

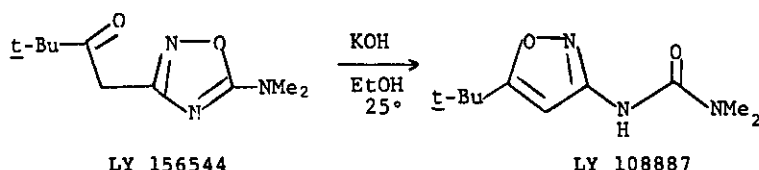
2. S. Gronowitz and J. Roe, *Acta Chem. Scand.*, **19**, 1741(1965), and J. D. Davenport, R. E. Hackler, and H. E. Taylor, British Patent 1,218,623; *Chem. Abstr.*, **75**, 15186h(1971).
3. T. J. Kress, *J. Org. Chem.*, **44**, 2081(1979).
4. A portion of this work has been reported, T. J. Kress and E. F. Szymanski, U. S. Patent 4, 252,955(1981); *Chem. Abstr.*, **94**, 192368m(1981).
5. *Org. Synthesis*, Coll. Vol. **4**, 688(1963).
6. Y. Hachilham, T. Shono, and S. Ikeda, *J. Org. Chem.* **29**, 1371(1964).
7. B. Lythgoe and L. Rayner, *J. Chem Soc.*, 2323(1951).

NEW APPLICATIONS OF MONONUCLEAR HETEROCYCLIC REARRANGEMENTS (MHR's)
IN ORGANIC SYNTHESIS

John C. Lechleiter and Bruce P. Gunn

The Lilly Research Laboratories, Eli Lilly and Company,
Indianapolis, Indiana 46285

Mononuclear heterocyclic rearrangements¹ represent a class of azole/azole interconversions first systematized by Boulton and Katritzky². Interest in the synthesis of LY 108887 prompted our consideration of a scarcely documented version of this rearrangement. Thus, reaction of methyl pivalate with 3-methyl-5-dimethylamino-1,2,4-oxadiazole in the presence of lithium diisopropylamide (LDA) at low temperature, followed by quench with aqueous acid at 0° gave LY 156544 in high yield. Treatment of this compound with ethanolic potassium hydroxide gave LY 108887 in quantitative yield.



Further examples of this condensation/rearrangement sequence and extensions to other heterocyclic ring systems are discussed.

-
1. Recent review: M. Ruccia, N. Vivona, and D. Spinelli, *Adv. Het. Chem.*, **29**, 141 (1981).
 2. A. J. Boulton, A. R. Katritzky, and A. M. Hamid, *J. Chem. Soc. C*, 2005 (1967).

6-SUBSTITUTED NICOTINIC ACIDS FROM 2-METHYL-5-ETHYLPYRIDINE

Author's Name and Current Address: Dr. Raimund J. Miller,
Lonza Inc., 22-10 Route 208, Fair Lawn, New Jersey 07410

Work was done by Dr. Daniel Quarroz, Lonza AG, 3930 Visp,
Switzerland

In our continuing exploration of the chemistry of isocinchomeric

acid, made by oxidation of 2-methyl-5-ethylpyridine, we observed a novel transformation of this pyridine dicarboxylic acid to variously 6-substituted nicotinic acids.

When isocinchomeric acid-N-oxide was reacted with acetic anhydride/triethylamine in methylenechloride 6-chloronicotinic acid was obtained in 50% yield, the chlorine originating from the solvent. 6-Hydroxynicotinic acid was identified as a side product in 40% yield. This unusual and unexpected chlorination with methylenechloride was also tried successfully on other pyridine carboxylic acids bearing a carboxyl group in the 2 position to the nitrogen. The carboxyl group was invariably replaced by chlorine.

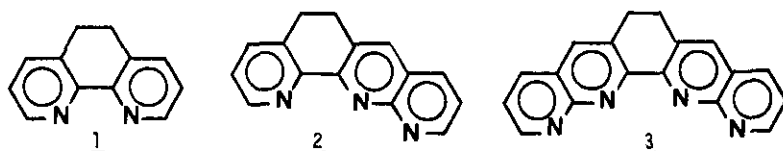
When in the system isocinchomeric acid-N-oxide/acetic anhydride/triethylamine the methylenechloride was replaced by another solvent, a radical of this solvent was found as substituent in the 2 position. In acetonitrile as solvent 6-aminonicotinic acid was isolated in 80% yield. In ethylacetate 6-hydroxynicotinic acid was formed in 80-86% yield. The benzene- and toluene-radical was also introduced into the 2 position.

We are continuing to study the scope of this reaction, which gives easy access to 6-substituted nicotinic acids hitherto available only on very cumbersome routes.

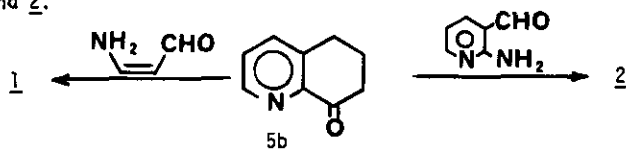
Annelated Derivatives of 2,2'-Bipyridine and 2,2'-Bi(1,8)naphthyridine

Randolph P. Thummel*, Ramanathan Mahadevan, Agha S. Saleem, and David Cantu

Department of Chemistry, University of Houston, Houston, Texas 77004



The series of ethano-bridged bi-aryl compounds 1-3 has been synthesized by application of the Friedlander Condensation method. Thus the reaction of 8-oxo-5,6,7,8-tetrahydroquinoline (5b) with β -aminoacrolein leads to the formation of 1 while condensation with 2-aminonicotinaldehyde gives compound 2.



The 2-oxocycloalkenopyridines (5 a-c) are readily prepared by a two step route from the corresponding commercially available cycloalkenopyridines.

