(C-5), 96.6 (C-3), 50.5 (OMe), 40.4 (C-8), 40 (C-4), 26.2 (Me), 22.4 (C-7).

3-Acetyl-6-methyl-2-phenyl-1,4,7,8-tetrahydroazocine (22c). **20c** (120 mg, 0.50 mmol) was thermolyzed for 20 h as described for **20a**. After evaporation the residue was recrystallized from 1:6 CH_2Cl_2/hexane, yielding 99 mg (82.5%) of enamine form **22c** as yellow needles: mp 166–167 °C; ^1H NMR δ (ppm) 1.46 (s, Ac), 1.72 (br s, Me), 2.49 (br t, J = 6.5 Hz, CH_2-7), 3.47 (d, J = 8.5 Hz, CH_2-4), 3.81 (br q, J = 6.5 Hz, CH_2-8), 4.5 (br, NH), 5.53 (tq, J = 8.5, 1.5 Hz, H-5), 7.39 (m, H-2); ^{13}C NMR δ (ppm) 198.1 (C=O), 161.8 (C-2), 141.3 (C-6), 128-134 (Ph), 122.8 (C-5), 109.7 (C-3), 44.6 (C-8), 36.9 (C-4), 29.9 (Ac), 25.9 (Me), 25.8 (C-7). Imine tautomer **21c**: ^{13}C NMR δ (ppm) 204.1 (C=O), 166.1 (C=N), 127–137 (Ph), 119.6 (C-5), C-6 not resolved, 66 (C-3), 50.2 (C-8), 33.8 (C-4), 29.6 (Ac), 27.5 (Me), 26.2 (C-7). Anal. Calcd for $C_{16}H_{19}NO$ (241.34): C, 79.63; H, 7.94; N, 5.80. Found: C, 79.74; H, 8.02; N, 5.84. MS, EI (24 eV), m/e (relative intensity) 241 (20, M^+), 226 (4), 198 (100), 170 (41), 156 (20), 83 (52).

Acknowledgment. We thank Dr. H. E. Gottlieb for helping interpretation of NMR-spectra, Dr. K. Murthy for valuable assistance and the Minerva Foundation for fellowship support (to N.W.). A grant from the Israel Academy of Sciences and Humanities in support of this research is greatfully acknowledged.

Registry No. **5a**, 96-33-3; **5b**, 78-94-4; **5c**, 107-13-1; **5d**, 20451-53-0; **5e**, 5535-48-8; **9c**, 16939-57-4; **10a**, 20012-94-6; **10b**, 103564-07-4; **10c**, 103564-07-4; **11a**, 103564-08-5; **11b**, 103564-09-6; **11c**, 103564-10-9; **12**, 103564-11-0; **13a**, 103564-12-1; **13b**, 103564-13-2; **13c**, 103564-14-3; **13d**, 103564-15-4; **13e**, 103564-16-5; **14**, 102-96-5; **15** (isomer 1), 103564-17-6; **15** (isomer 2), 103564-18-7; **16**, 17041-60-0; **17** (isomer 1), 103564-19-8; **17** (isomer 2), 103564-20-1; **19a**, 762-42-5; **19b**, 922-67-8; **19c**, 1817-57-8; **20a**, 103564-21-2; **20b**, 103564-22-3; **20c**, 103564-23-4; **21a**, 103564-24-5; **21c**, 103564-25-6; **22a**, 103564-26-7; **22b**, 103564-27-8; **22c**, 103564-28-9; $ClSO_2NCO$, 1189-71-5.

Reactions of Alkylidenecarbenes Derived from N,N-Disubstituted-2-oxopropanamides: The Formation of 3-Pyrrol-2-ones and 2-Butynamides

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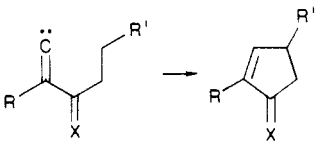
Activation of C–H bonds toward insertion by an alkylidenecarbene was examined in the reaction of N,N-disubstituted-2-oxopropanamides with diethyl (diazomethyl)phosphonate under basic reaction conditions. The intermediate alkylidenecarbene expected to be formed yielded two types of products, viz., 3-pyrrol-2-ones and 2-butynamides. A solvent effect that alters the relative ratio of the two products was observed. A mechanistic interpretation is offered for this effect and for the ratio of pyrrolones obtained from 2-oxopropanamides that are unsymmetrically substituted at nitrogen.

Development of methodologies for the formation of five-membered rings has recently been of considerable interest, primarily because of efforts to synthesize polyquinoids.[1] One of the approaches that has received increasing attention involves generation of a carbene and its subsequent intramolecular 1,5 C–H insertion.[2-4] For example, such an insertion reaction of alkylidenecarbenes (R_2C=C:), 1,[5] yields cyclopentenes and cyclopentenones (eq 1).[2]



X = H_2, O (1)

Several different synthetic approaches to alkylidenecarbenes have been developed, and they appear to produce intermediates sharing some common trends in their reactivities.[2] Preeminent among these is the preference for insertion into a tertiary C–H bond over a secondary C–H bond, which in turn is greatly favored over a primary C–H bond.[2d,i,k] On a first-order basis, the observed selectivity can be ascribed to the differences in bond dissociation energies of the various C–H bonds.[6] The present paper describes investigations intended to probe further the role of bond dissociation energies in defining the success of C–H insertion by alkylidenecarbenes **1**. Of particular interest was the possibility that heteroatoms would activate C–H bonds α to them toward the insertion reaction.

The effect of a heteroatom on the strength of a C–H bond α to it is substantial, as reflected in the reported bond

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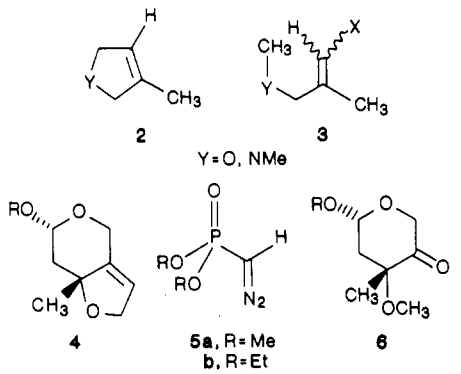
Table I. N,N-Disubstituted-2-oxopropanamides 9: Structure and Properties

entry	R^1	R^2	R^4	yield, %	bp (mmHg)/mp[a]	solid derivative (mp)[a]
a	H	H	H	78	105 (31)	
b	H	*n*-propyl	H	82	145–150 (31)	semicarbazone (168–169)
c	H	phenyl	H	86	125–130 (0.05)	2,4-DNP (177–178)
d	CH_3	CH_3	H	78	135 (31)	2,4-DNP (128–129)
e	$-(CH_2)_3-$		H	86	155–160 (31)	2,4-DNP (177–178)
f	$-(CH_2)_3-$		CH_3	72	95 (0.1)	semicarbazone (186–187)
g	$-CH_2CH(Bu\text{-}t)CH_2-$		H	80	115–120 (0.05)/36–37	

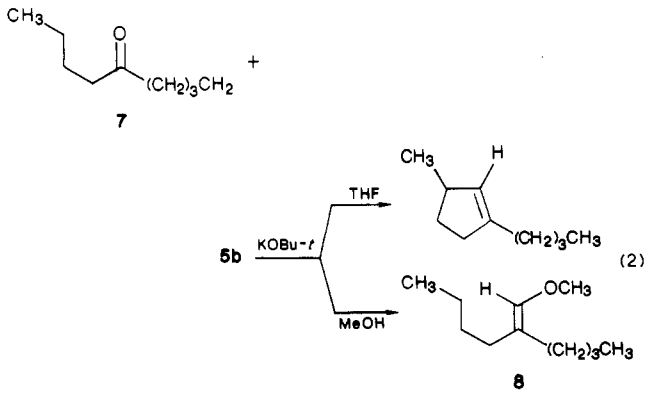
[a] Boiling and melting points are in °C.

dissociation energies for $H-CH_2OH$ and $H-CH_2NH_2$ of 93[6] and 94[7] kcal/mol, corresponding to stabilization energies[7] of 10 and 9 kcal/mol, respectively. These values are similar to those of secondary and tertiary aliphatic C–H bonds (94.5 and 91 kcal/mol, respectively[6]), and, according to a model based on bond dissociation energies, would make the 1,5 C–H insertion reaction into a *primary* H–C–Y bond, where Y is either N or O, of comparable efficiency to that into a secondary or tertiary H–C–C bond.

This anticipated activating effect of a heteroatom on the lability of a C–H bond α to it toward insertion by a carbene has experimental precedent. For example, insertion into a primary C–H bond occurs in very low yields in the absence of an α heteroatom.[2d,i] Bottini and Walsh, however, have noted the formation of **2** (Y = NCH_3), among other



products, in 17% yield upon reaction of **3** (Y = NCH_3) with KOBu-t[4a] and Hauske et al. obtained an 84% yield of the erythromycin A derivative **4** by the base-promoted reaction of dimethyl (diazomethyl)phosphonate (DAMP, **5a**) with the ketone **6**.[4b] Importantly, the cyclization of **6** proceeds without alteration in the presence of allyl alcohol, a carbene trap.[8] We had previously found that the cyclization of the alkylidenecarbene derived from the reaction of ketone **7** and DAMP, **5b**, under basic conditions in tetrahydrofuran (THF) as solvent, is quenched in the presence of methanol and yields the methyl enol ether **8** (eq 2).[2k] The



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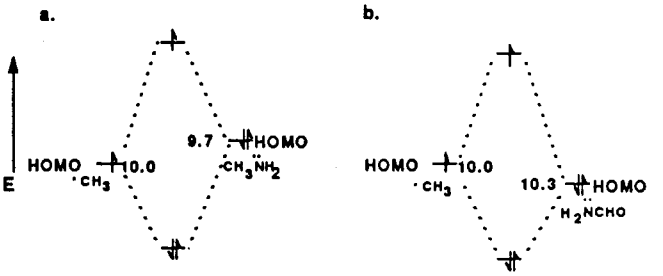

Figure 1. Interaction diagrams for transition states of insertion reaction.

preference of the carbene derived from **6** for *intramolecular* 1,5 C–H insertion to the exclusion of *intermolecular* O–H insertion signifies an important role of the heteroatom and suggests a possibly significant contribution of entropic factors (vide infra).

The purpose of the present work was to investigate activation of a C–H bond α to an amido nitrogen atom toward reaction with an alkylidenecarbene. The dissociation energy of this type of bond is unreported, but predictions based upon principles of PMO theory[9] support the supposition that the heteroatom effect on such energies, as noted for methylamine, should persist in amides. The necessary arguments can be developed by assuming that the transition state for C–H bond dissociation is radical-like, so that an important factor defining its energy will be interaction between a carbon-based radical and the nonbonding electron pair on nitrogen. Using the values of 9.7 eV,[10] 10.3 eV,[11] and 10.0 eV[12] for the vertical ionization potentials of methylamine, formamide, and methyl radical, respectively, the interaction diagrams shown in Figure 1 can be developed. It can be seen by this first-order analysis that comparable stabilization of the radical by orbital mixing should obtain in both systems.[13] Consequently, it is reasonable to predict that the lowering of C–H bond dissociation energies known to be caused by an amino function (Figure 1a) should also be observed for amides (Figure 1b). Furthermore, an alkyl radical α to an amido nitrogen has been postulated as an intermediate by Shono and co-workers in the anodic oxidation of amides and carbamates.[14]

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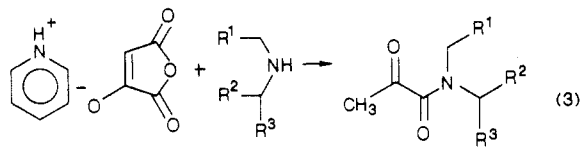
Table II. Product Distribution of Pyrrolones, 11 and 12, and Butynamides, 13

entry	amide	R^1	R^2	R^3	11 + 12[a]	11:12	13[a]	11:12[b]
1	**9a**	H	H	H	50		23	
2	**9b**	H	*n*-propyl	H	67 (43)[c]	70:30	32 (20)[c]	1.5:1.0
3	**9c**	H	phenyl	H	60 (56)[c]	80:20	35 (16)[c]	2.6:1.0
4	**9d**	CH_3	CH_3	H	67		31	
5	**9e**	$-(CH_2)_3-$		H	67		32	
6	**9f**	$-(CH_2)_3-$		CH_3	67 (63)[c]	50:50	32 (26)[c]	0.8:1.0
7	**9g**	$-CH_2CH(Bu\text{-}t)CH_2-$		H	70		29	

[a] Yield (%) as determined by ^1H NMR. [b] Statistically corrected ratio. [c] Isolated yield (%).

Results and Discussion

The expectation that the insertion reaction would be most efficient in cases in which the α amido C–H bond is four atoms away from the incipient carbene center[2k] dictated the selection of α-keto amides as substrates for our studies. Such compounds having a variety of alkyl or aryl substituents are readily prepared by reaction of a secondary amine with pyridinium hydroxymaleic anhydride[15] as described by Wohl and Osterlin (eq 3).[16] Table I

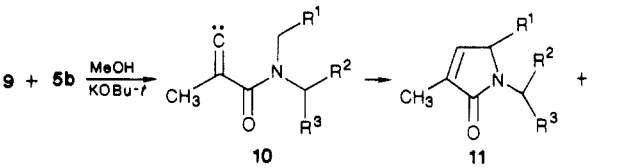


(3)

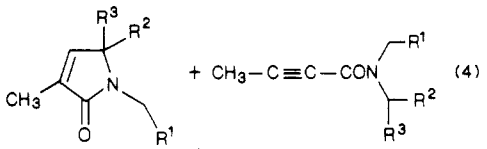
9

displays the N,N-disubstituted-2-oxopropanamides **9** prepared for this study along with isolated yields and some of their relevant physical constants. All of the previously unreported amides gave spectral data that were entirely consistent with their assigned structures (see Experimental Section).

Reaction of the N,N-disubstituted-2-oxopropanamides **9** with DAMP (**5b**), under the basic conditions expected[17] to produce the intermediate alkylidenecarbene **10**, afforded two types of products (eq 4). The predominant of these



10 **11**

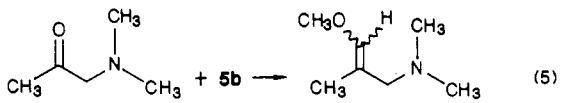


(4)

12 **13**

were the 3-pyrrol-2-ones **11** and **12**, the result of the anticipated 1,5 C–H insertion of **10**, and the other proved to be the 2-butynamides **13**, presumably arising from a 1,2 shift in **10**.[4c] A summary of the results obtained for the series of propanamides is found in Table II.[18]

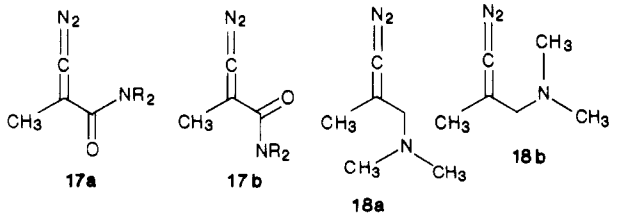
In no case was it possible to detect the methyl enol ether **14** that would have resulted from trapping of **10** by the solvent; it is estimated that the method used to probe for such a product, spectroscopy of crude reaction mixtures, would have shown the presence of as little as 5% of it had it been present. The preference of the alkylidenecarbene **10** for intramolecular 1,5 C–H insertion relative to intermolecular O–H insertion correlates with the aforementioned observation of Hauske et al. in the cyclization of the related carbene derived from **6**[4b] and is in sharp contrast to the results in aliphatic systems as illustrated in eq 2. Although such selectivity may be due solely to enthalpic factors associated with the presence of an activating heteroatom α to the site of insertion, there is evidence that entropic considerations are also of significance in the process. Specifically, the reaction of 1-(*N*,*N*-dimethylamino)-2-propanone (**15**) with DAMP and methanolic base provided the methyl enol ether (**16**) in 25% yield (eq 5); no C–H insertion product could be detected.



(5)

15 **16**

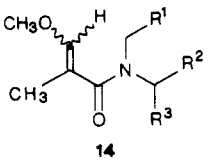
The formation of an enol ether from **15** but not from the α-ketopropanamides **9** is explained most economically by consideration of potential differences in conformational factors in the two systems. It is expected that the diazoalkenyl intermediate **17** derived by reaction of **9** with DAMP will be planar or nearly so in order to maintain optimal π-delocalization in the system. Should **17** preferentially adopt the s-trans conformation, **17a**, in order to minimize dipole–dipole repulsions, subsequent deazotization gives birth to an alkylidenecarbene that has its carbenic carbon atom in close proximity to the C–H bond that is subject to insertion. The corresponding diazo compound **18**, arising from **15**, is not as constrained conformationally as **17** and therefore more frequently decomposes to conformers, e.g., **18a**, that are inappropriate for successful



17a **17b** **18a** **18b**

intramolecular C–H insertion; consequently, intervention of solvent becomes more probable and production of enol ether results. Note that a comparable argument can be developed for the system investigated by Hauske et al.[4b]

Entries 2 and 3 of Table II, which contain data for unsymmetrically substituted amides, show that the normal trend in relative reactivities of C–H bonds toward alkylidenecarbenes noted earlier is not seen with **10**. Indeed, taken at face value the results would seem to suggest that primary C–H bonds are the *most* reactive toward the carbene. Such an interpretation, however, neglects the



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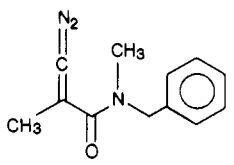
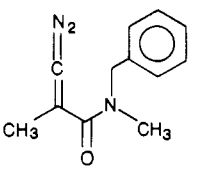
(16) Wohl, A.; Oesterlin, C. *Chem. Ber.* **1907**, *40*, 2312.
(17) Gilbert, J. C.; Weerasooriya, U. *J. Org. Chem.* **1982**, *47*, 1837.
(18) All new compounds were consistent with their structural assignment by their ^1H NMR, ^{13}C NMR, MS, HRMS, and IR spectra.

crucial role played by the conformational factors that define which of the two *N*-alkyl substituents is syn to the carbenic center at the time of reaction. Since it is probable that rotation associated with the amido group of the alkylidenecarbene **10** is not competitive with the rate of decomposition of **10** to products, the necessary analysis can be developed on the immediate precursor to **10**, the diazoalkene **17**.

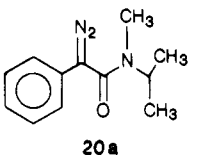
As noted above, the preferred conformation of **17** is **17a**, the same as that necessary for the insertion reaction. Unsymmetrical substitution of the amido nitrogen atom of such a conformer results in the existence of two rotamers, as illustrated by **19a** and **19b**, derived from reaction of **9c** and the anion of **5b**. Any energetic differences



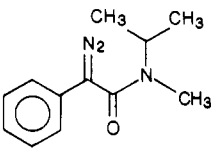
19a



19b



20a

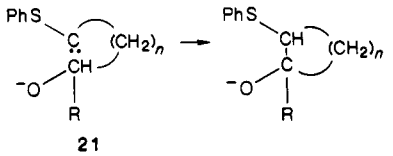


20b

between **19a** and **19b** would appear to be primarily associated with steric factors. Clearly, if the carbonyl oxygen is sterically less demanding than the diazoalkenyl group, conformer **19a** will be preferred since it has the smaller *N*-alkyl group syn to the latter functionality. Consequently, the favored C–H insertion product will be that derived from insertion into the smaller alkyl group.

Support for the assignment of relative steric requirements in **19** comes from unpublished studies of Rando.[19] By the use of low-temperature ^{1}H NMR spectroscopy, he was able to determine that **20a** was the more stable conformation of *N*-methyl-*N*-isopropyl-2-diazophenylacetamide (**20**) and concluded that steric factors accounted for the preference.

The activation of a C–H bond toward the insertion reaction by an α heteroatom may be due to initial complexation between the carbenic center and the heteroatom. Oku et al. have postulated such complexation to account for the regioselectivity observed in intramolecular C–H insertion reactions of carbenoids **21** (eq 6).[3i] However, our

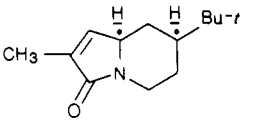


(6)

21

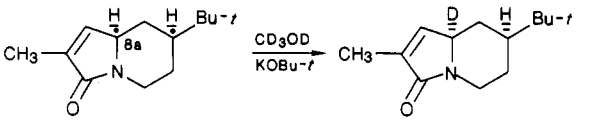
preferred interpretation of the effect is that orbital interaction between the nonbonded electrons of the heteroatom and the C–H bond α to it (Figure 1) provides significant stabilization at the transition state for the insertion process.

The results in entry 7 of Table II are of interest with respect to a possible stereochemical feature of the insertion process. As noted there, reaction of 1-(1,2-dioxopropyl)-4-(1,1-dimethylethyl)piperidine (**9g**) with DAMP yielded only the cis form of the bicyclic product **11g**, in addition to alkyne. The structural determination of **11g** was accomplished by use of two-dimensional homonuclear correlated spectroscopy (COSY)[20] and a series of proton decoupling experiments.



11g

Consideration of the relative strengths of the two types of C–H bonds leads to the prediction that insertion into the axial bond to produce the trans isomer should be preferred. This is because it is acknowledged that a C–H bond anti to the nonbonding electron pair on a nitrogen atom is weaker than one that is gauche to it,[21] although the source of the effect is not settled.[22] Therefore, the observed formation of the cis isomer may signal an unanticipated conformational requirement for the insertion reaction of the alkylidenecarbene that makes the equatorial C–H bond the more susceptible to the three-centered insertion process.[2j,m] A more likely explanation of the apparent stereoselectivity, in our opinion, is that the trans isomer is formed initially but is isomerized to the thermodynamically more stable cis isomer under the basic reaction conditions. The unavailablility of the trans isomer made a direct experimental test of this possibility impossible, but indirect support for its potential lability under the reaction conditions was provided by the observation that the proton at C-8a of the cis isomer underwent facile exchange with deuterium in the presence of base (eq 7).



(7)

11g **11g-D**

A viable pathway for the hypothesized trans to cis isomerization is thus available if it is assumed that the former isomer has a kinetic acidity comparable to that of the cis product.

As indicated by the data in Table II, the ratio of alkyne to insertion product is essentially constant throughout the series of propanamides **9** examined. This observation is consistent with the hypothesis that a common precursor is responsible for both types of products. This species most reasonably is the alkylidenecarbene **10**, which simply partitions between two unimolecular processes, C–H insertion, and 1,2 migration.

Because alkyl groups are loathe to migrate in alkylidenecarbenes,[23] it was thought that 1,2-shift of the carbamoyl moiety must be responsible for formation of the 2-butynamides. An experimental test of this proposal should be available from a labeling study in which the diazomethyl carbon atom of DAMP was enriched in carbon-13. If the migrating species leading to a 2-butynamide were the carbamoyl moiety, as suggested, then C-2 of the butynamide would retain all of the isotopic enrichment; the label

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(20) (a) Bax, A.; Freeman, R. R. *J. Magn. Reson.* **1981**, *44*, 542. (b) Review: Gunther, H.; Benn, R. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 350.

(21) (a) Hamlow, H. P.; Okuda, S.; Nagakawa, N. *Tetrahedron Lett.* **1964**, 2553. (b) Skolik, J.; Krueger, P. J.; Wiewiorowski, M. *Tetrahedron* **1968**, *24*, 5439. (c) Konarski, J. *J. Mol. Struct.* **1970**, *5*, 389. (d) Katritzky, A. R.; Taylor, P. J. *Phys. Methods Heterocycl. Chem.* **1971**, *21*, 245, 341. (e) Ernstbrunner, E. E.; Hudec, J. *J. Mol. Struct.* **1973**, *17*, 249.

(22) Wolfe, S.; Schlegel, H. B.; Whangbo, M.-H.; Bernardi, F. *Can. J. Chem.* **1974**, *52*, 3787.

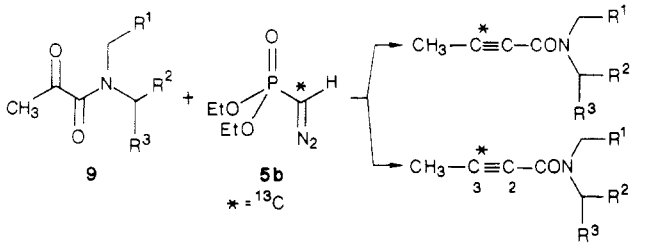
(23) See ref 17 and sources cited therin.

Table III. Effect of Solvent on the Ratio of 11a:13a

solvent	dielectric const[25]	insertion:rearranged[a]	combined yield[a]
dioxane	2.21	8.8:1	59
t-BuOH	12.47	4.3:1	63
MeOH	32.7	2.2:1	73
MeCN	36.5	1.2:1	37
water	78.5	0.6:1	31

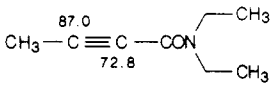
[a] Ratio and yield (%) as determined by ^{1}H NMR analysis.

would reside at C-3 if the unexpected migration of the methyl group were to occur (eq 8).



(8)

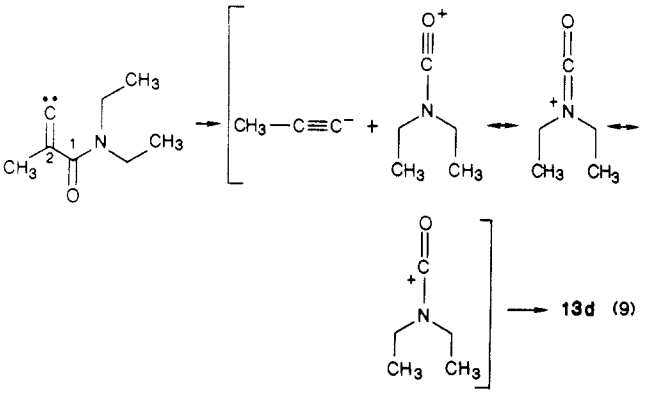
The substrate selected for this experiment was *N,N*-diethyl-2-oxopropanamide (**9d**), the alkynic product from which is *N,N*-diethyl-2-butynamide (**13d**). Since it was not possible to make an unambiguous assignment in **13d** of the two alkynyl carbon resonances at 87.0 and 72.8 ppm on the basis of literature data, a H-coupled ^{13}C NMR experiment was performed to make this determination. This experiment revealed that the downfield resonance was split into a quartet, J_{C-H} = 10.3 Hz, indicating two-bond coupling with the C-4 methyl protons, and that the resonance at 72.8 ppm was only broadened. Therefore, the resonance at 87.0 ppm was assigned to C-3 of the butynamide.



Reaction of **9d** with ^{13}C-enriched DAMP provided **13d** having all of the isotopic enrichment contained at C-2, within experimental error (see Experimental Section). Thus, the supposition that the migrating species in **10** would be the carbamoyl function is confirmed.

Further investigation into the mechanism of the reaction leading to the formation of pyrrolones and butynamides (eq 4) revealed a solvent effect that alters the relative ratio of the two products. As can be seen from the data contained in Table III, an increase in the dielectric constant of the solvent for the reaction results in a corresponding increase in the ratio of butynamide to pyrrolone.[24]

A mechanism that incorporates charge separation in the transition state is expected to become more favorable as the polarity of the solvent increases,[26] so the influence of solvent on the product distribution in the present case can be accounted for by invoking separation of charge in the transition state that leads to the butynamide. At the extreme, this can be achieved by proposing that heterolytic cleavage of the C-1, C-2 σ bond of the intermediate carbene, **10**, occurs to generate an ion pair constituted of an acetylide ion and a delocalized carbamoylonium ion; subsequent covalent bond formation by union of the ion pair produces the butynamide (eq 9).[27] In polar solvents,



(9)

therefore, the rate of formation of the butynamide from alkylidenecarbene **10** should increase faster than that for production of the insertion product, which does not involve as highly polarized a transition state.

As a synthetic method for the formation of 3-pyrrol-2-ones, the reaction described herein is best suited for substrates in which the nitrogen atom of the 2-oxopropanamide is symmetrically substituted. The production of butynamides as minor byproducts represents a drawback of this methodology, but separation of them from the desired pyrrolones by chromatographic means is straightforward. Advantages of the present approach over other methods for the production of 3-pyrrol-2-ones include the lack of formation of other isomeric pyrrolones and the availability of increased options with respect to the nature of substituents on the heterocycle. Previously reported methods for the synthesis of 3-pyrrol-2-ones are marred by structural limitations[28] or by generation of isomeric mixtures of 3- and 4-pyrrolones.[29]

Experimental Section

All IR spectra were recorded on a Beckman IR-5A spectrophotometer; the polystyrene absorption at 1944 cm^{-1} was used as reference. Samples were run as liquid films between salt plates; only major absorptions are reported and values are in cm^{-1}.

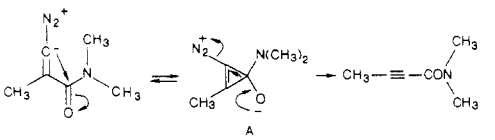
^{1}H NMR spectra were measured with a Varian EM-390, Nicolet NT-200, or Nicolet NT-360 spectrometer. The proton correlated spectrum was obtained on a Nicolet NT-360 spectrometer. The ^{1}H NMR assignments are described with the abbreviations s (singlet), d (doublet), t (triplet), q (quartet), p (pentuplet), b (broad). ^{13}C NMR spectra were recorded with a Bruker WH-90 spectrometer. Chemical shifts are reported in units of δ downfield of an internal standard, which was tetramethylsilane unless otherwise noted. ^{13}C NMR data are given with $CDCl_3$ as internal lock unless otherwise noted. Chloroform-*d* was used as the solvent

(24) The observed ratio for the series of solvents tested was also checked against the values of π^*, AN, and DN[25] but no correlation with these solvent parameters was evident.

(25) Lowery, T. H.; Richardson, K. S. *Mechanism and Theory in Organic Chemistry*, 2nd ed.; Harper and Row: New York, 1981; p 163.

(26) Szwarc, M. In *Ions and Ion pairs in Organic Reactions*; Szwarc, M., Ed.; Wiley-Interscience: New York, 1972.

(27) Another mechanism leading to the 2-butynamide that may account for the effect of solvent on the ratio of products is shown below.



The intermediate A, having the requisite separation of charge to conform with the observed solvent effect, is disfavored, however, due to energy considerations associated with the cyclization to the cyclopropene.

(28) (a) Black, D. St. C.; Blackman, N. A.; Johnstone, L. M. *Aust. J. Chem.* **1979**, *32*, 2041. (b) Farina, F.; Martin, M. V.; Paredes, M. C. *Heterocycles* **1984**, *22*, 1733. (c) Kricheldorf, H. R.; Regel, W. *Chem. Ber.* **1973**, *106*, 3753. (d) Guzman, A.; Muchowski, J. M.; Saldana, J. *Chem. Ind. (London)* **1977**, *9*, 357.

(29) (a) Masure, D.; Rio, G. *Bull. Soc. Chim. Fr.* **1972**, 4598. (b) Baker, J. T.; Sifiniades, S. *J. Org. Chem.* **1979**, *44*, 2798.

(30) (a) Aoyama, H.; Sakamoto, M.; Kuwabara, K.; Omote, Y. *J. Am. Chem. Soc.* **1983**, *105*, 1958. (b) Ozawa, F.; Yamamoto, A. *Chem. Lett.* **1982**, 865.

for both proton and carbon spectra.

Mass spectra (MS) were obtained with a Du Pont (CEC) 21-471 double-focusing mass spectrograph operating at 70 eV. Exact mass measurements were obtained with a Du Pont (CEC) 21-110 instrument.

All melting points were taken on a Thomas-Hoover capillary melting point apparatus and are uncorrected. Liquid samples were purified by distillation in a Kugelrohr apparatus; the boiling points quoted pertain to the oven temperature.

High-pressure liquid chromatography (HPLC) was performed on a Waters 6000A instrument with two contiguous 2 ft × $^1/_4$ in. columns packed with LC Porasil (type A) silica gel. The eluent used was 30% ethyl acetate–70% Skelly B.

Preparative GC was executed on a Varian Model 90-P gas chromatograph equipped with a thermal conductivity detector. Helium was used as the carrier gas at a rate of 60 mL/min. The following columns were used: A, 0.6 m × 0.25 in., 20% SF-96 on 60/80-mesh Chromosorb G column at an operating temperature of 140 °C; B, 1 m × 0.25 in., 50% Carbowax on 60/80-mesh Chromosorb P-A at an operating temperature of 160 °C.

A Finnigan-MAT 4023 gas chromatograph–mass spectrograph (GCMS) was used for analysis of **16**. The chromatograph contained a 40-m DB1 capillary column operating at 20 psi with helium as the carrier gas. Temperature programming: 40 °C, 1 min, to 280 °C at 10°/min. The ionizing voltage was 70 eV.

All reagents and solvents were purified and distilled according to standard methods unless otherwise specified. Skelly B was stirred over sulfuric acid for 24 h, over sodium carbonate for 12 h, and then was filtered and distilled.

2-Oxopropanamides 9. The 2-oxopropanamides **9** were prepared by using the procedure described by Wohl and Osterlin.[16]

***N,N*-Dimethyl-2-oxopropanamide (9a).** The material isolated was identical in all respects with that previously reported.[30a]

***N*-(1-Butyl)-*N*-methyl-2-oxopropanamide (9b):** ^{1}H NMR 3.40/3.27 (t, 2 H, NCH_2), 2.98/2.96 (s, 3 H, NCH_3), 2.41 (s, 3 H, CH_3CO), 1.60/1.34 (m, 2 H, NCH_2CH_2), 0.95 (m, 5 H, CH_2CH_3); ^{13}C NMR 199.20, 198.74, 167.14, 166.55, 49.62, 47.02, 34.99, 32.32, 30.44, 28.81, 27.77, 27.51, 19.96, 19.77, 13.79, 13.66; IR 2960, 1730, 1650; MS, *m/z* (relative intensity) 157 (M^+, 1.7) 114 (M – CH_3CO, 100); HRMS calcd for $C_8H_{15}NO_2$ 157.1102, found 157.1099. Combustion analysis of semicarbazone derivative[31] (mp 168–169 °C). Calcd for $C_9H_{18}N_4O_2$: C, 50.45; H, 8.47; N, 26.15. Found: C, 50.20; H, 8.61; N, 26.29.

***N*-Methyl-*N*-(phenylmethyl)-2-oxopropanamide (9c):** ^{1}H NMR 7.27 (m, 5 H, Ar H), 4.55/4.44 (s, 2 H, NCH_2), 2.77/2.75 (s, 3 H, NCH_3), 2.42/2.36 (s, 3 H, CH_3CO); ^{13}C NMR 198.74, 167.40, 166.81, 135.79, 129.03, 128.7, 127.92, 127.6, 127.01, 55.02, 53.33, 51.12, 50.47, 34.73, 34.6, 32.52, 27.77, 23.48; IR 3020, 2970, 1715, 1650 cm^{-1}; MS, *m/z* (relative intensity) 191 (M^+, 39.46), 91 (M – $C_7H_7^+$, 100); HRMS calcd for $C_{11}H_{13}NO_2$ 191.0946, found 191.0942; (2,4-dinitrophenyl)hydrazone[31] mp 177–178 °C.

***N,N*-Diethyl-2-propanamide (9d).** The material isolated is identical in all respects with that previously reported.[30,32] The solid derivative (2,4-dinitrophenyl)hydrazone was observed to have mp 128–129 °C.

1-(1,2-Dioxopropyl)piperidine (9e):[30] ^{1}H NMR 3.52 (t, 2 H, NCH_2), 3.33 (t, 2 H, NCH_2), 2.38 (s, 3 H, CH_3CO), 1.6 (m, 6 H, $-(CH_2)_3-$); ^{13}C NMR 199.20, 165.70, 46.82, 42.53, 27.83, 26.47, 25.43, 24.45; IR 2955, 1720, 1645 cm^{-1}; MS, *m/z* (relative intensity) 155 (M^+, 4.0), 112 (M – CH_3CO, 98), 69 (100); HRMS calcd for $C_8H_{13}NO_2$ 155.0946, found 155.0944; (2,4-dinitrophenyl)hydrazone mp 128–129 °C.

1-(1,2-Dioxopropyl)-2-methylpiperidine (9f): ^{1}H NMR 4.77, 3.92 (m, 1 H, $NCHCH_3$), 4.32/3.47 (dd, 1 H, NCH*H* equatorial), 3.19/2.81 (dt, 1 H, NCH*H* axial), 2.40/2.38 (s, 3 H, CH_3CO), 1.7 (m, 6 H, $-(CH_2)_3-$), 1.3/1.23 (d, 3 H, CH_3CH); ^{13}C NMR 199.33, 166.16, 166.03, 49.36, 44.03, 41.30, 36.29, 30.89, 29.72, 27.83, 26.27, 25.36, 18.86, 17.04, 15.54; IR 2950, 1725, 1645 cm^{-1}; MS, *m/z* (relative intensity) 169 (M^+, 1.29), 126 (M – CH_3CO, 100); HRMS calcd for $C_9H_{15}NO_2$ 169.1102, found 169.1098; semicarbazone mp 186–187 °C.

1-(1,2-Dioxopropyl)-4-(1,1-dimethylethyl)piperidine (9g): ^{1}H NMR 4.58 (bd, 1 H, NC*H*H equatorial), 3.83 (bd, 1 H, NC*H*H equatorial), 3.00 (bt, 1 H, NCH*H* axial), 2.6 (bt, 1 H, NCH*H* axial), 2.42 (s, 3 H, $CH_3C{=}O$), 1.78 (m, 2 H, NCH_2CH_2), 1.27 (m, 3 H, NCH_2CH_2CH), 0.92 (s, 9 H, $C(CH_3)_3$); ^{13}C NMR 198.58, 165.09, 46.58, 46.40, 42.24, 32.08, 27.50, 27.41, 27.02, 26.27; IR 2960, 2870, 1720, 1645, 1450, 1380, 1370, 1360, 1160, 980; MS, *m/z* (relative intensity) 211 (M^+, 0.79), 168 (M – CH_3CO 45.9), 57 (M $C_4H_9^+$, 100); HRMS calcd for $C_{11}H_{21}NO_2$ 211.1572, found 211.1576.

General Procedure for Insertion Reaction. To a solution of 1 mmol of 1,2-dioxopropanamide **9**, 2 mmol (0.28 mL, 0.356 g) of diethyl (diazomethyl)phosphonate (**5b**),[33] and 2 mL of methanol at −40 °C (anisole, dry ice) was added a solution of 2.7 mmol (0.3 g) of potassium *tert*-butoxide in 2 mL of methanol. After 2 min, the reaction mixture was allowed to warm slowly to 0 °C and was stirred for an additional 2 h. The mixture was warmed to room temperature, quenched with 10 mL water, and extracted with five 15-mL portions of ethyl acetate. The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated in vacuo to yield the crude products. Purification was achieved by distillation (Kugelrohr), during which the products co-distil, followed by high-pressure liquid chromatography. The isolated yields are shown below.

1,5-Dihydro-1,3-dimethyl-2(2*H*)-pyrrolone (11a). The ^{1}H NMR of **11** was identical in all respects with that reported previously.[34] ^{13}C NMR 171.80, 134.62 (overlapping olefinic carbon resonances), 52.61, 29.40, 11.38; MS, *m/z* (relative intensity) 111 (M^+, 98), 42 (100); HRMS calcd for C_6H_9NO 111.0684, found 111.0687.

1-(1-Butyl)-1,5-dihydro-3-methyl-2(2*H*)-pyrrolone (11b). The material was isolated in 26% yield: bp 75–80 °C/0.1 mmHg; ^{1}H NMR 6.68 (q, J = 2 Hz, 1 H, vinylic H), 3.83 (t, J = 2 Hz, 2 H, $NCH_2C{=}$), 3.46 (t, J = 7 Hz, 2 H, NCH_2CH_2), 1.91 (q, J = 2 Hz, 3 H, $CH_3C{=}$), 1.58 (m, 2 H, $CH_2CH_2CH_3$), 1.35 (m, 2 H, $CH_2CH_2CH_3$), 0.95 (t, J = 8 Hz, 3 H, CH_2CH_3); ^{13}C NMR 172.08, 136.11, 134.68, 50.66, 42.21, 30.89, 20.10, 13.79, 11.38; IR 2960, 2920, 2870, 1688, 1465, 1250 cm^{-1}; MS, *m/z* (relative intensity) 153 (M^+, 31.9), 110 (M – C_3H_7, 100); HRMS calcd for $C_9H_{15}NO$ 153.1153, found 153.1149.

1,5-Dihydro-1,3-dimethyl-5-(1-propyl)-2(2*H*)-pyrrolone (12b). The material was isolated in 17% yield: bp 75–80 °C/0.1 mmHg; ^{1}H NMR 6.63 (m, 1 H, vinylic H), 3.87 (m, 1 H, $NCHC_3H_7$), 2.95 (s, 3 H, NCH_3), 1.90 (t, J = 2 Hz, 3 H, $CH_3C{=}$), 1.85–1.25 (mm, 4 H, $CHCH_2CH_2CH_3$), 0.95 (t, J = 7 Hz, 3 H, CH_2CH_3); ^{13}C NMR 171.95, 139.76, 135.14, 61.91, 32.54, 27.05, 17.43, 14.05, 11.12; IR 2950, 2925, 2875, 1680, 1445 cm^{-1}; MS, *m/z* (relative intensity) 153 (M^+, 19.01), 138 (M – CH_3, 13.58), 110 (M – C_3H_7, 100); HRMS calcd for $C_9H_{15}NO$ 153.1153, found 153.1156.

1,5-Dihydro-3-methyl-1-(phenylmethyl)-2(2*H*)-pyrrolone (11c). This compound, bp 105–110 °C/0.1 mmHg, was isolated in 35% yield, and had ^{1}H NMR and IR spectra that were identical with those previously reported.[35] ^{13}C NMR (external D_2O lock) 171.04, 136.76, 135.01, 128.18, 127.79, 127.34, 127.07, 126.55, 49.30, 45.33, 10.34; MS, *m/z* (relative intensity) 187 (M^+, 100), 91 (M – $C_7H_7^+$, 86.34); HRMS calcd for $C_{12}H_{13}NO$ 187.0997, found 187.0999.

1,5-Dihydro-1,3-dimethyl-5-phenyl-2(2*H*)-pyrrolone (12c). The material was isolated in 21% yield: bp 105–110 °C/0.1 mmHg; mp 89–90 °C; ^{1}H NMR 7.35 (m, 3 H, Ar H), 7.12 (m, 2 H, Ar H), 6.63 (m, 1 H, vinylic H), 4.82 (bs, 1 H, $NCHC_6H_5$), 2.84 (s, 3 H, NCH_3), 1.98 (t J = 2 Hz, 3 H, $CH_3C{=}$); ^{13}C NMR 171.10, 140.60, 135.79, 134.53, 129.16, 128.83, 128.57, 127.21, 66.66, 27.38, 11.19; IR 3050, 3010, 2905, 1685, 1400 cm^{-1}; MS, *m/z* (relative intensity) 187 (M^+, 100), 172 (M – CH_3, 71.01); HRMS calcd for $C_{12}H_{13}NO$ 187.0997, found 187.0994.

1,5-Dihydro-3,5-dimethyl-1-ethyl-2(2*H*)-pyrrolone (11d): ^{1}H NMR 6.58 (m, 1 H, vinylic H), 4.02 (q, J = 7 Hz, 2 Hz, 1 H,

(31) Shriner, R. L.; Fuson, R. L.; Curtin, D. Y. *The Systematic Identification of Organic Compounds*, 5th ed.; John Wiley and Sons: New York, 1964; p 253.

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NCH), 3.78, 3.16 (dq, J = 15 Hz, 8 Hz, 2 diastereotopic H, NCH_2CH_3), 1.89 (t, J = 2 Hz, 3 H, CH_3CO), 1.23 (d, J = 7 Hz, 3 H, $CHCH_3$), 1.17 (dd, J = 8 Hz, 8 Hz, 3 H, CH_2CH_3); ^{13}C NMR (external D_2O lock) 169.80, 141.32, 132.99, 54.56, 33.49, 15.80, 12.94, 9.82; IR 2960, 2905, 2860, 1675, 1645, 1415 cm^{-1}; MS, m/z (relative intensity) 139 (M^+, 63.56), 124 (M - CH_3, 100); HRMS calcd for $C_8H_{13}NO$ 139.0997, found 139.0994.

2-Methyl-6,7,8,8a-tetrahydro-3(5*H*)-indolizinone (11e): ^1H NMR 6.65 (m, 1 H, vinylic H), 4.28 (dd, J = 14 Hz, 4 Hz, 1 H, NCHCH=), 3.7 (bd, 1 H, $NCHHCH_2$ equatorial), 2.85 (dt, J = 4 Hz, 14 Hz, 1 H, $NCHHCH_2$ axial), 2.2–1.5 (mm, 6 H, C-6,7,8 methylene H), 1.90 (t, J = 2 Hz, 3 H, CH_3C=); ^{13}C NMR 169.48, 139.82, 135.07, 59.18, 39.54, 31.09, 25.43, 23.54, 11.19; IR 2940, 2860, 1690, 1645, 1430, 1042 cm^{-1}; MS, m/z (relative intensity) 151 (M^+, 100), 136 (M - CH_3, 82.6), 108 (92.6); HRMS calcd for $C_9H_{13}NO$ 151.0997, found 151.1004.

2,5-Dimethyl-6,7,8,8a-tetrahydro-3(5*H*)-indolizinone (11f) and 2,8a-Dimethyl-6,7,8,8a-tetrahydro-3(5*H*)-indolizinone (12f). The two compounds were inseparable by HPLC. Isomer **12f** was isolated by GC, column A, during which **11f** was selectively destroyed. The spectra of the mixture are as follows: ^1H NMR 6.68 (d, J = 2 Hz, 1 H, vinylic H), 6.62 (t, J = 2 Hz, 1 H, vinylic H), 4.58 (bp, 1 H, NCHCH=), 4.23 (dd, J = 6 Hz, 14 Hz, 1 H, $NCHHCH_2$), 2.1–1.5 (mm, 8 H, $CH_2CNCH_2CH_2$ of both isomers), 1.9 (m, 6 H, CH_3C= of both isomers), 1.3–0.8 (mm, 4 H, $CH_2CH_2CH_2$ of both isomers), 1.23 (s, 3 H, CH_3C), 1.21 (d, J = 7 Hz, 3 H, $NCHCH_3$); ^{13}C NMR 169.35 (overlapping C=O), 147.75, 140.02, 135.07, 132.73, 60.61, 55.60, 42.92, 36.69, 35.24, 31.22, 30.31, 25.69, 20.10, 19.38, 18.99, 18.47, 11.19, 11.06; IR 2950, 2870, 1685, 1425 cm^{-1}; MS, m/z (relative intensity) 165 (M^+, 45.47), 150 (M - CH_3, 100), 122 (53.79); HRMS calcd for $C_{10}H_{15}NO$ 165.1153, found 165.1159.

2,8a-Dimethyl-6,7,8,8a-tetrahydro-3(5*H*)-indolizinone (12f): ^1H NMR (external D_2O lock) 6.68 (d, J = 2 Hz, 1 H, vinylic H), 4.23 (dd, J = 6 Hz, 14 Hz, 1 H, $NCHHCH_2$ equatorial), 2.82 (dt, J = 3 Hz, 14 Hz, 1 H, $NCHHCH_2$ axial), 2.0–1.5 (mm, 4 H, $CH_2C(CH_3)NCH_2CH_2$), 1.9 (d, J = 2 Hz, 3 H, CH_3C=), 1.3–1.0 (mm, 2 H, $CH_2CH_2CH_2$), 1.23 (s, 3 H, CH_3C); ^{13}C NMR 169.10, 147.95, 140.20, 60.68, 36.74, 35.44, 25.82, 20.16, 19.51, 11.06; IR 2950, 2870, 1685, 1425 cm^{-1}; MS, m/z (relative intensity) 165 (M^+, 42.81), 150 (M - CH_3, 100), 122 (97.7); HRMS calcd for $C_{10}H_{15}NO$ 165.1153, found 165.1147.

7-(1,1-Dimethylethyl)-2-methyl-6,7,8,8a-tetrahydro-3-(5*H*)-indolizinone (11g): ^1H NMR 6.65 (bs, 1 H, vinylic H), 4.32 (dd, J = 14 Hz, 4 Hz, 1 H, NCHH equatorial), 3.71 (bd, J = 11 Hz, 1 H, NCHC=), 2.86 (dt, J = 14 Hz, 4 Hz, 1 H, CHH axial), 2.1 (bd, 1 H, C-8 equatorial H), 1.9 (bs, 3 H, CH_3C=), 1.78 (bd, 1 H, C-6 equatorial H), 1.34 (tt, J = 12 Hz, 2 Hz, 1 H, C-6 axial H), 1.07 (dq, J = 12 Hz, 6 Hz, 1 H, $CHC(CH_3)_3$), 0.89 (s, 9 H, $C(CH_3)_3$), 0.71 (q, J = 12 Hz, 1 H, C-8 axial); ^{13}C NMR 169.18, 139.45, 135.06, 59.35, 46.12, 39.41, 32.20, 27.35, 26.76, 11.07; IR 3490, 2960, 2870, 1685, 1650, 1435, 1383, 1250, 852; MS, m/z 207 (relative intensity) (M^+, 74.33), 192 (M - CH_3, 38.04), 150 (M - C_4H_9 82.78), 122 (100); HRMS calcd for $C_{13}H_{21}$ NO 207.1623, found 207.1619.

***N*,*N*-Dimethyl-2-butynamide (13a).** The material isolated is identical with that which has been previously reported.[36]

***N*-(1-Butyl)-*N*-methyl-2-butynamide (13b).** The material was isolated in 20% yield: bp 75–80 °C/0.1 mmHg; ^1H NMR 3.56, 3.39 (t, J = 7 Hz, 2 H, NCH_2CH_2), 3.17, 2.93 (s, 3 H, NCH_3), 2.0 (s, 3 H, CH_3), 1.55 (m, 2 H, NCH_2CH_2), 1.35 (m, 2 H, CH_2CH_3), 0.95 (dt, J = 7 Hz, 3 H, CH_2CH_3); ^{13}C NMR (external D_2O lock) 153.87, 87.86, 87.34, 73.94, 73.81, 50.21, 45.72, 35.70, 29.00, 19.90, 19.64, 13.53, 3.06; IR 2945, 2930, 2850, 2235, 1630, 1400 cm^{-1}; MS, m/z (relative intensity) 153 (M^+, 4.3), 138 (M - CH_3, 14.85), 110 (M - C_3H_7, 100); HRMS calcd for $C_9H_{15}NO$ 153.1153, found 153.1157.

***N*-Methyl-*N*-(phenylmethyl)-2-butynamide (13c).** The material was isolated in 16% yield: bp 105–110 °C/0.01 mmHg; ^1H NMR 7.3 (m, 5 H, Ar H), 4.79, 4.62 (s, 2 H, $NCH_2C_6H_5$), 3.1, 2.88 (s, 3 H, NCH_3), 2.04, 2.01 (s, 3 H, CH_3); ^{13}C NMR (ref $CDCl_3$) 154.91, 136.31, 128.77, 128.57, 128.05, 127.79, 127.47, 89.49, 88.97, 73.29, 54.69, 49.62, 35.64, 31.61, 3.84; IR 3020, 2920, 2245, 1638, 1405, 1253, 1555; MS, m/z (relative intensity) 187 (M^+, 89.57), 91 (M - $C_7H_7^+$, 55.8), 67 (100); HRMS calcd for $C_{12}H_{13}NO$ 187.0997, found 187.1003.

***N*,*N*-Diethyl-2-butynamide (13d)**: ^1H NMR 3.65, 3.35 (q, J = 10 Hz, 4 H, CH_2CH_3), 2.05 (s, 3 H, CH_3), 1.23 (t, J = 10 Hz, 3 H, CH_2CH_3), 1.13 (t, J = 10 Hz, 3 H, CH_2CH_3); ^{13}C NMR 154.26, 87.86 (C-3), 73.75 (C-2), 43.42, 39.08, 14.31, 12.81, 3.90 (C-4 methyl); IR 2975, 2930, 2875, 2260, 2230, 1630, 1230, 1290 cm^{-1}; MS, m/z (relative intensity) 139 (M^+, 40.47), 124 (M - CH_3, 52.74), 67 (100); HRMS calcd for $C_8H_{13}NO$ 139.0997, found 139.1003.

1-(1-Oxo-2-butynyl)piperidine (13e): ^1H NMR 3.70 (dd, J = 4 Hz, 6 Hz, 2 H, NCH_2), 3.56 (dd, J = 5 Hz, 5 Hz, 2 H, NCH_2), 2.02 (s, 3 H, CH_3), 2.2–1.4 (mm, 6 H, $CH_2(CH_2)_3CH_2$); ^{13}C NMR (external D_2O lock) 152.96, 88.71, 73.55, 48.06, 42.21, 26.40, 25.62, 24.71, 3.77; IR 2930, 2850, 2220, 1635, 1440, 1275 cm^{-1}; MS, m/z (relative intensity) 151 (M^+, 50.19), 136 (M - CH_3, 23.19), 67 (100); HRMS calcd for $C_9H_{13}NO$ 151.0997, found 151.0999.

2-Methyl-1-(1-oxo-2-butynyl)piperidine (13f). The material was obtained in 26% yield: bp 78–81 °C/0.05 mmHg; ^1H NMR 4.87, 4.7 (m, 1 H, $NCH(CH_3)CH_2$), 4.42, 4.23 (dd, J = 4 Hz, 14 Hz, 1 H, NCHH equatorial), 3.16, 2.72 (dt, J = 3 Hz, 14 Hz, 1 H, NCHH), 2.02, 2.0 (s, 3 H, CH_3), 1.8–1.3 (mm, 6 H, $CH_2(CH_2)_3CH$), 1.27, 1.18 (d, J = 7 Hz, 3 H, $CHCH_3$); ^{13}C NMR 153.41, 88.97, 73.68, 73.36, 50.27, 43.90, 42.73, 36.55, 30.76, 29.79, 26.34, 25.43, 19.05, 16.97, 15.61, 4.10; IR 2940, 2855, 2250, 2220, 1619, 1425, 1280, 1182, 735; MS, m/z (relative intensity) 165 (M^+, 42.09), 150 (M - CH_3, 96.25), 84 (100), 67 (M $C_4H_3O^+$, 97.04); HRMS calcd for $C_9H_{13}NO$ 165.1153, found 165.1158.

4-(1,1-Dimethylethyl)-1-(1-oxo-2-butynyl)piperidine (13g). The material was obtained in 12% yield: bp 105–120 °C/0.05 mmHg; mp 116–118 °C; ^1H NMR 4.5 (dd, 2 H, HHCNCHH equatorial), 3.0 (bt, 1 H, NCHH axial), 2.6 (bt, 1 H, NCHH), 2.0 (s, 3 H, CH_3C), 1.75 (m, 2 H, NCH_2CH_2), 1.25 (m, 3 H, NCH_2CH_2CH), 0.9 (s, 9 H, $C(CH_3)_3$; ^{13}C NMR 152.78, 88.62, 73.24, 47.79, 46.83, 42.00, 32.19, 27.48, 27.17, 26.37, 3.87; IR 2978, 2850, 2224, 1634, 1440, 1317, 1288, 1250, 1000 cm^{-1}; MS, m/z (relative intensity) 207 (M^+, 45.32), 192 (M - CH_3, 23.04), 150 (M - C_4H_7, 59.35), 67 (100); HRMS calcd for $C_{13}H_{21}NO$ 207.1630, found 207.1617.

***cis*,*trans*-1-(Dimethylamino)-2-(methoxymethylene)-propane (16).** To a solution of 25 mL of MeOH, 2.0 mL (0.017 mol) of **15**, and 4.9 mL of **5b** (0.035 mol) at 0 °C under an atmosphere of nitrogen was slowly added a solution of 3.8 of potassium *tert*-butoxide (0.035 mol) in 15 mL of MeOH. Once the addition was complete the reaction mixture was magnetically stirred at 0 °C for 3 h. The mixture was allowed to warm to room temperature and stirred for an additional 14 h. The reaction mixture was quenched with 100 mL of water and extracted with 5 × 30 mL of *n*-pentane. The combined organic layers were dried over Na_2SO_4, filtered, and fractionally distilled to give 0.63 g of **16**, bp 82 °C. The mixture of isomeric enol ethers was isolated in an approximately 3:1 ratio as determined by GCMS and ^1H NMR analysis: ^1H NMR 5.90 (bs, 1 H, vinylic H), 3.56, 3.53 (two s, 3 H, CH_3O), 2.88 (bs, 0.6 H, CH_2N), 2.67 (bs, 1.4 H, CH_2N), 2.17, 2.15 (two s, 6 H, $N(CH_3)_2$), 1.62 (bs, 3 H, CH_3C=); ^{13}C NMR 144.49, 144.33, 111.85, 111.76, 63.69, 59.16, 59.11, 57.32, 48.21, 45.15, 44.89, 44.09, 16.51, 12.34; IR 2920, 2800, 1950, 1685, 1458, 1211, 1132, 1027; MS, m/z (relative intensity) (major isomer) 129 (M^+, 14.54), 114 (M - CH_3 7.44), 85 (M - C_2H_6N 60.83), 58 (69.46), 55 (100), (minor isomer) 129 (M^+, 13.63), 114 (M - CH_3, 8.14), 85 (M - C_2H_6N, 30.86), 58 (100), 55 (58.32); HRMS calcd for $C_7H_{15}NO$ 129.1153, found 129.1158.

^{13}C Labeling Experiment. Labeled diethyl (diazomethyl)-phosphonate (**5b**) was prepared[33] by using formaldehyde having ca. 12% isotopic enrichment.[37] The rearranged product, *N*,*N*-diethyl-2-butynamide (**13d**) was separated from the reaction mixture by GC, using column B. The ^{13}C NMR spectral data were obtained on a 1:10 (w:w) solution of **13d** in $CDCl_3$; the solutions were 0.1 M in $Cr(acac)_3$ to enhance relaxation.[38]

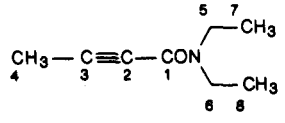
(36) Spassov, S. L.; Dimitrov, V. S.; Agora, M.; Kantschovska-Dimicoli, I.; Tudorova-Momchera, R. *Org. Magn. Reson.* **1974**, *6*, 508.

(37) A 40% aqueous solution of 90% ^{13}C formaldehyde was purchased from Isotope Labeling Corporation. The enriched ^{13}C solution was diluted to a 12% enrichment with a 40% aqueous solution of formaldehyde, having a natural abundance of ^{13}C.

(38) Gansow, O. A.; Burke, A. R.; LaMar, G. N. *J. Chem. Soc., Chem. Commun.* **1972**, 456.

Statistical analysis of the integrated ^{13}C NMR spectrum of the butynamide showed that the excess label was completely contained at C-2. The error in this analysis is estimated at ±6.3%, as was determined by comparison of the relative intensities of the resonances for carbons 5, 6, 7, and 8 of the ^{13}C NMR spectra of *N,N*-diethyl-2-butynamide having both enriched and natural abundance of ^{13}C.

intensities (C-5) + (C-6) + (C-7) + (C-8)



13d

unlabeled: 721.496 + 661.656 + 648.080 + 710.480

n = 685.428 s = 36.002 error = 5.25%

labeled: 286.951 + 319.452 + 336.462 + 294.133

n = 309.249 s = 22.879 error = 7.4%

average error of the compared spectra = 6.3%

The enrichment of ^{13}C over that of natural abundance of the alkynyl carbons was calculated by comparing the relative intensities of the alkynyl carbon atoms of the enriched and naturally abundant material. A multiplication factor (MF) was used to equate the two spectra.

multiplication factor (MF) =

n(unlabeled)/n(labeled) = 2.215

C-2

unlabeled: 494.104

labeled: 2954.616 × 2.215 = 6544.474

enrichment = 13.25 ± 6.3%

C-3

unlabeled: 443.680

labeled: 187.551 × 2.215 = 415.43

enrichment = 0.94 ± 6.3%

Solvent Effects. The reactions investigating the effect of solvent were performed as described above for the general procedure for insertion reaction between **5b** and **9a**, but the solvent used for the reactions was varied accordingly.

Deuterium Exchange of 11g. To a solution of 22.4 mg of **11g** (0.108 mmol) and 0.5 mL of methanol-d_4 at −40 °C and under an atmosphere of nitrogen was added a solution of 0.01 g (0.1 mmol) of potassium *tert*-butoxide and 0.5 mL of methanol-d_4. The reaction mixture was allowed to warm to 0 °C and stirred for 1 h. The solution was then warmed to room temperature, quenched with 1 mL of deuterium oxide, and extracted with three 10-mL portions of ethyl acetate. The combined organics were dried over sodium sulfate, filtered, and concentrated in vacuo. The resulting solid residue, 13 mg, was analyzed by ^1H NMR and found to have 81% deuterium at C-8a (bridgehead) position by integration of the residual resonance at δ 3.71 vs. the integration of the resonances at δ 4.32, 2.86, 2.10, and 1.78. Analysis of the mass spectrum of the resulting solid also showed an 81% incorporation of deuterium into **11g**: ^1H NMR 6.65 (bs, 1 H, vinylic H), 4.32 (dd, J = 14 Hz, 4 Hz, 1 H, NC*H*H equatorial), 2.86 (dt, J = 14 Hz, 4 Hz, 1 H, NCH*H* axial), 2.10 (dd, J = 13 Hz, 2 Hz, 1 H, C-8 equatorial H), 1.90 (bs, 3 H, CH_3C=), 1.78 (bd, 1 H, C-6 equatorial H), 1.34, (tt, J = 12 Hz, 2 H, 1 H, C-6 axial H), 1.07 (dq, J = 12 Hz, 6 Hz, C*H*C$(CH_3)_3$), 0.89 (s, 9 H, C$(CH_3)_3$), 0.71 (dt, J = 13 Hz, 4 Hz, C-8 axial); MS, m/z (relative intensity) 208 (M^+, 50.31), 193 (M − CH_3, 32.59), 151 (M − C_4H_9, 82.53), 123 (100).

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Registry No. 5b, 25411-73-8; **9a**, 19432-30-5; **9b**, 93953-12-9; **9b** (semicarbazone), 103438-35-3; **9c**, 93953-13-0; **9c** (2,4-DNP), 103438-36-4; **9d**, 22381-21-1; **9d** (2,4-DNP), 103438-37-5; **9e**, 22381-22-2; **9e** (2,4-DNP), 103438-38-6; **9f**, 93953-14-1; **9f** (semicarbazone), 103438-35-3; **9g**, 103438-34-2; **11a**, 55164-55-1; **11b**, 93953-15-2; **11c**, 27610-96-4; **11d**, 93953-20-9; **11e**, 93953-21-0; **11f**, 93953-23-2; **11g**, 103438-39-7; **11g**-*d*, 103438-40-0; **12b**, 93953-16-3; **12c**, 93953-18-5; **12f**, 93953-24-3; **13a**, 53099-32-4; **13b**, 93953-17-4; **13c**, 93953-19-6; **13d**, 51590-65-9; **13d**-^{13}C, 103438-42-2; **13e**, 93953-22-1; **13f**, 93953-25-4; **13g**, 103438-41-1; **15**, 15364-56-4; *cis*-**16**, 103438-43-3; *trans*-**16**, 103438-44-4; Me_2NH, 124-40-3; MeNHBu, 110-68-9; $MeNHCH_2Ph$, 103-67-3; Et_2NH, 109-89-7; pyridinium hydroxymaleic anhydride, 52060-80-7; piperidine, 110-89-4; 2-methylpiperidine, 109-05-7; 4-*tert*-butylpiperidine, 1882-42-4.

Supplementary Material Available: Two-dimensional correlated NMR spectrum (COSY) of **11g** (1 page). Ordering information is given on any current masthead page.