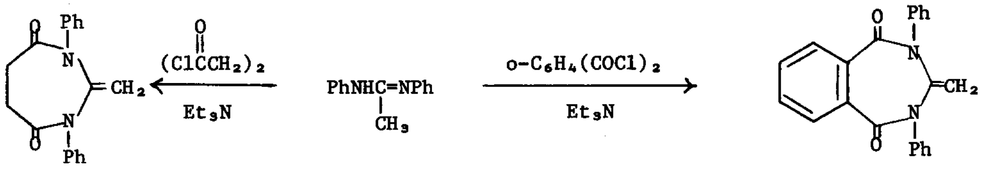
Tetrahedron Letters No. 1, pp 23 - 24, 1978. Pergamon Press. Printed in Great Britain.

THE SYNTHESIS OF A 2,4-BENZODIAZEPINE-1,5-DIONE AND A 1,3-DIAZEPINE-4,7-DIONE

Harold W. Heine* and Cornelis Tintel
Department of Chemistry, Bucknell University,
Lewisburg, PA 17837

(Received in USA 6 October 1977; received in UK for publication 8 November 1977)

The only known synthesis of an authentic 2,4-benzodiazepinedione is the chromic acid oxidation of 2,4-dibenzyl-1,2,4,5-tetrahydro-3H-2,4-benzodiazepin-3-one to 2,4-dibenzyl-4,5-dihydro-1H-2,4-benzodiazepine-1,3-(2H)-dione.[1] An earlier report[2] on the preparation of these elusive substances appears to be in error.[1] We describe here a facile synthesis of 3,4-dihydro-3-methylene-2,4-diphenyl-1H-2,4-benzodiazepine-1,5-(2H)-dione (I) and tetrahydro-2-methylene-1,3-diphenyl-1H-1,3-diazepine-4,7-dione (II). Addition of o-phthaloyl chloride to a stirred solution of N,N'-diphenylacetamidine and triethylamine in an 1:1:2 molar ratio respectively in diethyl ether solvent, followed by filtration of the formed triethylamine hydrochloride and evaporation of the solvent gave I in 80% yield.



II

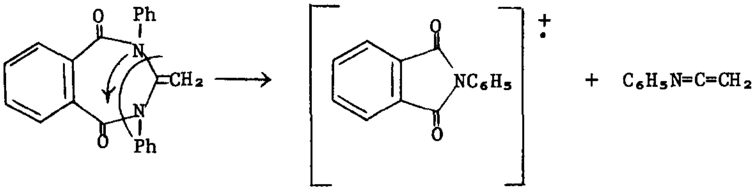
I

Aftėr recrystallization from methanol compound I[3] melted at 174-175°. Nmr (CDCl$_3$): δ7.52-8.15 (m, 4H, C$_6$H$_4$), 7.30 (s, 10H, 2C$_6$H$_5$), 5.43 (s, 2H, CH$_2$=); molecular ion, m/e 430.

For the successful preparation of II it is necessary to initially admix N,N'-diphenylacetamidine, triethylamine and succinoyl chloride in an 1:1:1 molar ratio, stir the reaction mixture for five minutes and then add another equivalent of triethylamine. Compound II[3] was obtained in 40% yield and after recrystallization from 50% aqueous methanol it melted at 139-140°. Nmr

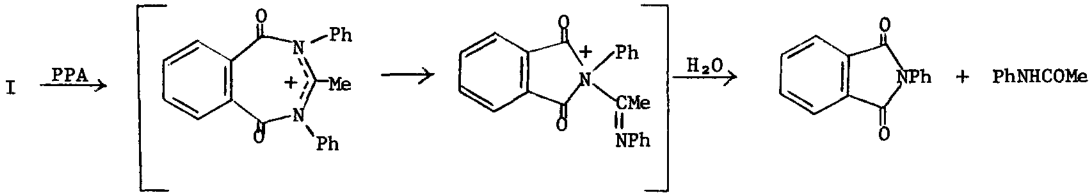
($CDCl_3$): δ7.1-7.5 (m, 10H, $2C_6H_5$), 5.1 (s, 2H, CH_2=), 3.09 (s, 4H, $-CH_2-CH_2-$); molecular ion m/e 288.

The mass spectra of I and II show intense peaks at 117 mass units lower then their respective molecular ions indicating the loss of the fragment $C_6H_5N=C=CH_2$ and the probable formation of N-phenylphthalimide and N-phenylsuccinimide: viz.



I

This loss of 117 is mirrored in the chemical reactivity of I. Thus, I was converted in hot polyphosphoric acid to N-phenylphthalimide (76%) and acetanilide (48%). A plausible mechanism for the reaction involves protonation of the double bond, followed by ring contraction and hydrolysis:



Attempts to oxidize I with chromic oxide in acetic acid also gave N-phenylphthalimide in 50% yield. Reaction of I with bromine in carbon tetrachloride resulted in the formation of N-phenylphthalimide as well.

Acknowledgement: The authors are grateful to Dr. William J. A. VandenHeuvel of Merck Sharp & Dohme Laboratories for the mass spectra of I and II.

References and Footnotes

1) A. M. Felix and R. I. Fryer, J. Heterocyclic Chem., 5, 291 (1968).
2) A. Rosenthal and S. Millward, Can. J. Chem., 42, 956 (1964).
3) Combustion analysis data of compound I and II were consistent with the proposed structures.