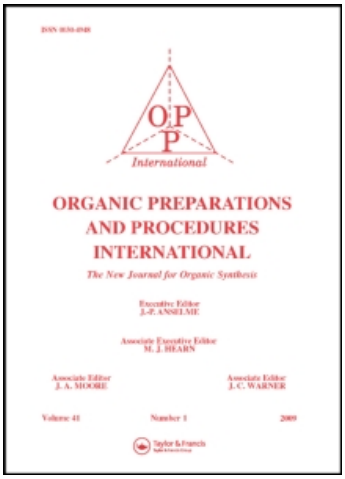


Organic Preparations and Procedures International
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t902189982

2-SUBSTITUTED-5-METHYL-2-OXAZOLINES

S. P. McManus[a]; J. T. Carroll[a]; P. M. Grohse[a]; C. U. Pittman Jr.[b]
[a] Department of Chemistry, University of Alabama in Huntsville, Huntsville, Alabama [b] Department of Chemistry, University of Alabama, University, Alabama

To cite this Article McManus, S. P. , Carroll, J. T. , Grohse, P. M. and Pittman Jr., C. U.(1969) '2-SUBSTITUTED-5-METHYL-2-OXAZOLINES', Organic Preparations and Procedures International, 1: 3, 183 — 186
To link to this Article: DOI: 10.1080/00304946909458377
URL: http://dx.doi.org/10.1080/00304946909458377

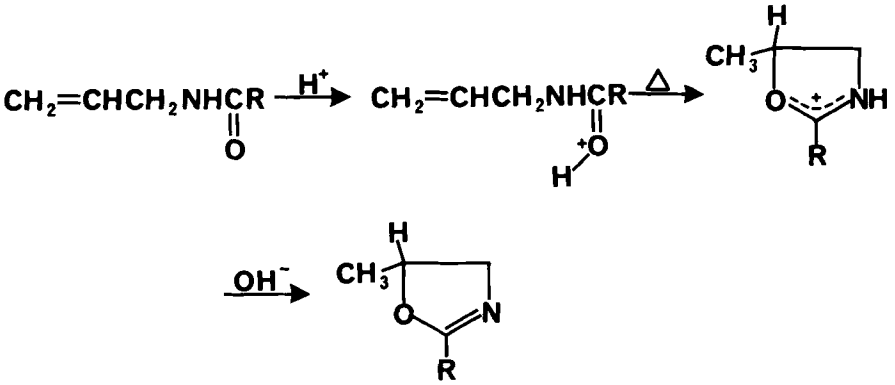
ORGANIC PREPARATIONS AND PROCEDURES 1(3), 183-186 (1969)

2-SUBSTITUTED-5-METHYL-2-OXAZOLINES[1]

S. P. McManus[2], J. T. Carroll and P. M. Grohse[3]
Department of Chemistry
University of Alabama in Huntsville, Huntsville, Alabama 35807

and

C. U. Pittman, Jr.[2a]
Department of Chemistry
University of Alabama, University, Alabama 35486



A future paper[4] will describe the facile cyclization of N-(β-methallyl)amides to 2,5,5-trisubstituted-2-oxazolines. The cyclization of N-allylamides to 2,5-disubstituted-2-oxazolines is much slower in strongly acidic media (H_2SO_4, FSO_3H). Thus, this method has not proved to be a general route to 2-oxazolines in the past, and only a few isolated examples have been reported. Kay[5] described the first acid-catalyzed formation of 5-methyl-2-phenyl-2-oxazoline from N-allylbenzamide in 1893. The use of n.m.r. has now permitted us to observe the species existing in the acid media during the cyclization.[6] At room temperature N-allylamides are protonated quantitatively at oxygen and they remain unchanged indefinitely. Upon heating to 80-90°, however, conversion to the corresponding 2-oxazolinium ion occurs. The kinetics are easily measured by following the disappearance of the vinyl

protons (or some other characteristic band) of the protonated amide and/or observing the appearance of the 5-methyl group's doublet of the stable oxazolinium ion which always arises at about 2.10 p.p.m. downfield from TMS (internal capillary).

This procedure describes the use of n.m.r. to determine and optimize the conditions for cyclization of N-allylamides in 96% sulfuric acid.[7] The technique is both convenient and general, and the availability of N-allylamides makes this procedure competitive with the more standard Wenker method.[8] Data for the preparation of several representative 2-oxazolines by this procedure are summarized in the Table.

Table

N-Allylamide	5-Methyl-2-oxazoline	m.p. (b.p.)	% Yield	Picrate m.p.
Acetamide	2-Methyl	(117-119°)	30(64)[a]	114-115°
Benzamide	2-Phenyl	(90-95°/1.5 mm)	39(77)[a]	168-169°
p-Toluamide	2-p-Tolyl[b]	oil	50	190-191.5°
p-Fluorobenzamide	2-p-Fluorophenyl[c]	oil	40	173-174°
p-Nitrobenzamide	2-p-Nitrophenyl[d]	133.5-134°	35(74)[a]	-
p-Dimethylaminobenzamide	2-p-Dimethylaminophenyl[e]	89.5-91°	52	223.5-224°
p-Methoxybenzamide	2-p-Anisyl[f]	oil	15[g]	182-182.5°

[a]Up to double the yield has been obtained when a 90% sulfuric acid solution of the oxazolinium ion is drowned into cold, dilute, excess sodium hydroxide with rapid stirring and continuous extraction with a petroleum ether-ether layer. However, most of these reactions do not allow for that technique since some residual amide and other biproducts normally remain. [b]A. Solomon, Ber., 26, 1321 (1893). [c]Anal. Calc. for picrate: N, 13.72; Found: 13.67. [d]M. T. Leffler and R. Adams, J. Amer. Chem. Soc., 59, 2252 (1937). [e]Anal. Calc. for monopicrate: N, 16.16; Found: 15.76. [f]Anal. Calc. for picrate: N, 13.33; Found: 13.28. [g]Low yield was probably due to ether cleavage during workup to give the amphoteric product which was soluble in base.

Procedure

The amide[9] is added to a rapidly stirred solution of 90 or 96% sulfuric acid at a temperature below 25° to a concentration of about 5% amide. A portion of the solution is placed

in an n.m.r. tube at room temperature. The spectrum of the protonated amide is recorded and then the tube is placed, along with the container holding the bulk of the sample, in a constant temperature bath maintained at 80-90°. The tube is removed at 15 - 20 minute intervals to record the spectrum. When the concentration of the oxazolinium ion reaches a maximum, the acid solution is removed from the bath, cooled, and added to a large excess of ice and the pH is quickly adjusted to about pH 6 with cold aqueous NaOH. The weakly acidic solution is extracted with $CHCl_3$ to remove excess amide and any neutral or acidic by-products. The aqueous fraction is then made basic with more NaOH solution. The aqueous layer is extracted several times with ether; the ether layer is dried and distilled.[11] The product should be stored in a clean container, preferably under nitrogen in the cold to prevent polymerization.[12]

The n.m.r. spectra of the protonated N-allylamides in H_2SO_4 resemble closely those of the unprotonated amides in CCl_4 with the exception of the expected downfield shifts[13] due to deshielding in the positively charged species. The n.m.r. spectra of the oxazolinium ions in both this and the preceding paper[4] will be reported in detail later.[6]

References

1. Acid-catalyzed Cyclization Reactions. V. For paper IV, see preceding paper (ref. 4).

2. (a) Authors to whom inquiries should be addressed; (b) Acknowledgement is made for partial financial support from the Petroleum Research Fund, administered by the American Chemical Society, and from the National Aeronautics and Space Administration.

3. Petroleum Research Fund Undergraduate Scholar.

4. S. P. McManus, J. T. Carroll, P. M. Grohse, and C. U. Pittman, Jr., Org. Preps. and Proc., to be published.

5. P. Kay, Ber., 26, 2848 (1893).

6. S. P. McManus, J. T. Carroll, P. M. Grohse, C. R. Taddei, and C. U. Pittman, Jr., 20th Annual Southeastern Regional Meeting, American Chemical Society, Tallahassee, Florida, Dec. 4-7, 1968, Abstracts p.69; paper in preparation for publication.

7. Other acids have been successfully used and no attempt here is made to show the particular acid media where the yield is maximized for each amide.

8. (a) H. Wenker, J. Am. Chem. Soc., 57, 1079 (1935); (b) W. Seeliger, E. Aufderhaar, W. Diepers, R. Feinauer, R. Nehring, W. Thier, and H. Hellman, Angew Chem. Internat. Edit., 5, 875 (1966).

9. All of the benzamides were prepared by the Schotten-Baumann procedure.[10] N-allylacetamide was prepared using ketene.[4] The allylamine used was Eastman "white label". The following derivatives of N-allylbenzamide have not previously been reported: p-CH_3, m.p. 75.5-76.5°, Anal. Calc.: N, 7.99, Found: 7.72 ; p-F, m.p. 67-68°, Anal. Calc.: N, 7.90, Found: 7.68 ; p-NO_2, m.p. 118-118.5°, Anal. Calc.: N, 13.59, Found: 13.37 ; p-$(CH_3)_2N$, m.p. 131-132°, Anal. Calc.: N, 13.71, Found: 13.98; p-CH_3O, m.p. 42.5-43.5°, Anal. Calc.: N, 7.32, Found: 7.40 . The i.r. and n.m.r. spectra of all new compounds were consistant with the assigned structures.

10. A. I. Vogel, "Textbook of Practical Organic Chemistry", 3rd Edition, p. 582, Longmans, London, 1956.

11. If conversion is complete, it is unnecessary to extract the solution while it is slightly acidic. Since hydrolysis of the 2-oxazolines is fairly rapid in some acidic media, exposure to dilute solutions is avoided where possible. See footnote a in the Table.

12. T. G. Bassiri, A. Levy and M. Litt, Polymer Letters, 5, 871 (1967).

13. G. A. Olah and C. U. Pittman, Jr., in "Advances in Physical Organic Chemistry", Vol. 4, p. 305, V. Gold, editor, Academic Press, New York, 1966.

(Received April 10, 1969)