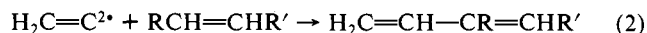
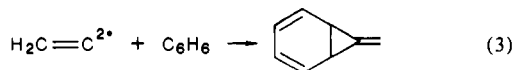


Figure 2. Mass spectra, 50 eV, of reacting mixtures of (a) C_2H_2 (0.13)/ C_6H_6 (0.87) at 49 torr, 942 K; (b) C_2H_2 (0.3)/ $C_6H_5CH_3$ (0.7) at 32 torr, 942 K; and (c) C_2H_4 (0.3)/ $C_6H_5CH_3$ (0.7) at 53 torr, 942 K, at early stages.

thermochemical grounds.¹⁵ After considering that formation of the lowest lying triplet state of acetylene is about 80 kcal/mol endothermic, we finally proposed the intermediacy of vinylidene.¹⁶ On the basis of the above evidence we conclude that this is indeed the case and that acetylene pyrolyses studied here can be described by a scheme comprising steps (1,-1) followed by addition/insertion reactions



(10) The estimated heat of formation of 7-methylenebicyclo[4.1.0]hepta-2,4-diene (A),¹¹ the primary product of vinylidene addition to benzene



$\Delta H_{f,300K}^{\circ}$ (A) = 90.2 kcal/mol leads to $\Delta H_3 = -23$ kcal/mol and to $\Delta H_4 = -55$ kcal/mol for its isomerization to styrene: $A = C_8H_8$.¹²

(11) Benson, S. W. *Thermochemical Kinetics*, 2nd ed.; Wiley: New York, 1976.

(12) Brinker et al. (Brinker, U. H.; König, L. *J. Am. Chem. Soc.* **1981**, *103*, 212) report that the closely related isomerization of 7-methylenebicyclo[4.1.0]hept-2-ene to vinylcyclohexa-1,3-diene takes place readily at temperatures as low as 200 °C.

(13) Stang, P. J. *Chem. Rev.* **1978**, *78*, 383.

(14) Ayrancy, G.; Back, M. H. *Int. J. Chem. Kinet.* **1983**, *15*, 83.

(15) Durán, R. P.; Amorebieta, V. T.; Colussi, A. J., submitted for publication in *J. Phys. Chem.*

(16) Wetmore, R. W.; Schaefer, H. F., III *J. Chem. Phys.* **1978**, *69*, 1648.

with $r_{-1} \gg r_2$, $E_2 = 0 \pm 1$ kcal/mol, $E_a = \Delta H_1 + E_2$, and $\Delta H_1 = 37$ kcal/mol, in good agreement with theoretical predictions.^{1,2,17} Further work is under way.

Acknowledgment. We are grateful to CIC and CONICET of Argentina for financial support.

(17) Canosa-Mas et al. (Canosa-Mas, E. C.; Frey, M. H.; Walsh, R. J. *Chem. Soc., Faraday Trans. 2* **1985**, *81*, 283) have measured a value of $k = 1.5 \times 10^{11} \text{ M}^{-1} \text{ s}^{-1}$ for the reaction ${}^1C_2H_2 + C_2H_2 \rightarrow C_3H_4$ at 300 K.

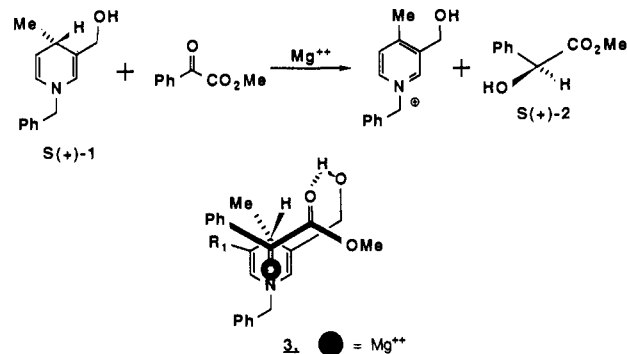
The First Nonenzymic Stereospecific Intramolecular Reduction by an NADH Mimic Containing a Covalently Bound Carbonyl Moiety

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We have recently described¹ the pure self-immolative chirality transfer between the stereochemically defined (*S*)-*N*-benzyl-3-(hydroxymethyl)-4-methyl-1,4-dihydropyridine (**1**) and benzoylformic ester. The methyl mandelate (**2**) produced was found to be greater than 95% enantiomerically pure (corrected for the enantiomeric purity of **1**) and possessed the *S* configuration. This



process, which occurred in the absence of any external or appended stereocenters, other than that present in the 4-position of **1**, was assumed to occur via the previously suggested ternary complex **3** consisting of **1**, benzoyl formic ester, and the magnesium ion. The stereochemical outcome was rationalized by assuming a hydrogen bond or dipole-dipole interaction between the hydroxyl group and the carbomethoxyl group in **3**, resulting in hydride transfer to the *re* face of the carbonyl group. In the natural NADH-NAD⁺ system the 4-position is achiral containing two hydrogens and the enzyme, alcohol dehydrogenase, must be employed.² An enormous quantity of work has been done with metal ions (Mg^{2+} , Zn^{2+}) in place of the enzyme in an effort to mimic the natural process and, along with successful redox behavior, impressive stereochemical control has been achieved.³ However, the metal ion mediated reductions of prochiral carbonyls to optically enriched carbinols required several days to reach completion, in dramatic contrast to the rate of the enzyme's rapid catalytic activity. Thus, these studies have been more mechanistically interesting rather than synthetically useful processes.

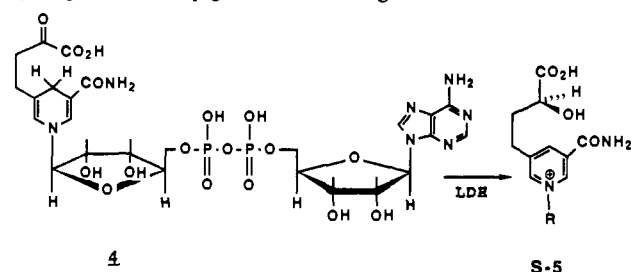
We now wish to report that we have succeeded in carrying out an *intramolecular* version of this metal ion mediated reduction

(1) Meyers, A. I.; Oppenlaender, T. *J. Am. Chem. Soc.* **1986**, *108*, 1989.

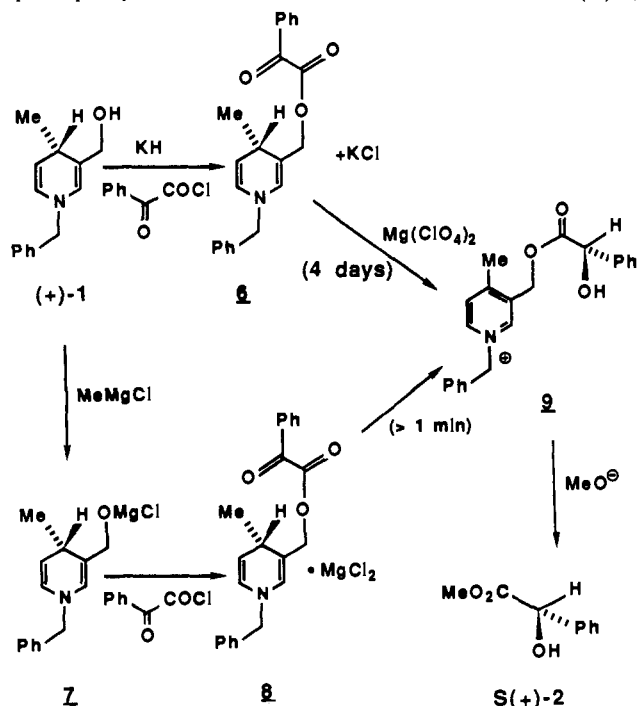
(2) Fischer, H. F.; Westheimer, F. H.; Conn, E. E.; Vennesland, B. *J. Am. Chem. Soc.* **1951**, *73*, 2403.

(3) For summaries of metal ion mediated NADH mimics for stereochemical reduction of prochiral carbonyls, see: (a) Ohno, A. *ACS Symp. Ser.* **1982**, *No. 185*, 1. (b) Ohno, A.; Lee, J. H.; Yasuma, T.; Oka, S. *Tetrahedron Lett.* **1984**, *25*, 1995. (c) Inouye, Y.; Oda, J.; Baba, N. *Asymmetric Synthesis*; Academic: New York, 1983; Vol. 2, p 1. (d) Kellogg, R. M. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 782. (e) Ohno, A.; Vishida, S. *Lecture Notes in Bioorganic Chemistry*; Springer Verlag: Heidelberg, 1986.

which proceeded with >99% stereoselectivity and reached completion in a matter of seconds. The intramolecular redox system has heretofore only been reported⁴ by using NADH with an appended pyruvate moiety **4** in the presence of lactate dehydrogenase from pig heart furnishing the lactate **5**. However,



this reduction occurred only at a rate 0.003, that of the natural *intermolecular* system. Our initial effort to study the intramolecular reduction was to transform the dihydropyridine carbinol **1** to an ester of benzoylformic acid **6**. This was accomplished by treatment of **1** with potassium hydride (THF) followed by addition of benzoylformyl chloride. The resulting ester **6** was then treated with 1.0 equiv of $Mg(ClO_4)_2$ and reduction to **9** was complete (TLC) after 4 days. Thus, there was very little difference from the rate of reduction in the intermolecular process reported earlier.¹ However, the situation was drastically altered when the dihydropyridine carbinol was transformed into its magnesium alkoxide **7** ($MeMgCl$, 1.0 equiv, THF, $-23^\circ C$). The THF solution containing **7** was then treated with 1.0 equiv of benzoylformyl chloride and gave an instantaneous red color indicative of the pyridinium salt, **9**. After addition of the acid chloride to **7** was complete (20 min), the red reaction mixture was concentrated and methanol-methoxide ion was introduced to solvolyze the ester **9**. Isolation gave methyl mandelate (**2**) in 65% yield with an optical rotation of $+127.2^\circ$ (c 0.10, MeOH) which corresponds to an optical purity of 90%.⁵ Based on the enantiomeric ratio of (+)-**1**,

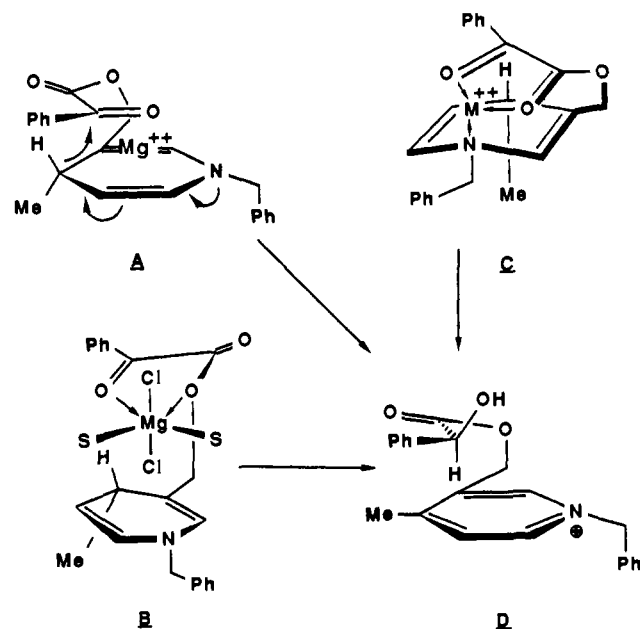


which was $96:4 \pm 2$, the extent of stereocenter transfer was greater than 99%. The extraordinary enhancement in reduction rate may be rationalized by assuming that the magnesium salt in **8** is closely associated in the solvent shell forming three ternary complexes

(4) Kapmeyer, H.; Pfeleiderer, G.; Trommer, W. E. *Biochemistry* **1976**, *15*, 5024.

(5) Based on $[\alpha]_D$ of methyl mandelate, 141.4° (MeOH), the optical purity of (S)-(+)-**2** was 90.0%. The dihydropyridine (+)-**1** had an observed $[\alpha]_D +56.7^\circ$ which was $90 \pm 2\%$ ee.¹

A, B, or C by virtue of the esterification reaction.⁶ The latter three complexes may be considered as pretransition states which result in rapid hydride transfer from the complex to generate the mandelate **D** with the observed absolute configuration. The



conformation A is analogous to the intermolecular version in a variety of NADH mimics^{3e} such that the π -system of the dihydropyridine and the carbonyl to be reduced form a sandwich around the metal ion. Other transition-state models, proposed by Kellogg,^{3d} rely on steric interactions when the magnesium is complexed in a chiral environment. Conformer (B), showing chelation of the magnesium to the two oxygen atoms and the hexacoordinated magnesium,⁷ may also be considered as a pre-transition-state model. This is relatively strain free; however, the distance that the hydride must travel appears to be large ($>2 \text{ \AA}$) and the ether oxygen in B may be a poor electron donor. Conformer C appears to us to be the most attractive at this stage of our knowledge, since it is reasonably strain free, incorporates the metal ion comfortably, and allows the pyridine ring to pucker as it is known to exist. Furthermore, electron donation to hexacoordinate magnesium (shown in C simply as M^{2+}) comes from both electron-rich carbonyl groups and the lone pair on nitrogen. The remaining three ligands are both chlorides and a solvent molecule, which are omitted to keep the structure from being too cluttered.

In summary we have demonstrated that an intramolecular reduction in this NADH model, mediated by magnesium ion placed in close proximity by the nature of the esterification, is an extremely rapid process and it now remains to give serious consideration to other prochiral carbonyl or imines as well as means to make this a catalytic process. Furthermore, that the reduction proceeded so efficiently in THF is significant since acetonitrile has always been suggested as the optimum solvent for the metal ion mediated reduction in the intermolecular process.

Acknowledgment. We are grateful to the National Institutes of Health for financial support of this work.

(6) In order to preclude the possibility that the reduction of benzoylformyl chloride occurred intermolecularly, the methyl ether¹ of (+)-**1** was examined. It was found that the reduction of the acid chloride, in the presence of $MgCl_2$, proceeded to only a trace of methyl mandelate after 3 days. Furthermore, when (+)-**1** was transformed to its magnesium salt **7** and treated with methylbenzyl formate (THF, $-23^\circ C$) no reduction occurred, and after it was warmed to $25^\circ C$, only a 23% yield of methyl mandelate was obtained. Therefore, no alkoxide exchange to **9** took place at $-23^\circ C$ or at room temperature, and thus, reduction occurred in the usually sluggish intermolecular sense.

(7) The hexacoordination of the magnesium ion has been verified by X-ray studies: Seebach, D.; Hansen, J.; Seiler, P.; Gromek, J. M. *J. Organomet. Chem.* **1985**, *285*, 1.