Pergamon

Tetrahedron Letters 41 (2000) 8189–8192

TETRAHEDRON LETTERS

Asymmetric synthesis of 1-alkynylcyclopropane-1-carboxylates

Huw M. L. Davies* and Timothy A. Boebel

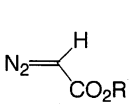
Department of Chemistry, State University of New York at Buffalo, Buffalo, NY 14260–3000, USA

Received 13 August 2000; revised 29 August 2000; accepted 1 September 2000

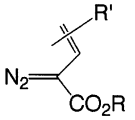
Abstract

Dirhodium tetrakis(*S*-(*N*-dodecylbenzenesulfonyl)prolinate) (Rh_2S–$DOSP_4$) catalyzed decomposition of methyl alkynyldiazoacetates in the presence of alkenes results in highly diastereoselective and enantioselective cyclopropanations. © 2000 Published by Elsevier Science Ltd.

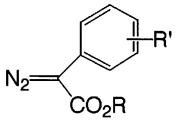
The metal catalyzed decomposition of α-diazocarbonyls in the presence of alkenes is a powerful method for the synthesis of highly functionalized cyclopropanes.[1] By far the most commonly used α-diazocarbonyls have been the diazoacetates **1**. Diastereoselective cyclopropanations, however, with this system have been challenging.[1,2] In recent years cyclopropanations by vinyldiazoacetates (**2**)[3] and phenyldiazoacetates (**3**)[4] have been extensively studied because these cyclopropanations are highly diastereoselective. Furthermore, these carbenoids display much greater chemoselectivity than the carbenoids derived from simple diazoacetates.[5] We have rationalized that carbenoids containing both electron-withdrawing (EWG) and electron-donating (EDG) groups undergo highly diastereoselective cyclopropanations because the trajectory of alkene approach to these carbenoids is very demanding, occurring side-on over the electron withdrawing group, as illustrated in transition-state model **5**.[3b] On the basis of this hypothesis, we predicted that alkynyldiazoacetates (**4**) would similarly undergo highly stereoselective and chemoselective cyclopropanations. The synthesis of alkynyldiazoacetates and their subsequent cyclopropanation chemistry is the basis of this paper.



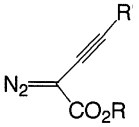
1



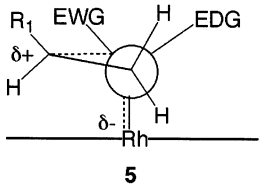
2



3



4

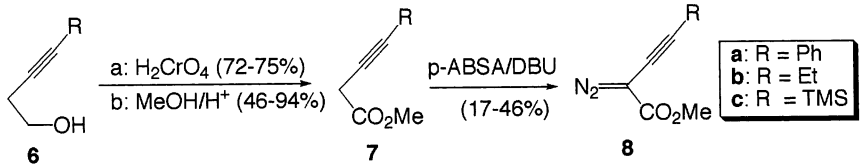


5

* Corresponding author.

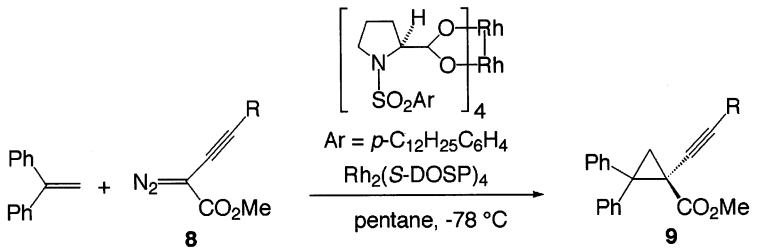
0040-4039/00/$ - see front matter © 2000 Published by Elsevier Science Ltd.
PII: S0040-4039(00)01453-2

In order to explore the chemistry of alkynyldiazoacetates, three representative examples were prepared as shown in reaction 1. The 3-alkyn-1-ols **6** were prepared by conventional procedures and were readily oxidized to the acid and then converted to the 3-alkynoates **7**. A diazo transfer reaction on **7** with *p*-(acetamido)benzenesulfonyl azide (*p*-ABSA)[6] and DBU as base gave the alkynyldiazoacetates **8**. Even though the yield for the formation of **8** was moderately low (17–46% yield), these compounds exhibit reasonable stability and can be stored in solution at 0°C for extended periods.



(1)

A further advantage of the aryl- and vinyldiazoacetate derived carbenoids is that highly enantioselective transformations can be achieved by using dirhodium tetraprolinates such as Rh_2(*S*-DOSP)$_4$ as catalyst.[7] These catalysts are especially well suited for aryl- and vinyldiazoacetates, while only low asymmetric induction is obtained with these catalysts in cyclopropanation by ethyl diazoacetate.[3b] Therefore, the test reactions of alkynyldiazoactetates were carried out using Rh_2(*S*-DOSP)$_4$ as the catalyst so that both the diastereoselectivity and the enantioselectivity of the cyclopropanation could be studied. It has been previously shown that Rh_2(*S*-DOSP)$_4$ catalyzed cyclopropanation of methyl phenyldiazoacetate (**3**, R = Me, R′ = H) occurs with very high enantioselectivity (97% ee).[4c] The parallel reaction with the alkynyldiazoacetates **8a**–**c** (Eq. (2)) also resulted in highly enantioselective cyclopropanations (87–93% ee). The catalyst is sufficiently active that these reactions could be carried out at −78°C (Table 1).

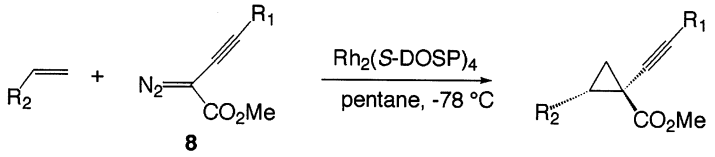


(2)

Table 1

	R	Yield (%)	ee (%)
a	Ph	68	93
b	Et	42	91
c	TMS	83	87

In order to explore the diastereoselectivity of these cyclopropanations, a series of reactions of **8a–c** was carried out with various mono-substituted alkenes. As summarized in Eq. (3), the reaction of all three diazo compounds with styrene resulted in cyclopropanation with high-diastereoselectivity (84–98% de) and enantioselectivity (56–89% ee).[8] Extension of the reaction of **8a** to other electron rich alkenes resulted in similarly high stereoselectivity (Table 2).

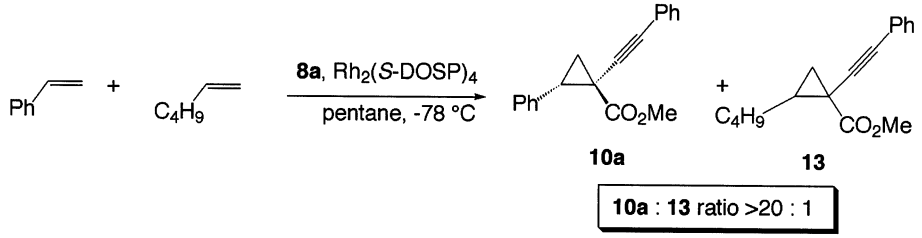


(3)

Table 2

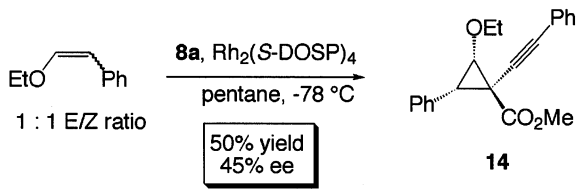
Diazo	R_1	R_2	Product	Yield (%)	de (%)	ee (%)
8a	Ph	Ph	**10a**	68	84	89
8b	Et	Ph	**10b**	91	98	56
8c	TMS	Ph	**10c**	84	88	65
8a	Ph	OBu	**11**	66	>94	87
8a	Ph	OAc	**12**	61	>94	95

We have recently described the considerable difference in chemoselectivity between vinyl- and aryldiazoacetates compared to simple diazoacetates.[5] For example, for vinyldiazoacetates and phenyldiazoacetates the chemoselectivity ratio for competing cyclopropanation between styrene versus 1-hexene is about 50:1, while for ethyl diazoacetate it is only about 3:1. The chemoselectivity of alkynyldiazoacetates appeared to be very high because 1-hexene was not effectively cyclopropanated. Indeed, decomposition of **8a** in the presence of styrene and 1-hexene led to selective cyclopropanation of styrene by a ratio of >20:1 (Eq. (4)).



(4)

One of the most distinctive features of vinyldiazoacetate intermolecular cyclopropanations is that no reaction occurs with *trans* alkenes.[3b,9] In order to explore if a similar reactivity profile is displayed by the alkynyldiazoacetates, **8a** was decomposed in the presence of a 1:1 mixture of methyl propenyl ether. This resulted in the formation of **14** as a single diastereomer in 45% ee (Eq. (5)). This result demonstrates that **8a** displays the same type of selectivity as the vinyldiazoacetates.



(5)

In summary, these studies demonstrate that alkynyldiazoacetates have a similar reactivity profile to aryl- and vinyldiazoacetates. The resulting carbenoids have high chemoselectivity and undergo highly stereoselective cyclopropanations. This reactivity appears to be a general feature of rhodium–carbenoids that contain both electron donor and acceptor groups, and is presumably caused by the stabilizing influence of the donor group. It is considered that the high stereoselectivity is due to a very demanding trajectory of approach of the alkene to the carbenoid, with approach occurring over the acceptor group. As the trajectory is based on an electronic argument, the same sense of enantioselectivity would be expected from the alkynyldiazoacetates. The observation of similar enantioselectivity and same sense of asymmetric induction is good supporting evidence for the proposed mechanism because if steric factors governed the approach of the alkene, attack over the linear alkynyl groups might have been expected leading to the opposite sense of asymmetric induction.

Acknowledgements

Financial support of this work by the National Science Foundation (CHE 9726124) is gratefully acknowledged. We also thank Pfizer, Inc. for a Pfizer Undergraduate Summer Research Fellowship to T.A.B. Technical assistance by Mr. Douglas Stafford is also greatly appreciated.

References

1. Doyle, M. P.; McKervey, M. A.; Ye, T. *Modern Catalytic Methods for Organic Synthesis with Diazo Compounds*; Wiley-Interscience: New York, 1998; pp. 163–239.
2. For recent advances in stereoselectivity of diazoacetate cyclopropanations, see (a) Doyle, M. P.; Bagheri, V.; Wandless, T. J.; Harn, N. K.; Brinker, D. A.; Eagle, C. T.; Loh, K. L. *J. Am. Chem. Soc.* **1990**, *112*, 1906. (b) Nishiyama, H.; Itoh, Y.; Matsumoto, H.; Park, S.-B.; Itoh, K. *J. Am. Chem. Soc.* **1994**, *116*, 2223. (c) Niimi, T.; Uchida, T.; Irie, R.; Katsuki, T. *Tetrahedron Lett.* **241**, *41*, 3647.
3. (a) Davies, H. M. L.; Clark, T. J.; Church, L. A. *Tetrahedron Lett.* **1989**, *30*, 5057. (b) Davies, H. M. L.; Bruzinski, P. R.; Lake, D. H.; Kong, N.; Fall, M. J. *J. Am. Chem. Soc.* **1996**, *118*, 6897.
4. (a) Paulini, K.; Reissig, H.-U. *J. Prakt. Chem./Chem. -Ztg.* **1995**, *337*, 55. (b) Davies, H. M. L.; Bruzinski, P. R.; Fall, M. J. *Tetrahedron Lett.* **1996**, *37*, 4133. (c) Doyle, M. P.; Zhou, Q.-L.; Charnsangavej, C.; Longoria, M. A.; McKervey, M. A.; Garcia, C. F. *Tetrahedron Lett.* **1996**, *37*, 4129. (d) Starmans, W. A. J.; Thijs, L.; Zwanenburg, B. *Tetrahedron* **1998**, *54*, 629. (e) Davies, H. M. L.; Rusiniak, L. *Tetrahedron Lett.* **1998**, *29*, 8811.
5. Davies, H. M. L.; Panaro, S. A. *Tetrahedron* **28192**, *56*, 4871.
6. Davies, H. M. L.; Cantrell Jr., W. R.; Romines, K. R.; Baum, J. S. *Org. Synth.* **1991**, *70*, 93.
7. (a) Davies, H. M. L. *Aldrichimica Acta* **1997**, *30*, 107. (b) Davies, H. M. L. *Eur. J. Org. Chem.* **1999**, 2459.
8. The absolute stereochemistry of **10a** was determined by catalytic hydrogenation of both **10a** and (1*S*,2*S*)-methyl 2-phenyl-1-(2-(*Z*)-styryl)cyclopropane-1-carboxylate (see Ref. 3b) to (1*S*,2*S*)-methyl 2-phenyl-1-(2-phenylethyl)cyclopropane-1-carboxylate. The absolute stereochemistry of the other products is drawn assuming a similar trajectory of attack as was observed for the vinyldiazoacetates (see Ref. 3b).
9. Davies, H. M. L.; Hu, B. *Heterocycles* **1993**, *35*, 385.