# 2,5-Diketo-D-Gluconate: A New Intermediate for the Synthesis of *N*-Methyl- and -Aryl-5-oxidopyridazinium Derivatives

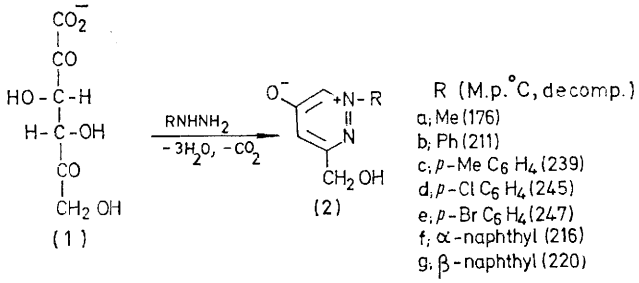
By KATSUMI IMADA

(*Research Institute, Daiichi Seiyaku Co. Ltd., Edogawa-Ku, Tokyo* 132, *Japan*)

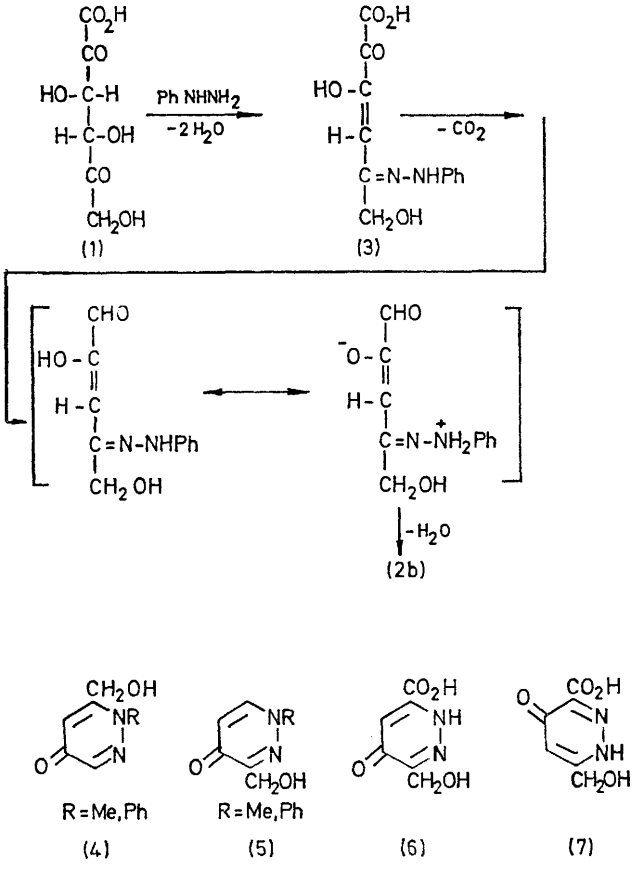
*Summary* Calcium 2,5-diketo-D-gluconate (**1**), prepared by microbial oxidation of D-glucose, reacts with methyl- and aryl-hydrazines to give *N*-methyl- and -aryl-5-oxidopyridazinium derivatives (**2a**—**g**), respectively.

DURING an investigation on the utilization of the calcium 2,5-diketo-D-gluconate (**1**),[1,2] obtained by the action of *Acetobacter* on D-glucose, it was found that (**1**) was a useful intermediate for the synthesis of *N*-methyl- and -aryl-5-oxidopyridazinium derivatives (**2a**—**g**) (Scheme 1).

The synthesis of $\gamma$-pyrone derivatives *via* (**1**) has been reported.[3]




SCHEME 1




SCHEME 2

The reaction is best explained in terms of hydrazone formation, dehydration, decarboxylation, and cyclization (see Scheme 2).

The initially formed hydrazone intermediate (**3**)† isolated from the reaction mixture, was spontaneously converted into the final product (**2b**) upon treatment with hot aqueous acid.

Better results (50—85%) were obtained by heating of a mixture of equimolar quantities of (**1**) and methyl- or aryl-hydrazine at 70—90 °C in a buffer solution (pH = 5·3), composed of pyridine, acetic acid, and water (2:1:2) for 3 h.

Compounds (**2a**—**g**) showed no i.r. absorption corresponding to a carboxyl and carbonyl band.

The u.v. spectra of (**2a**,**b**) in EtOH [$\lambda_{max}$ nm (log $\epsilon$): 258 (3·79), 313 (3·64) and 255 (4·30), 325 (3·78), respectively] were similar to that of authentic anhydro-5-hydroxy-1-methylpyridazinium hydroxide[4] and different from those of 1-methyl-4(1*H*)-pyridazinone[4] and 1-phenyl-6-methyl-4-(1*H*)-pyridazinone.[5]

The n.m.r. spectra of (**2a**,**b**) show a significant upfield shift for the pyridazine ring protons as compared with those of their hydrochlorides, indicating that negative charge from the oxygen atoms is delocalized into the pyridazine ring. Thus the alternate ketonic structures [(**4**) and (**5**)] were eliminated.

Analogous treatment of (**1**) with hydrazine hydrate, however, gave isomeric 3-hydroxymethyl-4(1*H*)-pyridazinone-6-carboxylic acid[6] (**6**), (85%) m.p. 219 °C (decomp.) and 6-hydroxymethyl-4(1*H*)-pyridazinone-3-carboxylic acid[6] (**7**), (5%) m.p. 206·5°C (decomp.).

The author wishes to thank Dr. Y. Maki, Gifu College of Pharmacy, for many helpful discussions and suggestions during this work.

(*Received*, 23*rd July* 1973; *Com.* 1068.)

† All compounds described herein gave satisfactory microanalytical results and spectral data consistent with their structure.

[1] H. Katznelson, S. W. Tanenbaum, and E. L. Tatum, *J. Biol. Chem.*, 1953, **204**, 43.
[2] Y. Wakisaka, *Agr. Biol. Chem.*, 1964, **28**, 819.
[3] S. Oga, K. Asano, and K. Imada, *U.S. P.*, 3,654,316/1972.
[4] K. Eichenberger, R. Romtesch, and J. Druey, *Helv. Chim. Acta*, 1956, **39**, 1755.
[5] A. Staehelin, K. Eichenberger, and J. Druey, *Helv. Chim. Acta*, 1956, **39**, 1741.
[6] K. Imada, to be submitted for publication.