Tetrahedron Letters, Vol.32, No 31, pp 3755-3758, 1991
Printed in Great Britain

0040-4039/91 $3 00 -
Pergamon Press plc

DOUBLE (INTERNAL/EXTERNAL) ALKYNE INSERTION REACTIONS OF α-DIAZOKETONES

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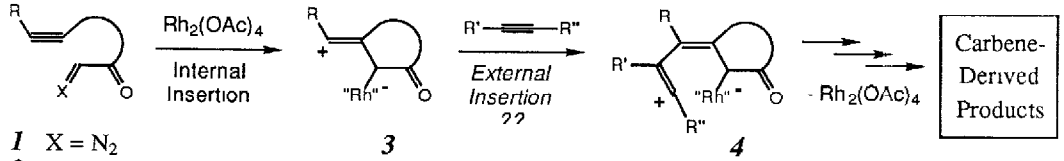
***Summary**: Acetylenic α-diazoketone 5, when treated with Rh2(OAc)4 and several different alkynes, gives alkyne insertion/cyclopropenation products Subsequent catalytic ring opening reactions demonstrate a highly regioselective net double alkyne insertion process and a new dihydropentalenone synthesis*

The propensity for α-diazoketones **1** to undergo internal insertion of the tethered alkyne unit upon exposure to catalytic dirhodium tetraacetate (**1** → **2** → **3**) has attracted recent interest.[2] The extent of metal involvement throughout this cycloisomerization has been investigated, as well as the ability of the resultant vinylcarbene equivalent **3**[3] to perform further intramolecular transformations such as cyclopropanation, C-H insertion, ylide rearrangement, and 1,3-dipole formation. In none of these studies, however, has **3** been trapped by a second alkyne unit, a process which should give the butadienylcarbene equivalent **4**. In this paper we report that a second *external* insertion can occur, providing a highly regioselective double cyclization strategy.

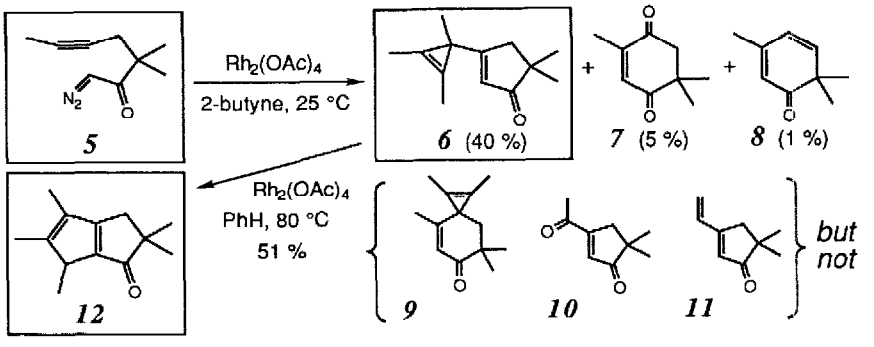


1 X = N_2
2 X = "Rh"

3 ***4***

This study focused on reactions of the readily prepared diazoketone **5**[4] (Scheme 1). A solution of **5** in 2-butyne (0.07 M) was stirred with $Rh_2(OAc)_4$ (5 mol%) at 25 °C under N_2 atmosphere and concentrated after 48 h Purification by SiO_2 chromatography yielded cyclopropene **6** (40%) and byproducts **7** (5%; from sequential proximal alkyne carbon activation and oxidation) and **8** (1%; from sequential proximal alkyne carbon activation and 1,2-hydrogen migration) The formation of **6** - **8** and the absence of **9** - **11** likely reflect the greater steric accessibility of 2-butyne to the 5-membered exocyclic intermediate "carbene" (cf., **3**) than to its isomeric 6-membered endocyclic intermediate

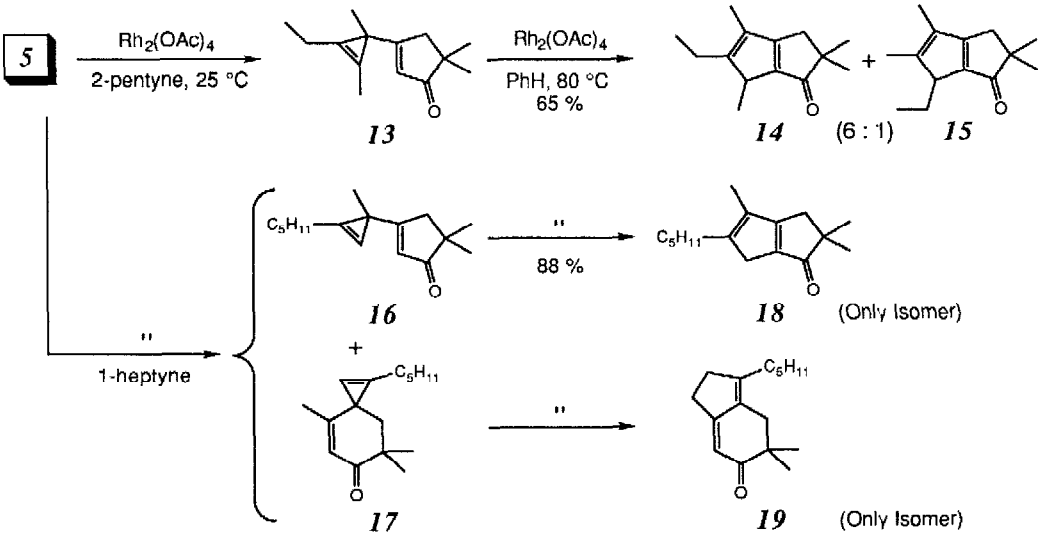
Scheme 1



In light of a recent account of Rh(II) carboxylate mediated cyclopropene rearrangements,[5] we resubjected **6** to $Rh_2(OAc)_4$ (10 mol%) in refluxing benzene (0.07 M) for 42 h. Monitoring this transformation by either GC/MS or ^1H NMR analysis showed a very clean isomerization to a single product. Filtration of the solution through SiO_2 and concentration gave the 3,6-dihydro-1(2*H*)-pentalenone derivative **12** (51%). A control experiment showed that **6** was unchanged when similarly heated for 40 h in the absence of catalyst.

In order to probe the regioselectivity of this rearrangement, **5** was converted to various other cyclopropenes (Scheme 2). Reaction with 2-pentyne at RT gave **13** (33% after MPLC), which was slowly but efficiently converted (required ~80 h) at 80 °C to a 6:1 SiO_2-inseparable mixture (65%) of regioisomeric pentalenones **14** and **15**. The use of 1-heptyne as solvent resulted in several cycloadducts after a 22 h reaction time at RT. The expected cyclopropene **16** (28%) was accompanied by the skeletal isomer **17** (9%), the pentalenone **18** (7%), and the previously observed diketone **7** (10%). This more facile formation of **18** suggests that the

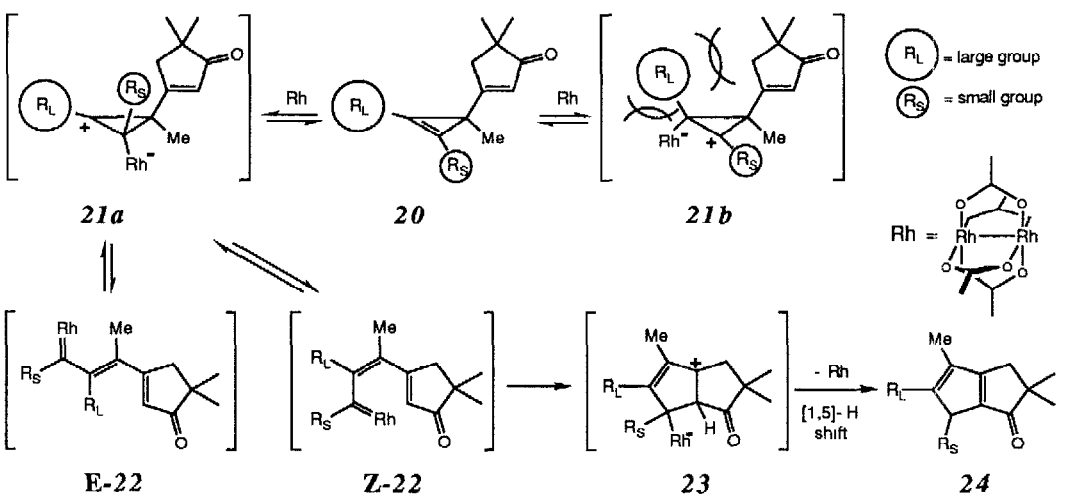
Scheme 2



ease of these cyclopropene rearrangements is sensitive to steric access of the catalyst to the cyclopropene π-bond. In a separate experiment **16** was catalytically converted (at 80 °C) exclusively to **18** (88%), denoting a possible electronic as well as steric origin to the regioselectivity (*vide infra*). Upon similar treatment **17** gave **19** (cleanly by GC/MS) via ring opening and subsequent insertion into a methyl C-H bond.[5,6]

Although many intermediates may be envisioned along the pathway from cyclopropenes like **20** (Scheme 3) to cyclopentadienes like **24**, a very plausible mechanism is analogous to that suggested by Doyle and Müller.[5] The manifold is entered by regioselective electrophilic attack by the bulky Rh(II) catalyst *trans* to the cyclopentenone ring and *ipso* to the smaller group (R_S) to give **21a**. The less stable cyclopropyl cation **21b** contains enhanced steric destabilizations between the acetate ligands of the catalyst and the larger group (R_L), as well as between the *cis*-oriented R_L and cyclopentenone groups. Electrocyclic ring opening of **21a** could give either of the butadienylogous α-ketocarbenes ***E*-22** or ***Z*-22**, but only the latter can proceed to **24**, presumably via **23**. Most likely, a rapid equilibrium among all of the possible regio- and stereoisomeric carbene intermediates is accompanied by preferential consumption of ***Z*-22**.

Scheme 3



The results demonstrate that alkynes are useful traps for vinylcarbene equivalents generated in the intramolecular alkyne insertion reaction of α-diazoketones. Moreover, the resultant cyclopropenes undergo further interesting and efficient metal-mediated transformations. Finally, the success of this double alkyne insertion process suggests the possibility of related internal/internal and external/internal versions which we are currently investigating.

Acknowledgment. This investigation was supported by grant GM-38854 awarded by the DHHS. We thank Rohm & Haas and Glaxo for Fellowship support.

References and Notes

1) Rohm & Haas Graduate Fellow, 1989-1990. Graduate Fellow of the ACS Division of Organic Chemistry, sponsored by Glaxo Research Laboratories, 1990-1991.

2) a) Padwa, A.; Krumpe, K. E.; Zhi, L. *Tetrahedron Lett.* **1989**, *30*, 2633. b) Padwa, A.; Chiacchio, U.; Garreau, Y.; Kassir, J. M.; Krumpe, K. E.; Schofftstall, A. M. *J. Org. Chem.* **1990**, *55*, 414. c) Hoye, T. R.; Dinsmore, C. J.; Johnson, D. S.; Korkowski, P. F. *J. Org. Chem.* **1990**, *55*, 4518. d) Padwa, A.; Krumpe, K. E.; Garreau, Y.; Chiacchio, U. *J Org. Chem.* **1990**, *56*, 2523.

3) Migration of $Rh_2(OAc)_4$ to the distal alkyne carbon is believed not to occur, hence the use of the zwitterionic structure **3**: Hoye, T. R.; Dinsmore, C. J. *J. Am. Chem. Soc.* in press.

4) The spectroscopic properties of all compounds reported herein are in full agreement with the assigned structures.[7] Yields have not been optimized.

5) Müller, P.; Pautex, N.; Doyle, M. P.; Bagheri, V. *Helv. Chim Acta* **1990**, *73*, 1233.

6) Ceccherelli, P.; Curini, M.; Marcotullio, M C.; Rosati, O.; Wenkert, E ; *J Org. Chem.* **1990**, *55*, 311.

7) Spectroscopic data for compounds; **6**: ^{1}H NMR ($CDCl_3$, 200 MHz): δ 5.84 (t, J = 1.5 Hz, C<u>H</u>CO), 2.03 (d, J = 1.5 Hz, C<u>H</u>$_2$CMe$_2$), 1.99 (s, C<u>H</u>$_3$C=CC<u>H</u>$_3$), 1 29 (s, C<u>H</u>$_3$CC=CH), and 1 05 [s, C(C<u>H</u>$_3$)$_2$]. IR ($CDCl_3$): ν(C=O) 1690 cm^{-1}. HRMS (CI, NH_3): Anal. calcd for $C_{13}H_{18}O$+H$^{\oplus}$ 191.1436. Found 191.1437. **12**: ^{1}H NMR ($CDCl_3$, 200 MHz): δ 2.97 (m, CH$_3$C<u>H</u>), 2.51 (bd, J = 14 Hz, C<u>H$_a$H$_b$</u>CMe$_2$), 2.48 (bd, J = 14 Hz, CH$_a$<u>H$_b$</u>CMe$_2$), 1.96 [bs, CH$_3$CHC(C<u>H</u>$_3$)], 1 86 (bs, CH$_3$CHC=CC<u>H</u>$_3$), 1.25 (d, J = 7.7 Hz, C<u>H</u>$_3$CH), and 1.17 [s, C(C<u>H</u>$_3$)$_2$]. IR ($CDCl_3$): ν(C=O) 1660 cm^{-1} HRMS (CI, NH_3): Anal. calcd for $C_{13}H_{18}O$+H$^{\oplus}$ 191.1436. Found 191.1428. **14**: ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.12 (m, CH$_3$C<u>H</u>), 2.5 (m, C<u>H</u>$_2$CMe$_2$), 2.46 (dq, J = 14.6 and 7.6 Hz, CH$_3$C<u>H$_a$H$_b$</u>), 2.30 (dq, J = 14.6 and 7.6 Hz, CH$_3$CH$_a$<u>H$_b$</u>), 1.87 (bs, C=CC<u>H</u>$_3$), 1.20 (d, J = 7.9 Hz, C<u>H</u>$_3$CH), 1.17 [s, C(C<u>H</u>$_3$)$_2$], and 1 08 (t, J = 7.6 Hz, C<u>H</u>$_3$CH$_2$). GC/MS (EI): m/z 204 (43). **15**: ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.05 (m, CH$_2$C<u>H</u>), 2.5 (m, C<u>H</u>$_2$CMe$_2$), 1.94 [bs, CH$_2$CHC(C<u>H</u>$_3$)], 1.87 [bs, CH$_2$CHC=C(C<u>H</u>$_3$)], 0.70 (t, J = 7.4 Hz, C<u>H</u>$_3$CH$_2$), other signals obscured by resonances from **14** GC/MS (EI): m/z 204 (48). **16** (selected data): ^{1}H NMR ($CDCl_3$, 200 MHz): δ 6.68 [bs, (CH$_2$)$_4$C=C<u>H</u>], 5.89 (dd, J = 1.4 and 1.4 Hz, C<u>H</u>CO), and 1.37 (s, C<u>H</u>$_3$CC=CHCO). IR ($CDCl_3$): ν(C=O) 1680 cm^{-1}. HRMS (CI, NH_3): Anal. calcd for $C_{16}H_{24}O$+H$^{\oplus}$ 233.1905. Found 233.1900. **17** (selected data): ^{1}H NMR ($CDCl_3$, 200 MHz): δ 6.73 [bs, (CH$_2$)$_4$C=C<u>H</u>], 5.87 (bs, C<u>H</u>CO), and 1.54 (d, J = 1.2 Hz, C<u>H</u>$_3$C=CH). IR ($CDCl_3$) ν(C=O) 1650 cm^{-1}. HRMS (CI, NH_3): Anal. calcd for $C_{16}H_{24}O$+H$^{\oplus}$ 233.1905. Found 233.1887. **19**: ^{1}H NMR ($CDCl_3$, 200 MHz): δ 5.66 (bs, C<u>H</u>CO), 2.65-2.69 (m, C=CC<u>H</u>$_2$CH$_2$C=C), 2.52-2.57 (m, C=CCH$_2$C<u>H</u>$_2$C=C), 2.42 (bs, C<u>H</u>$_2$CMe$_2$), 2.29 [bt, J = 7 Hz, C<u>H</u>$_2$(CH$_2$)$_3$CH$_3$], 1.49 [m, C<u>H</u>$_2$(CH$_2$)$_2$CH$_3$], 1.23-1.35 (m, C<u>H</u>$_2$C<u>H</u>$_2$CH$_3$), 1.07 [s, C(C<u>H</u>$_3$)$_2$], and 0.89 (t, J = 6.7 Hz, CH$_2$C<u>H</u>$_3$). IR ($CDCl_3$): ν(C=O) 1640 (br) cm^{-1}. GC/MS (EI)· m/z 232 (50).

(Received in USA 18 February 1991)