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Zinc reduction of alkynes

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Abstract—The dissolving zinc metal reduction of ethyl phenylpropiolate to the corresponding cinnamate ester can be stereochemically controlled by changing the proton source in the reaction. The results of this study, while not fully understood, may imply that surface phenomena, coupled with a relatively slow forming equilibrium between the intermediate cis and trans anion or radical anion, competes with the rate determining protonation step in the mechanism.

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Our investigations into the Rieke zinc dissolving metal reductions of various functional groups have recently included the reduction of alkynes to alkenes. Previous studies involving the Rieke zinc reduction of alkynes, where substituted propargylic alcohols, 1,3-diynes, and 1,3-enynes served as the reactants, illustrated that the corresponding cis-alkenes are the major products of the reaction.¹ In our efforts to expand the scope of this reduction, we noted that only certain substituted alkynes undergo Rieke zinc reduction.² For instance, ferrocenylethyne and some arylethynes are quantitatively and rapidly reduced to their corresponding alkenes (Scheme 1). However, 1-phenylpropyne and 1-octyne are not reduced and diphenylethyne reacts only sluggishly and in low yield. Of extreme significance to us was the fact that the Rieke zinc reduction of ethyl phenylpropiolate gave predominantly (>90%) the transcinnamate ester.



 $Ph-C\equiv C-CH_3$ $C_6H_{13}-C\equiv CH$

Scheme 1. Ease of Rieke zinc reduction of alkynes.



Scheme 2. Mechanism of dissolving metal reduction of alkynes.

Traditional methods for the reduction of alkynes to trans-alkenes have typically been achieved by the dissolving metal reduction using sodium or lithium in ammonia.³ The stereochemistry of the product in these methods has been explained by considering the mechanism of the reaction (Scheme 2).⁴ It has been proposed that in the first step, electron donation from the metal to the alkyne forms the more stable trans-radical anion. The rate determining step, protonation of the radical anion by the solvent, gives rise to the trans-radical. A second one-electron transfer gives the trans-anion, which is then protonated to give the trans-alkene.

It has been noted that increasing the temperature of the dissolving metal reduction of an alkyne results in an increased yield of the cis-alkene. This presumably arises due to the increased propensity for equilibration between the initially formed trans-radical anion and

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Scheme 3. Equilibrium between cis- and trans-vinyl radical anions.

the cis-radical anion (Scheme 3).⁵ However, since the trans-radical anion is considered to be more stable due to steric hindrance, the equilibrium, once reached, still favors the trans-radical anion. Thus, the trans-alkene is not only the kinetic product (arising from the initially formed trans-radical anion), but is also the thermo-dynamic product of the reaction.

To further explore this assumption, we examined the dissolving zinc metal reduction (using zinc powder instead of Rieke zinc) of ethyl phenylpropiolate. Interestingly, we noted a marked difference in product stereochemistry as a function of the pK_a of the added proton source (Table 1).⁶ As shown in the table, when the alkyne was treated with powdered zinc under conditions similar to those used in Rieke zinc reductions, no alkene products were detected. However, when the methanol solvent was replaced with hydrochloric acid (6.0 M), the reduction proceeded rapidly and in high yield. Moreover, the stereochemistry of the product mixture closely resembled that of the Rieke zinc reduction; 90% of the alkene product was the *trans*-alkene. When hydrogen sulfate was used as the proton source, however, only 63% of the trans-isomer was produced. And when acetic acid was used as the proton source, the trans-isomer was found to be less than 10% of the product alkene. A reduction in the percent of trans-alkene formed in the reaction could be due to a slow forming equilibrium between the more thermodynamically stable and kinetically formed trans-radical anion and the cisradical anion as shown in Scheme 3. However, such an argument does not account for the relatively high percent of the *cis*-cinnamate ester formed when acetic acid was used as the proton source.

Verification that the stereochemistry of the product alkene was determined during the course of the reduction of the alkyne, and not as a result of isomerization of the alkene after its formation, was determined by treating *cis*-ethyl cinnamate to the conditions of the dissolving metal reduction. In all attempts to affect the isomerization of the product, no *trans*-cinnamate was noted by nuclear magnetic resonance spectroscopy.

The pK_a of the proton source in the reaction appears to correlate well with the cis-trans ratio of the product.⁷ As the pK_a of the proton source increases, the time required to consume the zinc increased and the percent transalkene decreased. This correlation could imply that surface phenomena described below, which are often overlooked, may play a large role in the mechanism of the reduction. Moreover, the rate determining step of the mechanism, in the case of the dissolving zinc reductions, may be the protonation of the anion instead of the radical anion. In such a case, the stereochemistry of the product mixture may be explained by considering the geometry of the carbanion-zinc ion paired intermediate (Scheme 4). The trans ion pair, in equilibrium with the cis ion pair, should be less fully ion paired with the zinc because of steric requirements. In HCl, the proton source is most likely H_3O^+ , and the small hydronium ion is more able to protonate the trans-isomer due to its less fully ion paired nature and smaller size. The trans-anion-zinc ion pair arising from the use of HCl as a proton source may also be more solvent separated due to the large quantity of chloride counterion in the reaction mixture. The chloride anions would ion pair with the zinc ion, resulting in a solvent separated ion pair between the zinc cation and carbanion. In acetic acid, however, the trans- and cis-anions should be more tightly ion paired with zinc due to the lack of a large quantity of anions in the reaction mixture. The larger acetic acid proton source would then more rapidly protonate the more sterically accessible cis-anion-zinc ion pair.

A useful outcome of this study, in addition to an increased understanding of the mechanism of the dissolving zinc metal reduction, is the ability to stereochemically select either the cis- or trans-cinnamate ester by simply changing the proton source in the reduction of the corresponding alkyne. Moreover, the

Table 1. The reduction of an alkyne with powdered zinc

Reaction	Acid	Trans ^a (%)	Conv ^a (%)	pK_a^{d}
1	MeOH	nd	0	15.5
2 ^b	HCl	90 ^c	80	-7
3	$\mathrm{HSO_4}^-$	63	40	2.0
4	H_3PO_4	54	71	2.1
5	PhCOOH	12	98	4.2
6	AcOH	9	74	4.8

^a Determined by averaging multiple runs.

^b Reaction performed at room temperature.

^c Determined spectroscopically.

^d Ref. 7.



Scheme 4. Proposed mechanism of zinc metal reduction of alkyne.

reduction can be effected using readily available and inexpensive zinc powder.

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References and notes

- Chou, W.-N.; Clark, D. L.; White, J. B. *Tetrahedron Lett.* 1991, 32, 299–302; Rieke, R. D.; Uhm, S. J. *Synthesis* 1975, 452–453.
- 2. Kaufman, D.; Mosher, M. D., unpublished results.
- For reviews, see House, H. O. In Modern Synthetic Reactions, 2nd ed.; W.A. Benjamin: Menlo Park, CA, 1972, pp 205–209; Olah, G. A.; Molnár, A. In Hydrocarbon Chemistry; J. Wiley and Sons: New York, NY, 1995, pp 472–473; Smith, H. In Organic Reactions in Liquid Ammonia; Wiley-Interscience: New York, NY, 1963; Vol. 1, Part 2, pp 213–216.

- See: Ref. 3; Campbell, K. N.; Eby, T. L. J. Am. Chem. Soc. 1941, 63, 216–219, 2683–2685; Henne, A. L.; Greenlee, K. W. J. Am. Chem. Soc. 1943, 65, 2020–2023.
- House, H. O.; Kinloch, E. F. J. Org. Chem. 1974, 39, 747– 755.
- 6. The general procedure for the dissolving zinc metal reduction: To a stirred solution of ethyl phenylpropiolate (4.60 mmol) in tetrahydrofuran (10 mL) and water (1.0 mL) was added zinc powder (40 mesh, 11.5 mmol) and the appropriate proton source (34.5 mmol). The slurry was then refluxed for 48 h under an inert atmosphere, cooled to room temperature, and poured into 250 mL diethyl ether. The mixture was then filtered by gravity through a Celite pad and extracted with water (2 × 50 mL), 10% sodium bicarbonate (2 × 50 mL), 10% ammonium chloride (50 mL), and brine (50 mL). The organic phase was then dried over anhydrous magnesium sulfate, filtered, and the solvent removed by rotary evaporation. The yield and composition of the crude product mixture was then determined by proton NMR.
- pK_a Values taken from: Wade, L. G. In Organic Chemistry, 5th ed.; Prentice Hall: Upper Saddle River, NJ, 2003, pp 1218–1220; Brown, H. C. In Determination of Organic Structures by Physical Methods; Braude, E. A., Nachod, F. C., Eds.; Academic Press: NY, 1955; Dippy, J. F. J.; Hughes, S. R. C.; Rozanski, A. J. Chem. Soc. 1959, 2492– 2498; Bjerrum, J.; Scharzenbach, G.; Sillen, L. G. Stability Constants; Chemical Society: London, 1958.