Tetrahedron Letters No. 19, pp 1633 - 1634, 1978. 0040-4039/78/0501-1633. $02.00/0.

© Pergamon Press Ltd. Printed in Great Britain.

ON THE STEREOCHEMISTRY OF REDUCTION OF 9-METHYL-1-CARBOXY-Δ⁴-3-OCTALONE: A REMARKABLE LITHIUM-AMMONIA REDUCTION

John E. McMurry, Larry C. Blaszczak[1], and Mark A. Johnson
Thimann Laboratories, University of California, Santa Cruz, CA 95064

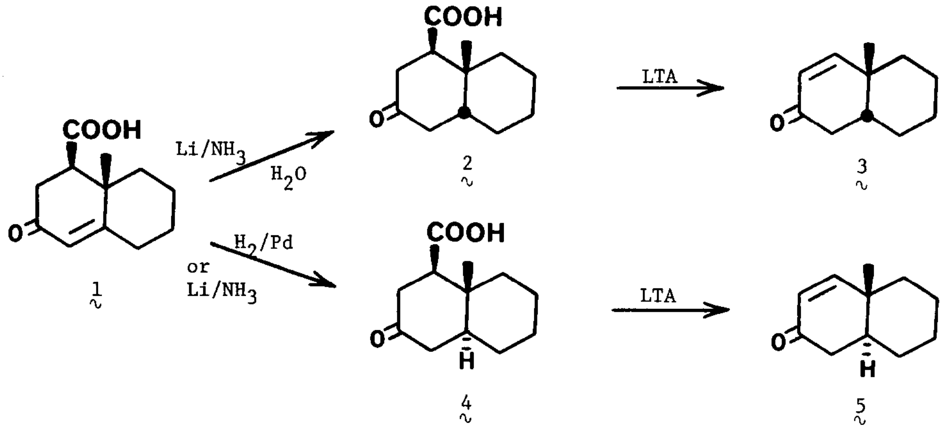
(Received in USA 11 January 1978; received in UK for publication 23 March 1978)

Some time ago, we reported[2] a method for the synthesis of enones whereby β-carboxy ketones were oxidatively decarboxylated by treatment with lead tetraacetate (LTA). Among the examples we discussed were decarboxylations of the cis and trans 9-methyl-1-carboxy-3-decalones, prepared by reduction of 9-methyl-1-carboxy-Δ^4-3-octalone (1). We reported that octalone 1 could be catalytically reduced (H_2/Pd/EtOH) to a single dihydro derivative which, on treatment with LTA, gave a pure enone product (nmr: angular methyl 1.08δ, $CDCl_3$). We assigned cis stereochemistry to the product based on many well-known analogous results.[3] Similarly, we found that octalone 1 could be reduced with lithium in liquid ammonia to a different dihydro derivative which, on treatment with LTA, gave a different enone product (nmr: angular methyl 1.23δ, $CDCl_3$) Trans stereochemistry was assigned based, once again, on extensive literature analogies.[4]

Recently, however, these stereochemical assignments have been called into question. Boger[5] has synthesized the true cis-9-methyl-Δ^1-3-octalone (3) by an unequivocal route and has found it to be spectrally identical to our "trans" material. Since our "trans" enone is in fact cis, it follows that our isomeric "cis" material is probably the true trans enone. The simplest explanation of the error is to assume that we inadvertently transposed spectral data for the two enones in our original paper. This is not the case however. Both we and Boger[5] have now repeated our original experiments. We both find that when octalone (1) is catalytically reduced and then oxidatively decarboxylated, the product enone does indeed have spectral characteristics identical to those we originally reported. *Thus catalytic reduction of 1 gives exclusively the trans product, literature precedent to the contrary.*

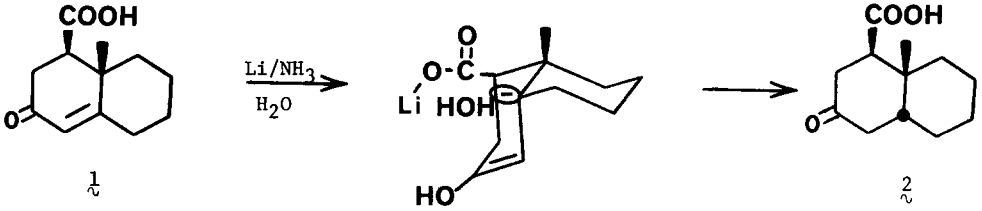
Even more surprising is the corollary that lithium ammonia reduction of 1 must give a cis product with, presumably, the less stable ring junction stereochemistry. On attempting to reproduce this result, however, neither we nor Boger were able to do so using the most careful conditions (liq. NH_3 distilled from sodium); lithium/ammonia reduction of octalone 1 under anhydrous conditions, followed by LTA decarboxylation, gave only trans enone.

In searching for reasons for the discrepancy, we noticed that our original lithium/ammonia reduction of 1 was carried out under "classic" Birch conditions; i.e., the reaction was carried out using undistilled ammonia in an open flask, and water was undoubtedly present. When we reproduced the reduction of 1 under these "wet" conditions, rather than under careful anhydrous conditions, *true cis was found to be the major product* (75:25 cis/trans).



That water is responsible for the difference in course of the reduction was shown by the fact that when we carried out the reaction under carefully controlled conditions with 10 equivalents water added to otherwise anhydrous distilled ammonia, cis product again predominated (70:30 cis/ trans).

We view this remarkable result as arising by protonation of an intermediate carbanion from the β face by water held in the solvent shell of the β-oriented lithium carboxylate grouping.[6] Water is clearly unique in its ability to affect the course of this reduction, since the use of methanol or ethanol in its place gave only the normal trans product.



References

1. Present Address: Eli Lilly & Co., Indianapolis, Indiana.
2. J. E. McMurry and L. C. Blaszczak, J. Org. Chem., 39, 2217 (1974).
3. See for example: a) C.B.C. Boyce and J. S. Whitehurst, J. Chem. Soc., 2680 (1960); b) J. McMurry, J. Am. Chem. Soc., 90, 6821 (1968).
4. For a discussion, see H. O. House, "Modern Synthetic Reactions, 2nd Ed.," W. A. Benjamin, Menlo Park, CA 1972, pp. 173-183.
5. D. L. Boger, Tetrahedron Lett., 17, (1978). We thank Dr. Boger for informing us of his results prior to publication.
6. The stereochemistry of the carboxyl in octalone 1 is assigned the β-equatorial configuration based on equilibration experiments on the corresponding ester.