Tetrahedron Letters No. 51, pp 5069 - 5072, 1973. Pergamon Press. Printed in Great Britain.

THE SYNTHESIS OF 2,3-DIHYDRO-1H-IMIDAZO[1,2-a][1,3,5]BENZOTRIAZEPIN-5/6H/--ONES AND -THIONES

G. Doleschall, Gy. Hornyák, B. Ágai, Gy. Simig, J. Fetter and K. Lempert

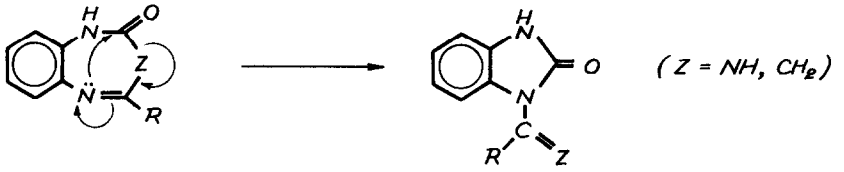
Department of Organic Chemistry, Technical University 1111-Budapest, Hungary

(Received in UK 22 October 1973; accepted for publication 8 November 1973)

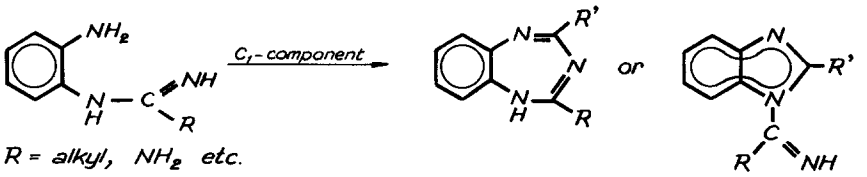
The chemistry of the 1,3,5-benzotriazepine system has yet scarcely been explored and only very few authenticated derivatives of this system have been described [1-3]. This is probably partly the consequence of the expected easy ring contraction of these compounds to yield the isomeric benzimidazole derivatives /Scheme 1, Z = NH/, and partly of the fact that the most obvious syntheses of these benzotriazepines /see e.g. Scheme 2/ may directly lead to these ring contraction products. Thermal ring contractions of the above type /Scheme 1, Z = CH_2/ have been described in the related 1H-1,5-benzodiazepin-2/3H/-on series [6,7].

In order to restrict the number of those conformers of the o-aminophenylguanidine type starting compounds /Scheme 2/ which are unfavourable for the formation of the benzotriazepine system and, at the same time, to minimize the danger of subsequent ring contraction of the desired products, 1-/2-aminophenyl/-2-iminoimidazolidines /1/ were selected as the starting compounds, and a general method for the synthesis of 2,3-dihydro-1H-imidazo[1,2-a][1,3,5]benzotriazepin-2/3H/-ones /2a/ and -thiones /2b/ has been developed by reacting compounds 1 with phosgen and carbon disulfide, respectively, or their equivalents. The complete sequence is shown in Scheme 3. The structures of the products follow from the microanalytical

Scheme 1

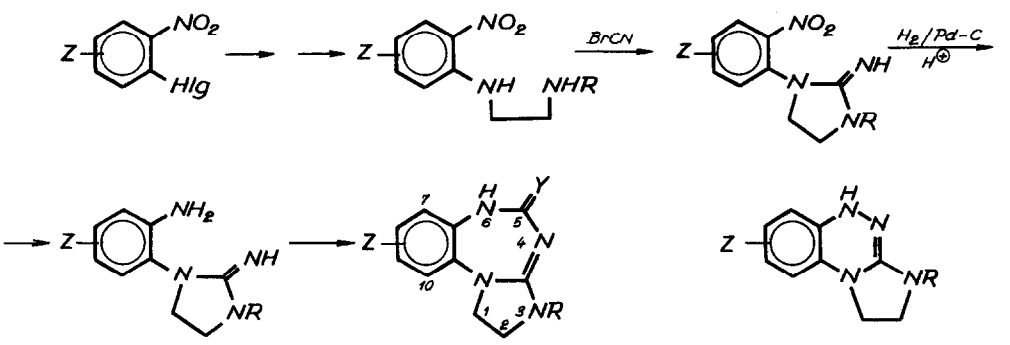


Scheme 2



R = alkyl, NH_2 etc.

Scheme 3



1 **2** **3**

a: Y = O
b: Y = S

Table I.

2,3-Dihydro-1H-imidazo[1,2-a][1,3,5]benzotriazepin-5/6H/-ones /2a/ and -thiones /2b/

Z	R	Mp. /°C/	
		2a	2b
H	H	255-7 /d./	264-5 /d./
8-Cl	H	--	257-8 /d./
8-OCH_3	H	—	260-61 /d./
8-$COOCH_3$	H	272 /d./	>300 /d./
8-$CONHC_4H_9$-/n/	H	--	248-9
H	n-C_4H_9	205-7	187-8 /d./
8-Cl	n-C_4H_9	220	214-6
8-$CONHC_4H_9$-/n/	n-C_4H_9	244-5	207-8
9-Cl	n-C_4H_9	197-8	217-8

results [8] and from their non-identity with their isomers which might also have been formed in the course of the above synthesis and which were prepared by unambiguous routes. The spectral data of the compounds 2 /which will be published elsewhere/ were also in agreement with the proposed structures.

The catalytic reduction of the nitrophenyliminoimidazolidines had to be performed in the presence of strong mineral acids; otherwise only 2/3 of the calculated amount of hydrogen was taken up and what are believed to be compounds of structure 3 were formed.

The newly prepared compounds 2a and b have been compiled in Table 1. The results of their biological screening will be described elsewhere by Mrs. Dr. L. Petőcz.

The financial assistance of the EGyT Pharmaceutical Works, Budapest is acknowledged.

References and Notes

1 F.E. King, R.M. Acheson and P.C. Spensley, J. Chem. Soc. 1948, 1366

2 R.M. Acheson and N.F. Taylor, ibid. 1956, 4727

3 A series of compounds for which the 1,3,5-benzotriazepine structure has earlier been claimed [4] apparently possess different structures. The structures of the 1,3,5-benzotriazepinediones described in Ref. [5] should also be accepted with caution.

4 T.N. Ghosh and P.Ch. Guha, J. Indian Chem. Soc. 6, 181 /1929/; Chem. Abstr. 24, 617 /1930/

5 H. Hagemann, Ger. Offen 2,036,172 /Jan. 27, 1972/; Chem. Abstr. 76, 99722 /1972/

6 M. Israel, L.C. Jones and E.J. Modest, Tetrahedron Letters 1968, 4811

7 M. Israel, L.C. Jones and M.M. Jouillé, J. Heterocyclic Chem. 8, 1015 /1971/ and earlier references cited therein.

8 All new compounds gave satisfactory microanalytical results.