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THE SYNTHESIS OF NITROCYCLOPROPANES FROM NITRODIAZOMETHANES

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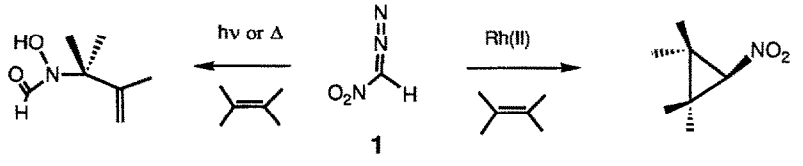
Summary: The synthesis of novel 1-substituted nitrocyclopropanes using the rhodium(II) acetate catalyzed cyclopropanation reaction of several nitrodiazomethanes with electron rich alkenes is described.

The transition metal mediated cyclopropanation of alkenes with diazo compounds is a valuable synthetic reaction.[1] It is especially useful in instances where the desired free singlet carbene is unstable to rearrangement.[2] If free singlet nitrocarbene is ever formed, high level *ab initio* calculations predict that it will quickly rearrange to the reactive intermediate nitrosoformaldehyde. This compound undergoes ene reactions or Diels-Alder reactions with alkenes and 1,3-dienes, respectively.[3] On the other hand, rhodium(II) acetate catalyzed decomposition of nitrodiazomethane in the presence of alkenes produces nitrocyclopropanes.[4]



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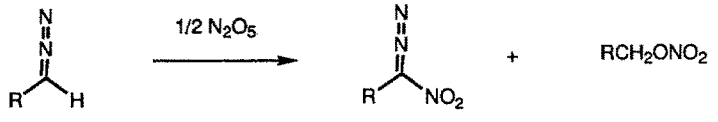
We have further investigated the generality of this rhodium(II) catalyzed cyclopropanation reaction using other substituted nitrodiazomethanes. Schöllkopf and co-workers reported the syntheses of several nitrodiazomethanes by nitration of electronegatively substituted diazomethanes with N_2O_5.[5] The parent nitrodiazomethane (**1**) is prepared by deprotection of **4** with trifluoroacetic acid followed by decarboxylation in wet methylene chloride.[6] The solution is dried and used without further purification. Like nitrodiazomethane, **2** is treacherously explosive when neat, but it can be safely and conveniently handled as the crude solution obtained from the nitration procedure. We have not experienced any problems with the purification of **3**, **4**, **5**, **6**, or **7**.



2, R = CN
3, R= CO_2Et
4, R = CO_2t-Bu
5, R = (CO)Ph
6, R = SO_2PhCH_3
7, R = CF_3

When a solution of nitrodiazomethane (**1** - **7**)[7] is slowly added to neat styrene containing 1 mole % $Rh_2(OAc)_4$, a smooth reaction takes place. The corresponding nitrocyclopropanes[8] can be isolated by silica gel chromatography in moderate to good yields. Several other alkenes behave similarly. The results are shown in Table 1.

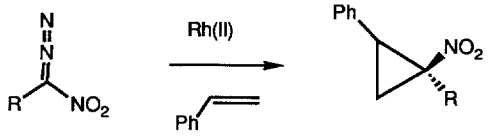
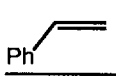
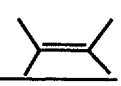
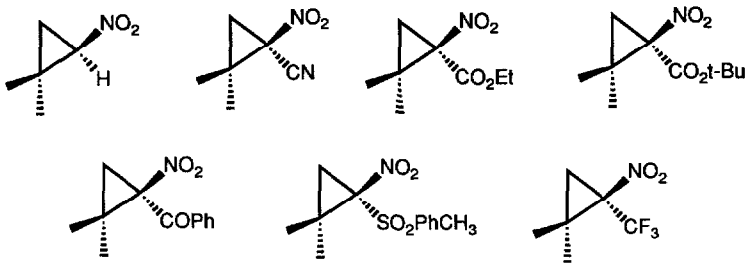


Table 1. Yields and diastereoselectivities[a] for the cyclopropanation of alkenes with several nitrodiazomethanes in the presence of rhodium(II) acetate.

						
1	54% 2.4:1	50% b	50% 1:1	30% 3:1	40% b	20% b
2	55% 2:1	50% b	40% 15:1	40% >20:1	30% b	35% b
3	75% 8:1	75% b	65% 4:1	35% 6:1	0	0
4	83% 2:1	80% b	50% 4:1	30% 4:1	c	0
5[d]	75% 1:6	58% b	45% 1:10	20% <1:20	c	0
6[d]	73% 1:2.4	72% b	53% 10:1	42% >20:1	c	0
7	30% 1:1	6% b	c	c	c	0

a. Diastereoselectivities are given as trans/cis relative to the nitro group. b. Only one diastereomer possible. c. Reaction was not performed. d. Tentative stereochemical assignments based on NMR data from reference 10.

As detailed in Table 1, the yields of cyclopropane products depend on the structure of both the alkene and the nitrodiazo precursor. The reaction works best with electron rich, unhindered alkenes. While diazo compounds **1** and **2** cyclopropanate all of the alkenes chosen for this study, compounds **3** - **6** which bear sterically demanding substituents generally do not cyclopropanate trans di-substituted and tetra-substituted alkenes. We have recently reported a detailed study of this steric effect using diazo compound **3**.[9] The cyclopropanes derived from isobutylene that are available by this route are shown below.



The diastereoselectivities of the cyclopropanation reaction are given in Table 1. They are determined by integration of the peaks corresponding to the cyclopropyl protons in the NMR spectrum. The assignment of stereochemistry for cyclopropanes derived from **2**, **3** and **4** is based on the observation that the nitro group deshields syn cyclopropyl protons more effectively than a carboxylate group.[9] For cyclopropanes derived from **5** and **6**, our assignments are tentative and based on NMR data gathered by others.[10] In many cases, the diastereomeric excess is quite good. It is generally found that the nitro group prefers a position trans to the alkyl or aryl substituent of the alkene. We have extended Doyle's model[11] for ethyl diazoacetate to account for this preference.[9] Nitrodiazoacetophenone (**5**) is an exception to this model, and we have no satisfactory explanation for the difference in stereochemical preference exhibited by **5** and **6**.

There are relatively few examples of 1-substituted nitrocyclopropanes in the literature[12, 13] and there are no general methods available for their synthesis. Our present methodology allows the ready synthesis of a variety of new 1-substituted nitrocyclopropanes in good yields and with a reasonable degree of diastereoselection. Further transformations of these compounds, for instance reduction to the corresponding amines, will make other cyclopropanes available for study. The chemistry of these nitrocyclopropanes will be reported at a later time.[14]

CAUTION: All diazo compounds, especially nitrodiazo compounds, should be treated as potential explosives and appropriate precautions should be taken.

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References

1. Doyle, M. P. *Chem. Rev.* **1986**, *86*, 919.

2. Arnold, Z. *J. Chem. Soc., Chem. Comm.* **1967**, 299.

3. O'Bannon, P. E. and Dailey, W. P. *Tetrahedron Lett.* **1988**, 5719.

4. O'Bannon, P. E. and Dailey, W. P. *Tetrahedron Lett.* **1988**, 987.

5. (a) Schöllkopf, U.; Tonne, P.; Schafer, H., Markusch, P. *Ann. Chem.* **1968**, *722*, 45.
(b) Schöllkopf, U. and Markusch, P. *Ann. Chem.* **1971**, *753*, 143.

6. O'Bannon, P. E. and Dailey, W. P. *Tetrahedron Lett.* **1988**, 6031.

7. Diazo compound **1** was used as a crude solution from the deprotection and decarboxylation of ester **4** and yields are based on **4**. Diazo compounds **2** and **5** were also used as crude solutions from the nitration reaction and yields are reported for the two steps together.

8. All new compounds were completely characterized by ^{1}H NMR, ir, and high resolution mass spectral and/or satisfactory elemental analyses.

9. O'Bannon, P. E. and Dailey, W. P. *J. Org. Chem.* **1989**, in press.

10. For simple methyl substituted phenylcyclopropyl ketones, it has been observed that the benzoyl group shields cis methyl groups relative to trans methyl groups (Watson, J. M.; Irvine, J. L.; Roberts, R. M. *J. Am. Chem. Soc.* **1973**, *95*, 3348 and Cowan, D. O.; Couch, M. M.; Kopecky, K. R.; Hammond, G. S. *J. Org. Chem.* **1964**, *29*, 1922). On the other hand, the sulfonyl group deshields cis methyl groups relative to trans methyl groups in aryl sulfonylcyclopropanes (van Leusen, A. M.; Mulder, R. J.; Strating, J. *Tetrahedron Lett.* **1964**, 543 and van Leusen, A. M.; Mulder, R. J.; Strating, *J.; Rec. Trav. Chim.* **1967**, *84*, 225). Thus we assign the major isomer from the reaction of **5** with cis-2-butene {δ 1.35 (m, 6 H), 2.15 (m, 2 H), 7.4 - 7.8 (m, 5 H)} as having the methyl groups cis to the nitro group and the minor isomer {δ 1.11 (m, 6 H), 2.52 (m, 2 H), 7.4 - 7.8 (m, 5 H)} as trans. Similarly for the major isomer obtained from the reaction of **6** with cis-2-butene{δ 1.59 (m, 6 H), 2.39 (s, 3 H), 2.63 (m, 2 H), 7.28 (d, 2 H), 7.83 (d, 2 H)} is assigned trans and the minor isomer {δ 1.11 (m, 6 H), 2.36 (m, 2 H), 2.41 (s, 3 H), 7.28 (d, 2 H), 7.83 (d, 2 H)} cis.

11. Doyle, M. P.; Griffin, J. H.; Bagheri, V.; Dorow, R. L. *Organometallics* **1984**, *3*, 53.

12. 1-alkyl nitrocyclopropanes may be prepared by cyclopropanation of nitroolefins with dimethylsulfoxonium methylide: Asunskis, J. and Shechter, H. *J. Org. Chem.* **1968**, *33*, 1165.

13. For an attempted functionalization of nitrocyclopropane see: Kai, Y.; Knochel, P.; Kwiatkowski, S.; Dunitz, J. D.; Oth, J. F. M.; Seebach, D.; Kalinowski, H.-O. *Helv. Chim. Act.* **1982**, *69*, 1655.

14. O'Bannon, P. E. and Dailey, W. P. unpublished results.

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