H), 4.42 (d, J = 5 Hz, 2H), 4.10 (m, broad, 1H), 2.05-1.20 (m, broad, 10H)
9i	7.48-7.00 (m, 11H), 4.40 (s, 1H), 4.36 (d, J = 5 Hz, 2H), 3.60 (m, 4H), 1.82 (m, 4H)
9j	8.11-7.85 (m, 2H), 7.50-6.95 (m, 14H), 6.25 (m, 1H), 4.55 (s, 1H), 4.18 (d, J = 5 Hz, 2H)
9k	9.10 (m, 1H), 7.63-7.00 (m, 10H), 4.32 (d, J = 5 Hz, 2H), 3.20 (s, 3H)

experimental) indicates that the compound contains 10 carbon atoms of which two appear to be carbonyls. The mass spectrum produces a molecular ion at m/z 177 which corresponds to a molecular formula of $C_{10}H_{11}NO_2$. This data strongly suggests structure **21**. The structural assignment was corroborated by synthesizing an authentic sample of **21** by an alternate route [11].
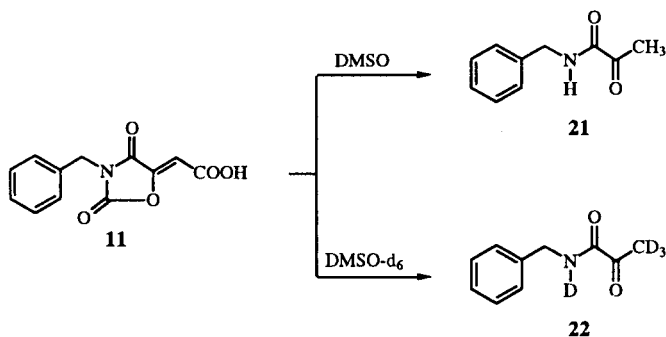
By analogy therefore the 1H-nmr sample in DMSO-d$_6$ must be the deuterated pyruvamide **22**. The lack of the methyl signal at δ 2.45 in addition to a molecular ion at m/z 181 supports the structure.

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° pulse angle (3 msec), 1.8 second pulse repetition time, and 16K time-domain points. The mass spectra were determined on LKB 9000 or Finnegan 4600 spectrometers either in EI or CI modes.

All carbanion generating reactions were conducted under argon atmosphere using tetrahydrofuran which was freshly distilled over lithium aluminum hydride.

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 **9** (Table 1).

To a solution of 0.05 mole of diisopropylamine in 300 ml of tetrahydrofuran at -30° was added 0.05 mole of *n*-butyllithium (1.6*M* in hexane). This solution was cooled to -65° then a solution of 0.05 mole of *N*-benzyl-2-propynamide (**4**) [1] in 50 ml of tetrahydrofuran was added dropwise. The mixture was allowed to warm to -20° (carbon tetrachloride/dry ice bath) and stirred there for 1 hour. To this was added dropwise a solution of 0.05 mole of the aldehyde or ketone in 50 ml of tetrahydrofuran and the mixture was stirred at -20° for 30 minutes. Saturated ammonium chloride solution was then added and the organic layer was separated. The aqueous phase was extracted with methylene chloride and the organic solutions were combined and dried over sodium sulfate. The solvent was removed under reduced pressure and the residue was chromatographed on a column of silica gel using 2% methanol/chloroform to elute the product.

3-Benzyl-2,4-dioxo-5-oxazolidinylacetic Acid (**11**).

To a solution of 2.5 g (0.025 mole) of diisopropylamine in 100 ml of tetrahydrofuran at -30° was added 1.67 g (0.026 mole) of *n*-butyllithium (1.6*M* in hexane). After cooling to -65°, a solution of 2.0 g (0.125 mole) of *N*-benzyl-2-propynamide (**4**) [1] in 20 ml of tetrahydrofuran was added dropwise. The mixture was warmed to -20° (carbon tetrachloride/dry ice bath) and stirred there for 1 hour after which time carbon dioxide gas was bubbled through the mixture for 20 minutes. Initially a green precipitate formed which slowly dissolved to produce a yellow solution. The flask was stoppered and the mixture was allowed to stir at room temperature under the carbon dioxide atmosphere for 48 hours. Saturated sodium chloride solution was added, then the mixture was acidified with 2*N* hydrochloric acid. The organic phase was separated and dried over sodium sulfate. The solvent was removed under reduced pressure and the residue triturated with methylene chloride to give 1.8 g (58%) of **11**, mp 179-181°; ir (potassium bromide): 1850, 1750, 1705, 1680 cm^{-1}; ^{1}H-nmr (DMSO-d$_6$): δ 14.0-12.0 (s, 1H, broad, COOH), 7.4 (s, 5H), 6.0 (s, 1H), 4.7 (s, 2H); ms: (70 ev) m/z 247 (M$^+$).

Anal. Calcd. for C$_{12}$H$_9$NO$_5$: C, 58.3; H, 3.7; N, 5.7. Found: C, 58.0; H, 3.4; N, 5.6.

N-Benzyl-3-trimethylsilyl-2-propynamide) (**13**).

Lithium diisopropylamide (0.1 mole) in 200 ml of tetrahydrofuran was generated as in the previously described examples. After cooling to -65°, a solution of 8.0 g (0.05 mole) of **4** in 50 ml of tetrahydrofuran was added dropwise then the mixture was stirred at -20° for 1 hour. To this solution was added 6.5 g of chlorotrimethylsilane (containing approximately 15% by weight of triethylamine) and the mixture was stirred at -20° for 3 hours. Saturated ammonium chloride solution was added and the organic phase was separated and dried over sodium sulfate. The solvent was removed under reduced pressure and the residue was chromatographed on a column of silica gel using chloroform to elute the product, 10.0 g (87%) of **13**. A sample was crystallized from ether/pentane, mp 73-76°; ir (chloroform): 3460, 3320, 2180, 1650 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 7.3 (s, 5H), 6.4 (m, broad, 1H), 4.45 (d, J = 6 Hz, 2H), 0.1 (s, 9H).

N-(α-Trimethylsilylbenzyl-3-trimethylsilyl-2-propynamide) (**14**).

Lithium diisopropylamide (0.03 mole) in 50 ml of tetrahydrofuran was generated as in the previously described examples.

After cooling to -65°, a solution of 1.6 g (0.01 mole) of **4** in 20 ml of tetrahydrofuran was added dropwise then the mixture was stirred at -20° for 1 hour. To this solution was added 3.3 g of chlorotrimethylsilane (containing approximately 15% by weight of triethylamine) and the mixture was stirred at -20° for 3 hours. Saturated ammonium chloride solution was added and the organic phase was separated and dried over sodium sulfate. The solvent was removed under reduced pressure to give 3.0 g (95%) of **14**. Chromatography on a column of silica gel, using methylene chloride to elute the product, furnished 0.9 g of analytically pure material (a glasslike solid); ir (chloroform): 3450, 3320, 2115, 1650 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 7.3-6.8 (m, 5H), 6.25 (m, 1H, NH), 4.55 (d, J = 10 Hz, 1H), 0.15 (s, 9H), -0.05 (s, 9H); ms: (70 ev) m/z 303 (M$^+$).

N-Benzyl-4-hydroxy-4-phenylbutanamide (**15a**).

A solution of 3.6 g (0.0136 mole) of **9a** in 100 ml of ethyl acetate was hydrogenated at one atmosphere over 0.5 g of platinum oxide for 6 hours. The catalyst was filtered from the mixture and the solvent was removed under reduced pressure. The residue was chromatographed on a column of silica gel using ethyl acetate to elute the product, 1.8 g (50%) of **15a**. An analytical sample was crystallized from methylene chloride/ether, mp 70-73°; ir (chloroform): 3620, 3460, 3330, 1655 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 7.25 (s, 5H), 7.21 (s, 5H), 6.6 (m, 1H), 4.8-4.4 (m, 1H), 4.38 (d, J = 4 Hz, 1H, OH), 4.27 (d, J = 6 Hz, 2H), 2.4-1.65 (m, 4H); ms: (70 eV) m/z 269 (M$^+$).

Anal. Calcd. for C$_{17}$H$_{19}$NO$_2$: C, 75.8; H, 7.1; N, 5.2. Found: C, 75.5; H, 7.2; N, 5.1.

N-Benzyl-4,4-diphenyl-4-hydroxybutanamide (**15b**).

A solution of 1.0 g (0.0029 mole) of **9f** in 100 ml of ethyl acetate was hydrogenated at one atmosphere over 0.1 g of platinum oxide for 3.5 hours. The catalyst was filtered from the mixture and the solvent was removed under reduced pressure to give 0.9 g (89%) of **15b**. An analytical sample was crystallized from methylene chloride/ether, mp 132-135° (lit [12] mp 132°); ir (chloroform): 3610, 3460, 1650 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 7.7-7.1 (m, 15H), 6.0 (m, 1H, NH), 4.35 (d, J = 6 Hz, 2H), 4.33 (s, 1H, OH), 2.8-2.1 (m, 4H).

Anal. Calcd. for C$_{23}$H$_{23}$NO$_2$: C, 80.0; H, 6.7; N, 4.1. Found: C, 79.8; H, 6.7; N, 3.8.

General Procedure for the Preparation of 4-Substituted-4-hydroxy-2-butenamides **16a-d**.

A solution of 0.01 mole of butynamide **9a**, **9b**, **9c**, or **9e** in 50 ml of ethanol was hydrogenated at one atmosphere over 0.25 g of palladium on calcium carbonate for 10-30 minutes until the theoretical amount of hydrogen had been absorbed. The catalyst was filtered from the mixture and the solvent evaporated under reduced pressure to give the product **16a-d**. These products were carried on to the next reaction without further purification.

General Procedure for the Preparation of 4-Substituted-γ-oxobutenamides **17a-d** (see Table 2).

A solution of 0.01 mole of **16** in 50 ml of toluene was refluxed for the amount of time specified in the table. The solvent was removed under reduced pressure and the residue was chromatographed on a column of silica gel using 2% methanol/chloroform to elute the product. All products were crystallized from methylene chloride/ether.

N-Benzyl-3-(5-hydroxy-5*H*-dibenzo[*a,d*]cyclohepten-5-yl)-2-propenamide (**18**).

A solution of 2.7 g (0.0074 mole) of **9j** in 50 ml of ethanol was hydrogenated at one atmosphere over 0.4 g of 5% palladium on calcium carbonate for 30 minutes. The catalyst was filtered from the mixture and the solvent was removed under reduced pressure. The residue was chromatographed on a column of silica gel using 1% methanol/chloroform to elute the product, 1.8 g (67%) of **18** as a glass-like solid; ir (chloroform): 3240 (very broad), 1635 cm⁻¹.

N-Benzyl-3-trimethylsilyl-2-propenamide (**19**).

A solution of 3.5 g (0.015 mole) of **13** in 100 ml of ethanol was hydrogenated at one atmosphere over 0.4 g of 5% palladium on calcium carbonate for 4 hours. The catalyst was filtered from the mixture and the solvent was removed under reduced pressure. The residue was chromatographed on a column of silica gel using hexane/ethyl acetate (2:1) to elute the product, 1.9 g (54%) of **19**, mp 68-72°; ir (chloroform): 3460, 1660 cm⁻¹; ¹H-nmr (deuteriochloroform): δ 7.2 (s, 5H), 6.4 (d, J = 13 Hz, 1H), 6.25 (m, 1H, NH), 6.1 (d, J = 13 Hz, 1H), 4.3 (d, J = 6 Hz, 2H), 0.2 (s, 9H).

Anal. Calcd. for $C_{13}H_{19}NOSi$: C, 66.9; H, 8.2; N, 6.0. Found: C, 66.2; H, 8.6; N, 6.2 (silicon forms a carbon complex which did not allow total carbon analysis).

N-Benzyl-3-trimethylsilyl-2-propynamide (**20**).

A solution of 4.0 g (0.0173 mole) of **13** in 100 ml of ethanol was hydrogenated at 3.5 atmospheres (50 psi) over 0.4 g of 10% palladium on carbon for 5 hours. The catalyst was filtered from the mixture and the solvent was removed under reduced pressure. The resulting oil was chromatographed on a column of silica gel using hexane/ethyl acetate (95:5) to elute the product, 2.8 g (68%) of **20** as an oil; ir (chloroform): 3465, 1660 cm⁻¹; ¹H-nmr (deuteriochloroform): δ 7.15 (s, 5H), 6.4 (m, 1H, NH), 4.25 (d, J = 6 Hz, 2H), 2.3-1.9 (m, 2H), 1.0-0.55 (m, 2H), -0.05 (s, 9H); ms: (70 eV) m/z 235 (M⁺).
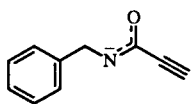
Anal. Calcd. for $C_{13}H_{21}NOSi$: C, 66.3; H, 9.0; N, 6.0. Found: C, 66.5; H, 9.4; N, 6.0.

N-Benzylpyruvamide (**21**).

To a solution of 0.5 g (0.002 mole) of **11** in 4 ml of dimethyl sulfoxide was added enough water until the solution turned cloudy. The mixture was then heated at 60° for 3 days. The solvent was removed at 40° under high vacuum and the resulting

oil was dissolved in methylene chloride. The solution was washed with 10% sodium bicarbonate and was dried over sodium sulfate. The solvent was removed under reduced pressure and the residue was chromatographed on a column of silica gel using chloroform to elute the product, 0.2 g (56%) of **21** as an oil; ir (chloroform): 3430, 1720, 1680 cm⁻¹; ¹H-nmr (deuteriochloroform): δ 7.3 (s, 6H, contains the NH proton), 4.4 (d, J = 6 Hz, 2H), 2.45 (s, 3H); ¹³C-nmr (deuteriochloroform): δ 197.5, 160.4, 137.3, 129.2, 128.2, 43.4, 24.6; ms (70 eV) m/z 177 (M⁺).

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