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RHODIUM(II) CATALYZED INTRAMOLECULAR REACTIONS BETWEEN VINYLDIAZOMETHANES AND PYRROLES. NOVEL SYNTHESIS OF FUSED 7-AZABICYCLO[4.2.0]OCTADIENES

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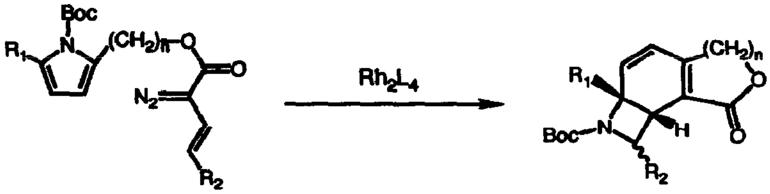
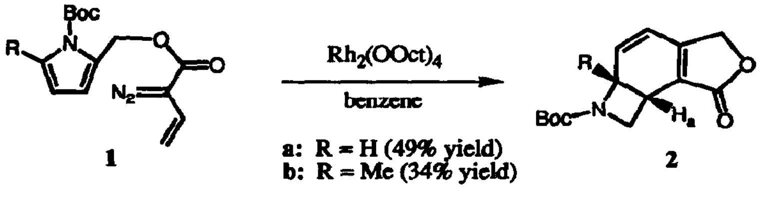
Abstract: Intramolecular capture by pyrroles of vinylcarbenoids generated by rhodium(II) carboxylate catalyzed decomposition of vinyldiazomethanes results in the formation of fused 7-azabicyclo[4.2.0]octadienes or fused tropanes.

The reaction between metal stabilized carbenoids and pyrroles can proceed by several pathways to form a variety of products. Pyrrole alkylation occurs on reaction of carbenoids with pyrrole or N-alkyl pyrrole.[1] The reaction of carbenoids with N-acylated pyrroles can lead to several different types of products, such as dihydropyridines,[2] alkylation products,[2] formal 2 + 3 cycloadducts[3] and formal 3 + 4 cycloadducts.[4] All of these products are considered to be derived from initially formed pyrrolocyclopropanes. The formal 3 + 4 cycloaddition has been developed as a general method for the synthesis of tropanes by a tandem cyclopropanation/Cope rearrangement between vinylcarbenoids and pyrroles.[4] Attempts to extend this chemistry to the synthesis of conformationally constrained tropanes by means of an intramolecular reaction between vinylcarbenoids and pyrroles resulted in a novel synthesis of fused 7-azabicyclo[4.2.0]octadienes (Scheme 1).[5] The details of this unusual transformation are the basis of this paper.



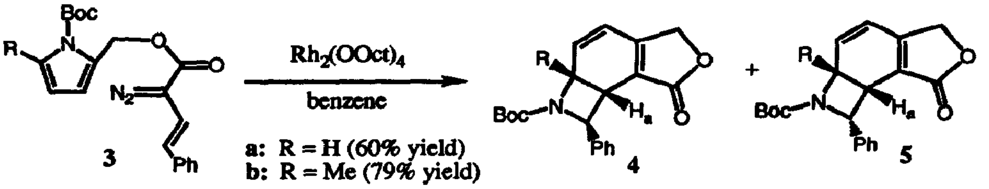
(1)

A series of vinyldiazomethanes was prepared by general procedures that have been previously described.[6] Rhodium(II) octanoate catalyzed decomposition of **1a** in refluxing benzene resulted in a clean transformation as determined from the NMR of the crude reaction mixture. The product was slightly unstable to chromatography but could be isolated in 49% yield after recrystallization from ether/petroleum ether. The structural assignment of **2a** was based on its distinctive NMR spectrum at 95 °C, which included signals for the two vinyl protons, the diastereotopic butyrolactone protons and the four azetidine protons.[7] Particularly distinctive is the methine proton H_a which displays coupling to all the other azetidine protons as well as homoallylic coupling to one of the butyrolactone methylene protons. A similar reaction was observed with substituted pyrrole **1b** leading to a clean transformation and the eventual isolation of **2b** in 34% yield.



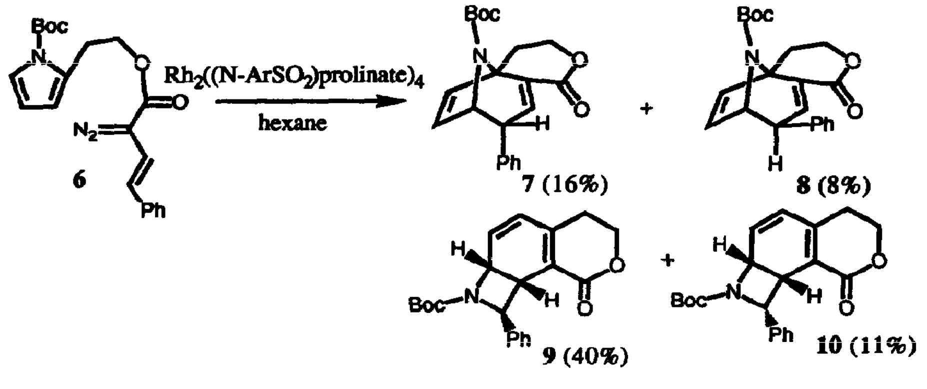
(2)

Fused 7-azabicyclo[4.2.0]octadienes could also be formed using the phenyl substituted vinyldiazomethanes **3**. These products were stable to chromatography, and consequently were isolable in higher yields. A mixture of isomeric products **4** and **5** was obtained (~2 : 1 ratio); these were readily distinguished on the basis of coupling constants for the azetidine protons and the shielding effect of the phenyl ring.



(3)

Extension of this chemistry to the higher homolog **6** led to intriguing results. The rhodium(II) octanoate/hexane reaction conditions resulted in inefficient capture of the carbenoid and the only isolable products were the fused tropanes, **7** and **8** in less than 10% combined yield. On the assumption that a more electrophilic carbenoid would likely lead to more effective reaction with the pyrrole, the reaction was repeated using rhodium(II) (N-p-(*tert*butyl)phenylsulfonyl)prolinate[8] as catalyst, and this lead to the formation of two isomeric

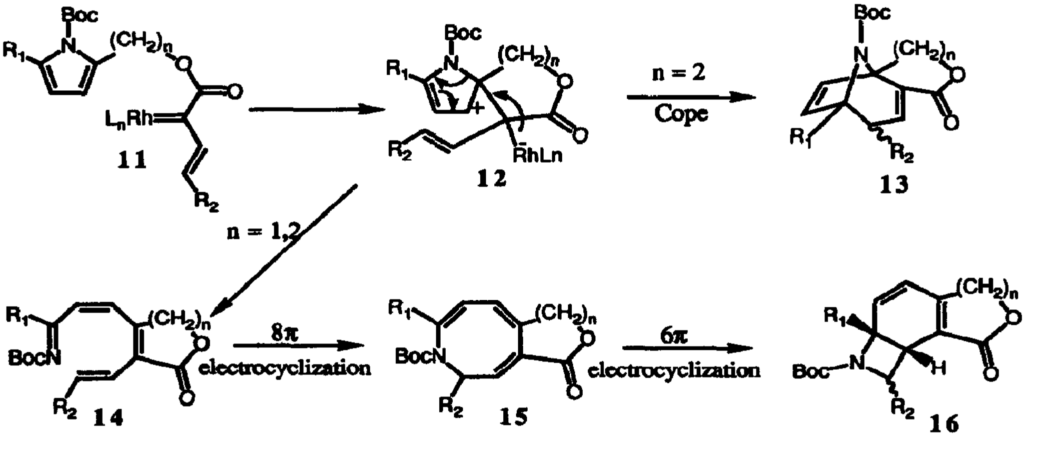


(4)

tropanes **7** and **8** (24% combined yield), as well as two fused 7-azabicyclo[4.2.0]octadienes **9** and **10** (51% combined yield). The stereochemistry for **7** and **8** was readily assigned based on the distinctive coupling constant for the bridgehead proton.[6b] The formation of both endo (**7**) and exo (**8**) isomers of the tropanes was unexpected because the Cope rearrangement of divinylcyclopropanes generally proceeds through a well defined boat transition state and this would have led to the formation of only the endo product **7**.[9] The formation of the exo product **8** was not due to isomerization of the endo product **7** because **7** was stable when subjected to the reaction conditions of its formation.

A reasonable mechanism to explain these transformations is shown in Scheme 1. The reaction is considered to proceed by initial intramolecular capture of the rhodium carbenoid by pyrrole leading to a zwitterionic structure **12** rather than direct cyclopropanation.[10] The involvement of a cyclopropane intermediate has been ruled out based on the lack of stereospecificity in the formation of the fused tropanes, whereas the zwitterionic structure **12** offers the opportunity for bond rotation, which could then lead to the formation of both endo and exo isomers of **13**. Due presumably to the constraints caused by the tether in **12**, rearrangement involving interactions of both vinyl groups (analogous to a stepwise Cope rearrangement) proceeding to the tropane **13** is only possible in the case of the more flexible system where n=2. Instead an alternative rearrangement occurs to form the unsaturated imine **14**. This type of rearrangement is known for furanocyclopropanes[11] and has been observed on flash vacuum pyrolysis of a pyrrolocyclopropane.[2] The presence of two Z double bonds in **14** means that the system can readily undergo a thermally allowed conrotatory 8π electrocyclization to form the dihydroazocine **15**. This type of electrocyclic ring closure is well doccumented for the formation of cyclooctatrienes.[12] The resulting dihydroazocine **15** then undergoes a well-precedented disrotatory 6π electrocyclization[5] to form the 7-azabicyclo[4.2.0]octadiene **16**.

Scheme 1



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References and Notes

1. (a) Maryanoff, B. E. *J. Org. Chem.* **1979**, *44*, 4410. (b) Maryanoff, B. E. *J. Org. Chem.* **1982**, *47*, 3000. (c) Jefford, C. W.; Tang, Q.; Zaslona, A. *Helv. Chim. Acta* **1989**, *72*, 1749. (d) Jefford, C. W.; Tang, Q.; Zaslona, A. *J. Am. Chem. Soc.* **1991**, *113*, 3513.
2. Tanny, S. R.; Grossman, J.; Fowler, F. W. *J. Am. Chem. Soc.* **1972**, *94*, 6495.
3. Pirrung, M. C.; Zhang, J.; McPhail, A. T. *J. Org. Chem.* **1991**, *56*, 6269
4. Davies, H. M. L.; Saikali, E.; Young, W. B. *J. Org. Chem.* **1991**, *56*, 5696.
5. Paquette, L. A.; Kakihana, T.; Kelly, J. F. *J. Org. Chem.* **1971**, *36*, 435.
6. (a) Davies, H. M. L.; Hougland, P. W.; Cantrell, W. R., Jr. *Synth. Commun.* **1992**, *22*, 971. (b) Davies, H. M. L.; Clark, T. J.; Smith, H. D. *J. Org. Chem.* **1991**, *56*, 3817.
7. Representative ^{1}H NMR data: **2a** (DMSO d_6, 95 °C): 6.35 (d, *J*=9.8 Hz, 1H), 6.26 (dd, *J*=9.8, 4.3 Hz, 1H), 5.16 (dd, *J*=9.8, 4.3 Hz, 1H), 4.98 (br. d, *J*=17.8 Hz, 1H), 4.85 (dd, *J*=17.8, 2.5 Hz, 1H), 4.31 (t, *J*=8.1 Hz, 1H), 3.85 (dd, *J*=8.1, 4.8 Hz, 1H), 3.52 (dddd, *J*=9.8, 8.1, 4.8, 2.5 Hz, 1H), 1.40 (s, 9H). **4a** (DMSO d_6, 95 °C): 7.25-7.45 (m, 5H), 6.50 (dd, *J*=9.9, 3.9 Hz, 1H), 6.41 (d, *J*=9.9 Hz, 1H), 5.40 (dd, *J*=9.8, 3.9 Hz, 1H), 5.23 (d, *J*=5.0 Hz, 1H), 5.05 (br. d, *J*=17.9 Hz, 1H), 4.90 (dd, *J*=17.9, 2.4 Hz, 1H), 3.40 (ddd, *J*=9.8, 5.0, 2.4 Hz), 1.27 (s, 9H). **5a** (DMSO d_6, 95 °C): 7.25-7.45 (m, 5H), 6.32 (m, 2H), 5.70 (d, *J*=8.6 Hz, 1H), 5.20 (m, 1H), 4.70 (dd, *J*=17.8, 2.6 Hz, 1H), 4.55 (br. d, *J*=17.8 Hz, 1H), 4.05 (ddd, *J*=8.6, 8.6, 2.6 Hz, 1H), 1.27 (s, 9H). **7** ($CDCl_3$): 7.24-7.36 (m, 3H), 7.03-7.10 (m, 2H), 7.02 (dd, *J*=2.8, 1.2 Hz, 1H), 6.42 (d, *J*=6.1 Hz, 1H), 5.51 (dd, *J*=6.1, 2.8 Hz, 1H), 4.92 (ddd, *J*=5.3, 2.8, 1.2 Hz, 1H), 4.60 (m, 1H), 4.32 (ddd, *J*=14.6, 9.6, 2.9 Hz, 1H), 4.22 (dd, *J*=5.3, 2.8 Hz, 1H), 3.25 (ddd, *J*=16.5, 9.6, 3.8 Hz, 1H), 2.08 (ddd, *J*=16.5, 5.8, 2.9 Hz), 1.45 (s, 9H). **8** ($CDCl_3$): 7.10-7.34 (m, 5H), 6.88 (dd, *J*=3.4, 1.8 Hz, 1H), 6.36 (d, *J*=6.0 Hz, 1H), 6.24 (dd, *J*=6.0, 2.8 Hz, 1H), 4.73 (dd, *J*=2.8, 1.8 Hz, 1H), 4.66 (ddd, *J*=14.0, 6.7, 3.5 Hz, 1H), 4.36 (ddd, *J*=14.0, 8.4, 2.9 Hz, 1H), 3.33 (d, *J*=3.4 Hz, 1H), 3.30 (ddd, *J*=14.8, 8.4, 3.5 Hz, 1H), 2.16 (ddd, *J*=14.8, 6.7, 2.9 Hz, 1H), 0.99 (s, 9H).
8. Davies, H. M. L.; Hutcheson, D. K. *Tetrahedron Lett.* **1993**, *34*, 7243.
9. Davies, H. M. L. *Tetrahedron* **1993**, *49*, 5203.
10. Many examples are known on intramolecular reactions of carbenoids with aromatic systems proceeding through dipolar intermediates. See: (a) Doyle, M. P.; Shanklin, M. S.; Pho, H. Q.; Mahapatro, S. N. *J. Org. Chem.* **1988**, *53*, 1017. (b) Davies, H. M. L.; McAfee, M. J.; Oldenburg, C. E. M. *J. Org. Chem.* **1989**, *54*, 930.
11. Padwa, A.; Wisnieff, T. J.; Walsh, E. J. *J. Org. Chem.* **1989**, *54*, 299 and references cited therein.
12. (a) Marvell, E. N.; Seubert, J. *J. Am. Chem. Soc.* **1967**, *89*, 3377. (b) Huisgen, R.; Dahmen, A.; Huber, H. *Tetrahedron Lett.* **1969**, 1461. (c) Huisgen, R.; Dahmen, A.; Huber, H. *J. Am. Chem. Soc.* **1967**, *89*, 7130. (d) Huisgen, R.; Dahmen, A.; Huber, H. *Tetrahedron Lett.* **1969**, 1465

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