Table I. Tandem Michael/1,3-Dipolar Cycloaddition Sequence[a]

entry	R	% yield 17	18	19	total
1	Me[b]	43	39	–	82
2	Me[c]	34	26	2	62
3	Et[b]	41	26	2	69
4	Et[c]	21	28	7	57
5	$^{S}CH(Me)CO_2Et$[c]	26[d]	22[d]	9	57

[a] To a 0.09 M solution of **11** in dry CH_3CN was added 3 equiv of $BF_3{\cdot}OEt_2$ and either [b] 40 equiv or [c] 10 equiv of acrylate. The mixture was refluxed under N_2 until no starting material remained as judged by TLC. Aqueous (bicarbonate) workup followed by silica gel chromatography afforded **17**, **18**, and **19** in the yields shown. [d] High field ^1H NMR analysis indicated a (1:1) mixture of diastereomers.

With compound **11** in hand we began to investigate conditions that might lead to the generation of unsymmetrical azomethine ylides III as discussed above. It was thus found that heating a mixture of **11** and boron trifluoride etherate in the presence of excess methyl acrylate (40 equiv) resulted in the formation of an approximately equimolar mixture of two isomeric substances possessing the diazabicyclo[3.2.1]octane skeleton in 82% combined yield (Table I, entry 1).[11] These products were readily identified as the endo- and exo-cycloadducts **17a** and **18a**, respectively, on the basis of their respective $^3J_{5,6}$ values as noted previously for related systems.[1,3] The *E*-trisubstituted olefin geometry was confirmed (for **17a**) by a series of NOE difference experiments that showed reciprocal enhancements for both H-5 and H-11 as well as H-10 and a benzylic resonance. When the reaction was stopped before **11** had been completely consumed, a cyclobutane **13a** could be isolated and was, in fact, the only product when trimethylsilyl triflate was substituted for $BF_3{\cdot}OEt_2$.[12] Subjection of pure **13a** to the original cycloaddition conditions (i.e. excess $CH_2{=}CHCO_2Me$, $BF_3{\cdot}OEt_2$, Δ) also resulted in the production of a 1:1 mixture of adducts **17a** and **18a**, though some transient reversion to **11** could also be detected during this reaction.[13] Similar results were obtained with ethyl acrylate (series b) and ethyl (*S*)-lactylacrylate[14] (series c). During some runs—especially those involving lower acrylate concentrations—small amounts of the (ring-opened) pyrrolidine **19** were isolated as well.

These data are consistent with the sequence shown in Scheme II whereby the β-cyano enamine moiety of **11** undergoes a reversible Michael addition to the BF_3-activated acrylate to give a zwitterionic species **12**, which is in equilibrium with the cyclobutane **13** and the azomethine ylide **14** (or BF_3 complex thereof). The reactive ylide **14** can now be "trapped" by the excess acrylate acting this time as a dipolarophile to give the initial 1,3-dipolar cycloadducts **15**, which eliminate HCN by way of the *N*-acyliminium species **16** to yield the cycloadducts **17** and **18**. The pyrrolidine **19** apparently results from hydrolytic cleavage of **16**. Finally, we speculate that the increased proportion of endo selectivity during these cycloadditions may reflect some sort of BF_3-mediated "chelation" between the azomethine ylide and dipolarophile. This novel tandem Michael addition/1,3-dipolar cycloaddition protocol may prove quite useful for the assembly of complex pyrrolidine structures such as those embodied in targets **1** and **2** since three carbon–carbon bonds are formed in a single synthetic operation.[15] Further studies aimed at delineating the scope of this unique entry to functionalized azomethine ylides (and thus pyrrolidines) from enamine-like structures are currently underway in our laboratory.

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Supplementary Material Available: Complete characterization data (IR, ^1H and ^{13}C NMR, and HRMS) for compounds **17a**, **18a**, **17b**, **18b**, **17c**, and **18c** (4 pages). Ordering information is given on any current masthead page.

(11) Attempted substitution of other Lewis acids (Et_2AlCl, $SnCl_4$, $TiCl_4$, and $TiCl(O^iPr)_3$) for $BF_3{\cdot}OEt_2$ gave decidedly inferior results with adducts **17a** and **18a** not even being detected in the crude reaction mixtures.

(12) Cf.: Cook, A. G. In *Enamines: Synthesis, Structure, and Reactions*; Cook, A. G., Ed.; Marcel Dekker: New York, 1969; p 211.

(13) When **13a** was reacted with ethyl acrylate there was obtained **13b**, **17b**, and **18b** (indicating that $k_{-1} > k_2$) along with small amounts of the "mixed" ester adducts corresponding to **17** and **18** that result from addition of ethyl acrylate to dipole **14a**. This seems to rule out the possibility of a Michael–Michael–Michael type of process and is further supported by our failure to observe any intermediate Michael addends.

(14) Poll, T.; Sobczak, A.; Hartmann, H.; Helmchen, G. *Tetrahedron Lett.* **1985**, 3095.

(15) for a recent review of pyrrolidine synthesis via [3 + 2] cycloadditions with a particular emphasis on natural product synthesis, see: Pearson, W. H. In *Studies in Natural Product Chemistry*; Atta-Ur-Rahman, Ed.; Elsevier: Amsterdam, 1988; Vol. 1, Stereoselective Synthesis (Part A), p 323.

Generation of Vinylcarbenes by the Intramolecular Addition of α-Diazo Ketones to Acetylenes

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Summary: Treatment of several α-diazo alkynyl substituted ketones with rhodium(II) carboxylates results in intramolecular addition to the acetylenic π-bond to give a transient cyclopropene which spontaneously rearranges to a vinyl carbene intermediate.

Vinylcarbenes have attracted considerable interest as intermediates in a variety of reactions.[1,2] Methods for generating these species include the pyrolysis[3] or singlet-

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(1) For a recent review, see: Steinmetz, M. G.; Srinivasan, R.; Leigh, W. J. *Rev. Chem. Intermed.* **1984**, *5*, 57.

(2) Pincock, J. A.; Boyd, R. J. *Can. J. Chem.* **1977**, *55*, 2482.

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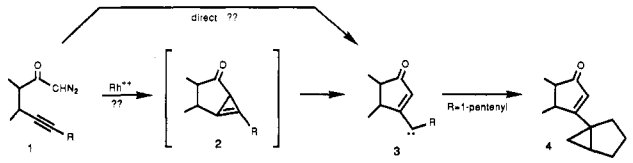
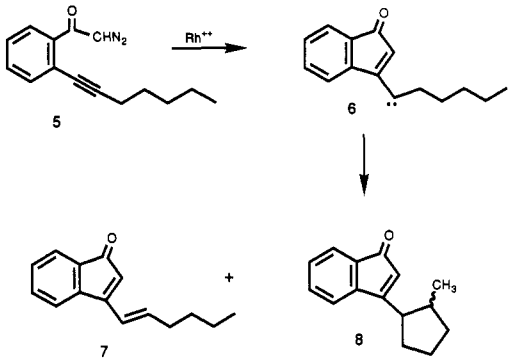
induced photochemistry of cyclopropenes[4] and the photolysis or thermolysis of vinyldiazomethanes.[5] We have recently developed an approach to vinylcarbenes (3) which is based on the rhodium(II)-catalyzed intramolecular addition of an α-diazo ketone (1) to a suitably tethered alkyne.[6,7] Products are formed from 3 by intramolecular addition to a neighboring olefinic π-bond. The simplest

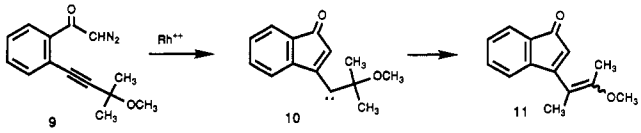


mechanism accounting for the results involves addition of a rhodium-stabilized carbenoid onto the acetylenic π-bond to give the vinylcarbene 3 directly or possibly the highly strained cyclopropene derivative 2. It is well known that cyclopropenes ring open to vinylcarbenes at ambient temperature[8] and that these reactive intermediates may be trapped by alkenes both in an inter-[9] and intramolecular fashion.[10] We have now investigated the rhodium(II)-catalyzed behavior of several related diazo ketones and describe below our results concerning these reactions and also present evidence for the intermediacy of cyclopropene 2.

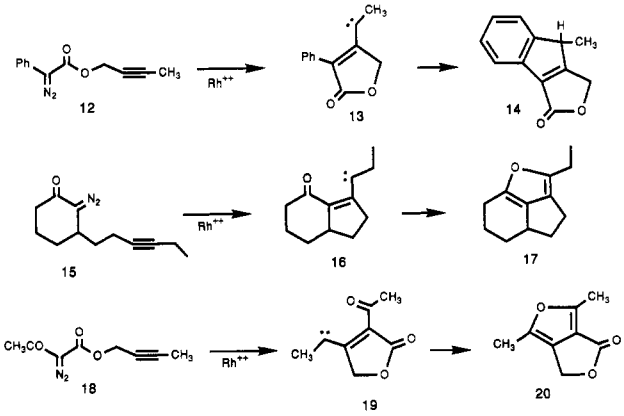
Cyclization of vinylcarbenes to cyclopropenes is considered to be their most common reaction.[11] However, this intramolecular process is not always observed, and a number of competing reactions have been reported. These include insertion into a C–H bond,[12] alkyl group migration,[13] and electrocyclization.[14] Since we were interested in exploiting the intramolecular addition of α-diazo ketones to alkynes as a synthetic method, we carried out a number of experiments designed to probe the scope and generality of the reaction. Initial efforts focused on the rhodium(II)-catalyzed reaction of o-alkynyl-substituted α-diazoacetophenone derivative 5. Treatment of 5 with a catalytic quantity of rhodium(II) octanoate at 25 °C in benzene afforded a 1:1 mixture of indenones 7 and 8 in 94% yield. The observed products are formed from vinylcarbene 6 by way of a 1,2-hydrogen shift giving 7 or insertion into a δ-hydrogen shift giving 8.[15] The formation of indenone



7 suggests that other 1,2-shifts to a carbene center could also occur. We have confirmed this possibility by treating α-diazo ketone 9 with rhodium(II) mandelate. In this case a 3:2 mixture of (E)- and (Z)-indenones (11) was formed in 83% yield. The simplest rationale to accomodate this result is one which involves a 1,2-methyl shift of a transient vinylcarbene intermediate (i.e. 10).



One of the more frequently encountered reactions of dienylcarbenes involves rearrangement to indenes, cyclopentadienes, or furans.[16] In an attempt to document the 1,5-electrocyclization process using α-diazoacetylenic ketones, we studied the rhodium(II)-catalyzed behavior of diazo ketone 12. The major product isolated in 60% yield corresponded to indenyl lactone 14. The formation of this compound can also be rationalized in terms of a 1,5-electrocyclization of a transient vinylcarbene (i.e. 13). Further



examples which support the generality of the cyclization reaction were sought. With this in mind, we investigated the rhodium(II)-catalyzed behavior of diazo ketones 15 and 18. In both cases the initially formed vinylcarbene (i.e. 16 or 19) cyclized cleanly to give furans 17 and 20 in 85%

(3) York, E. J.; Dittmar, W.; Stevenson, J.; Bergman, R. G. *J. Am. Chem. Soc.* **1973**, *95*, 5680.
(4) Padwa, A. *Acc. Chem. Res.* **1977**, *12*, 310 and references cited therein.
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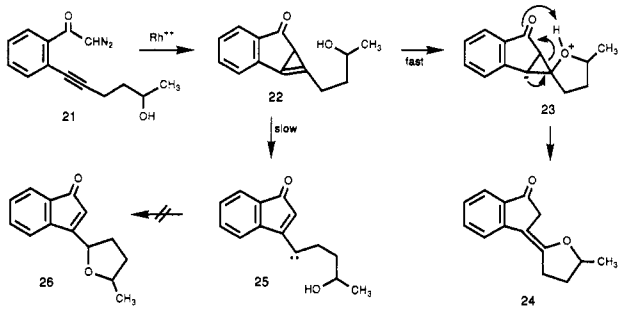
(7) For an earlier example, see: Mykytka, J. P.; Jones, W. M. *J. Am. Chem. Soc.* **1975**, *97*, 5933. A set of related results has also been uncovered by Professor T. Hoye. See: Korkowski, P. F.; Hoye, T. R. Abstracts 196th ACS National Meeting (1988), Abstract No. 271.
(8) Baird, M. S. Synthetic Applications of Cyclopropenes. *Topics in Current Chemistry*; de Meijere, A., Ed.; Springer-Verlag: New York, 1988; Vol. 144, p 138. Halton, B.; Bansell, M. G. *Cyclopropenes*. In *The Chemistry of Cyclopropanes*; Rappoport, Z., Ed.; Wiley: New York, 1988; Vol. 2.
(9) Baird, M. S.; Buxton, S. R.; Whitley, J. S. *Tetrahedron Lett.* **1984**, 1509. Al-Dulayymi, J.; Baird, M. S.; Clegg, W. *Tetrahedron Lett.* **1988**, 6149. Petiniot, N.; Anciauz, A. J.; Noels, A. F.; Hubert, A. J.; Teyssie, P. *Tetrahedron Lett.* **1978**, *1239*.
(10) Padwa, A.; Blacklock, T. J. *J. Am. Chem. Soc.* **1984**, *106*, 4446.
(11) Sevin, A.; Arnaud-Danon, A. *J. Org. Chem.* **1981**, *46*, 2346. Yoshimine, M.; Pacansky, J.; Honjou, N. *J. Am. Chem. Soc.* **1989**, *111*, 2785.
(12) Streeper, R. D.; Gardner, P. D. *Tetrahedron Lett.* **1973**, 767.
(13) Newmann, M. F.; Buchecker, C. *Tetrahedron Lett.* **1973**, 2875.
(14) Zimmerman, H. E.; Aasen, S. M. *J. Am. Chem.* Soc. **1977**, *99*, 2342; *J. Org. Chem.* **1978**, *43*, 1493. Zimmerman, H. E.; Kreil, D. J. *J. Org. Chem.* **1982**, *47*, 2060. Padwa, A.; Blacklock, T. J.; Getman, D.; Hatanaka, N. *J. Am. Chem. Soc.* **1977**, *99*, 2344; *J. Org. Chem.* **1978**, *43*, 1481.
(15) Intramolecular carbene insertion into a δ C–H bond has been previously reported; see: Taber, D. F.; Petty, E. H. *J. Org. Chem.* **1982**, *47*, 4809.
(16) For a review, see: Padwa, A. *Rearrangements in Ground and Excited States*; DeMayo, P., Ed.; Academic Press: New York, 1980; Vol. 3, p 501.

and 52% yield, respectively.

We have carried out a number of experiments designed to provide evidence for the intermediacy of a strained cyclopropene in these transformations. Our strongest evidence for a cyclopropene comes from studies which take advantage of the addition reaction of alcohols with cyclopropenes.[17] Compound **21** was prepared by treating methyl (*o*-bromophenyl)benzoate with the ethylene ketal of hex-1-yn-5-one under typical Heck arylation conditions.[18] The palladium-coupled product was easily converted into **21** using traditional methods. A sample of **21** was allowed to react with rhodium(II) mandelate in benzene at 25 °C. The only product isolated in 85% yield corresponded to structure **24**.[19] No signs of product **26** derived by vinylcarbene insertion into the neighboring OH group could be detected in the crude reaction mixture. We can account for **24** in the following manner. Intramolecular addition of the rhodium stabilized carbenoid onto the acetylenic π-bond generates the highly strained cyclopropene **22**. This species is too strained to survive at ambient temperature, but attack of the hydroxyl group onto the double bond would result in **23**, which rapidly undergoes ring cleavage to give **24**. In this case, intramolecular nucleophilic addition of the hydroxyl group on the cyclopropene ring is faster than ring opening to vinylcarbene **25**, which if formed, would have produced indenone **26**.



In conclusion, the facility with which the intramolecular rhodium(II)-catalyzed cyclization reaction of alkynyl-substituted diazo ketones occurs makes this process particularly attractive for the synthesis of a variety of polycyclic ring systems. We are continuing to explore the scope and mechanistic details of these cyclization reactions and will report additional findings at a later date.

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(17) Hauck, G.; Durr, H. *J. Chem. Res.* **1981**, 180. Gardner, P. D.; Shields, T. C. *J. Am. Chem. Soc.* **1967**, *89*, 5425. Hashem, A.; Weyerstahl, P. *Tetrahedron* **1984**, *40*, 2003. Padwa, A.; Wannamaker, M. W.; Dyszlewski, A. D. *J. Org. Chem.* **1987**, *52*, 4760.

(18) Heck, R. F. *Acc. Chem. Res.* **1979**, *12*, 146.

(19) All new compounds were characterized by ^{1}H and ^{13}C NMR, by high-resolution mass spectra, and by proper analytical data: NMR **24** ($CDCl_3$, 300 MHz) δ 1.39 (d, 3 H, J = 6.2 Hz), 1.70–1.85 (m, 1 H), 2.25–2.40 (m, 1 H), 2.85–3.10 (m, 2 H), 3.25 (s, 2 H), 4.50 (m, 1 H), 7.18 (t, 1 H, J = 7.5 Hz), 7.41 (d, 1 H, J = 7.5 Hz), 7.55 (t, 1 H, J = 7.5 Hz), and 7.35 (d, 1 H, J = 7.5 Hz).

Articles

Chemistry and Structure of Phenylcubanes

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Phenylcubanes show unusual reactivity toward metalation and oxidation. Metalation of 1,4-bis((diisopropylamino)carbonyl)-2,7-diphenylcubane, **1**, occurs at the cubane skeleton while oxidation of 1,4-bis((diisopropylamino)methyl)-2,7-diphenylcubane, **7**, resulted in the formation of benzoic acid. The X-ray structure of **7** shows a short phenyl–cubane bond length of 1.484 Å, and the C_1–C_2 bond, the cubane bond between the two substituents, is substantially longer than in an unsubstituted cubane (1.607 vs 1.558 Å). The selective functionalization of either the phenyl or the cubane moiety and the synthesis of 1,4-diphenylcubane-2,7-dicarboxylic acid, **8**, via oxidation of the (diisopropylamino)methyl group under mild conditions, were achieved.

There has been renewed interest in the chemistry of cubane since some of its derivatives, particularly nitrocubanes, have shown promise as high-density energetic materials.[1] In this connection we became interested in

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