Tetrahedron Letters,Vol.30,No.42,pp 5747-5750,1989 0040-4039/89 $3.00 + .00
Printed in Great Britain Pergamon Press plc

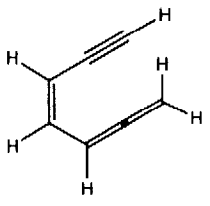
ALLENE SYNTHESIS FROM 2-ALKYN-1-OLS

Andrew G. Myers,* Nathaniel S. Finney and Elaine Y. Kuo
Contribution No. 8005 from the Arnold and Mabel Beckman Laboratories of Chemical Synthesis
California Institute of Technology, Pasadena, California 91125

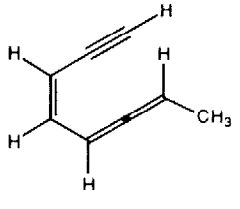
Summary: Activation of 2-alkyn-1-ols as their methanesulfonate esters and displacement with hydrazine furnishes the corresponding alkynyl hydrazine derivatives which undergo smooth oxidative rearrangement with diethyl azodicarboxylate (DEAD) or 4-methyl-1,2,4-triazoline-3,5-dione (MTAD) to form allenes.

As targets for chemical synthesis, (Z)-1,2,4-heptatrien-6-yne (**1**) and (Z)-3,5,6-octatrien-1-yne (**2**) present two challenges: (1) stereospecific construction of the vinylallene linkage and (2) a requirement for methodology in the final stage which is compatible with the low thermal stability and high reactivity of these compounds.[1] We describe herein the development of methodology which meets these criteria and which may prove of general value in the preparation of allenes.

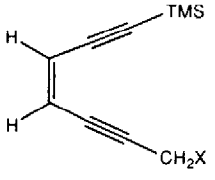
The formation of allenes and transposed alkenes upon hydridic reduction of conjugated alkynyl and alkenyl tosyl hydrazones, respectively, has been rationalized as arising via sigmatropic rearrangement (with extrusion of dinitrogen) of a propargylic or allylic diazene intermediate (e.g. **5**).[2] Corey and co-workers have recently developed a useful transposition sequence which, presumably, also involves an allylic diazene intermediate, produced in this case by air oxidation of an allylic hydrazine.[3]



1

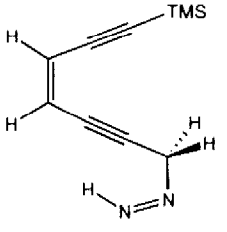


2



3 X = OH

4 X = $NHNH_2$

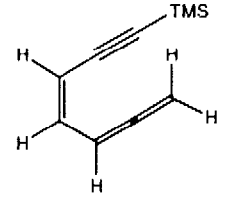


5

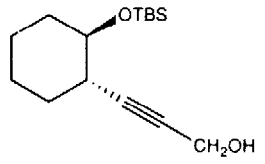
We find that while propargylic hydrazines are similarly oxidized in air to form allenes, reaction is much more rapid and efficient when diethyl azodicarboxylate (DEAD) or 4-methyl-1,2,4-triazoline-3,5-dione (MTAD) is used as the oxidant.[4]

The transformation of the acetylenic alcohol **3** to the allene **6** is representative.[5] Activation of the hydroxyl group of **3** with methanesulfonyl chloride and direct addition of the resulting mesylate to a solution of excess dry hydrazine in methanol at 0 °C afforded, after extractive isolation, the corresponding acetylenic hydrazine **4**. A survey of several oxidants revealed the commercially available azo compounds DEAD and MTAD as superior reagents in terms of rapidity and efficiency in oxidative rearrangement of **4**.[6] Thus, treatment of an ice-cooled ethereal solution of **4** with DEAD (1.1 equiv) led to spontaneous evolution of dinitrogen with formation of the allene **6** in 62% yield (from **3**) after flash column chromatography. A similar sequence of events transformed the acetylenic alcohol **8**[7] into the allene **9** (70%) and the (racemic) secondary alcohol **7** into allene **2** (48%).[8]

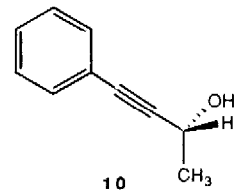
The latter example is notable for the high reactivity and volatility of the product allene and also suggests that the method may find use in the synthesis of optically active allenes. This was demonstrated with (*R*)-alcohol **10** (76 ± 2% ee), obtained by reduction of the corresponding ketone with (*R*)-Alpine–Borane®.[9] Implementation of the standard protocol furnished the (*S*)-allene **11** ($[\alpha]_{21}^{D} = -176°$, C = 1.26 in acetone) in 81% yield.[10] ^{1}H NMR analysis with the chiral shift reagent combination Ag(fod)–Yb(hfc)$_3$ showed the product to be 75 ± 2% ee, demonstrating that the displacement-rearrangement sequence had proceeded with essentially complete stereospecificity.[11] Experimental detail is provided in the procedure which follows.



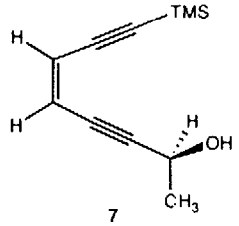
6



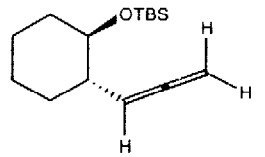
8



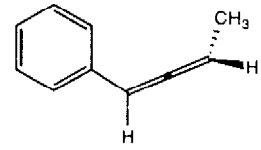
10



7



9



11

Experimental

Materials (*R*)-4-Phenyl-3-butyn-2-ol (76 ± 2% ee) was prepared by the method of Midland et. al.[9] Methylene chloride and triethylamine were freshly distilled from calcium hydride under dry nitrogen. Methanesulfonyl chloride was purified by vacuum distillation. Anhydrous hydrazine in methanol was prepared by addition of equal volumes of hydrazine (98%, Aldrich Chemical) and dry methanol (reagent grade "anhydrous") and was stored over 4 Å molecular sieves for at least 24 h *prior to use*. Diethyl azodicarboxylate (95%, Aldrich Chemical) was used as received. Reactions were performed under an atmosphere of dry argon.

Method Methanesulfonyl chloride (0.714 mL, 9.23 mmol, 1.10 equiv) was added dropwise over 5 min to a stirring solution of (*R*)-4 phenyl-3-butyn-2-ol (76 ± 2% ee, 1.225 g, 8.38 mmol, 1 equiv) and triethylamine (1.750 mL, 12.6 mmol, 1.50 equiv) in methylene chloride (15 mL) at 0 °C.[12] After 5 min, the ice-cooled reaction mixture was transferred via cannula to a solution of anhydrous hydrazine in methanol (1:1, 30 mL) at 0 °C and the resulting solution was stirred at 0 °C for 24 h. The product solution was partitioned between half-saturated brine (60 mL) and 5% methanol-methylene chloride solution (2 x, 40 mL). After washing with brine (40 mL), the combined organic layers were dried with sodium sulfate and concentrated *in vacuo*. The liquid residue was dissolved in ether (20 mL) and the resulting solution was cooled to 0 °C. Diethyl azodicarboxylate (95%, 1.53 mL, 9.23 mmol, 1.10 equiv) was introduced by dropwise addition over 2 min and was accompanied by the evolution of dinitrogen. After 5 min, pentane (100 mL) was added to the reaction mixture and the resulting solution was washed with brine (100 mL) and dried (Na_2SO_4). Careful concentration of this solution *in vacuo* at 0 °C and purification of the residue by flash column chromatography with pentane as eluent afforded (*R*)-(−)-1-phenyl-1,2-butadiene ($[\alpha]_{21}^{D} = -176^{\circ}$, C = 1.26 in acetone, 0.887 g, 81%)[10] as a colorless liquid. ^{1}H NMR analysis with the chiral shift reagent Ag(fod)–Yb(Hfc)$_3$ (allene: Ag: Yb = 1:2:1.5) showed the product to be 75 ± 2% ee.[11]

Acknowledgment

Generous financial assistance from the National Science Foundation and a Kodak fellowship to EYK are gratefully acknowledged.

References and Notes

1. Myers, A. G.; Kuo, E. Y.; Finney, N. S., submitted for publication in *J. Am. Chem. Soc.*

2. (a) Hutchins, R. O.; Milewski, C. A.; Maryanoff, B. E. *J. Am. Chem. Soc.* **1973**, *95*, 3662; (b) Hutchins, R. O.; Kacher, M.; Rua, L. *J. Org. Chem.* **1975**, *40*, 923; (c) Kabalka, G. W.; Yang, D. T. C.; Baker, J. D., Jr. *J. Org. Chem.* **1976**, *41*, 574; (d) Kabalka, G. W.; Chandler, J. H. *Synth. Commun.* **1979**, *9*, 275. For the related rearrangement of allylic tosylhydrazides see: (e) Sato, T.; Homma, I.; Nakamura, S. *Tetrahedron Lett.* **1969**, 871; (f) Corey, E. J.; Cane, D. E.; Libit, L. *J. Am. Chem. Soc.* **1971**, *93*, 7016. Similarly, Wolff-Kishner reduction of α,β-unsaturated carbonyl compounds often leads to olefin transposition, see: (g) Reusch, W. In *Reduction*; Augustine, R. L., Ed., Marcel Dekker: New York, 1968; p. 182.

3. Corey, E. J.; Wess, G.; Xiang, Y. B.; Singh, A. K. *J. Am. Chem. Soc.* **1987**, *109*, 4717.

4. For the oxidation of 1,1- and 1,2-dialkylhydrazines, respectively, with diethyl azodicarboxylate, see: (a) Fahr, E.; Koch, K.-H. *Liebigs, Ann. Chem.* **1980**, 219; (b) Stone, K. J.; Greenberg, M. M.; Blackstock, S. C.; Berson, J. A. *J. Am. Chem. Soc.* **1989**, *111*, 3659. *N*-Phenyltriazolinedione has been used for the oxidation of 1,2-dialkylhydrazines: (c) Gisin, M.; Wirz, J. *Helv. Chim. Acta.* **1976**, *59*, 2273.

5. Use of an acetylenic precursor for the allene functional group allows stereospecific formation of the vinylallene linkage (see reference 1), satisfying one of the criteria set forth above.

6. Oxidation with the less expensive DEAD typically produced small amounts (≤5%) of products of carboethoxy transfer to the hydrazine. Oxidation with MTAD was more rapid and could be carried out at lower temperature (−78 °C). Yields with each reagent were roughly comparable and both led to complete reaction within 5 min at 0 °C.

7. Alcohol **8** was synthesized as follows: Reaction of cyclohexene oxide with the 1:1 complex of boron trifluoride etherate and the lithiated tetrahydropyranyl ether of propargyl alcohol in tetrahydrofuran at −78 °C produced the *trans*-cyclohexanol in 82% yield [Yamaguchi, M.; Hirao, I. *Tetrahedron Lett.* **1983**, *24*, 391]. Silylation with *t*-butyldimethylsilyl chloride-4-dimethylaminopyridine-triethylamine and selective removal of the tetrahydropyranyl protecting group with hydrogen peroxide-trichloroacetic acid in *t*-butyl alcohol-methylene chloride (Myers, A. G.; Fundy, M. M.; Lindstrom, P. A., Jr. *Tetrahedron Lett.* **1988**, *29*, 5609) then furnished alcohol **8** in 70% yield for the two steps. Other methods for removal of the tetrahydropyranyl protecting group induced competitive desilylation.

8. Unlike substrate **3**, alcohol **7** underwent clean desilylation when subjected to conditions leading to allene formation.

9. Midland, M. M.; McDowell, D. C.; Hatch, R. L.; Tramontano, A. *J. Am. Chem. Soc.* **1980**, *102*, 867.

10. Estimates of the maximum rotation of (*S*)-**11** are in the range −197.7 to −237±23°. For discussion, see reference 11.

11. Mannshreck, A.; Munninger, W.; Burgemeister, T.; Gore, J.; Cazes, B. *Tetrahedron*, **1986**, *42*, 399.

12. Crossland, R. K.; Servis, K. L. *J. Org. Chem.* **1970**, *35*, 3195.

(Received in USA 7 August 1989)