Chemistry of Heterocyclic Compounds, Vol. 31, No. 10, 1995

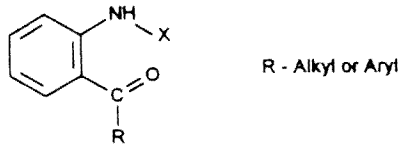
PREPARATION OF SOME 3,4-DIHYDRO-(5H)-1,3,5-BENZO-TRIAZEPINES

Štefan Stankovský, Michal Bodajla, and Katarína Špirková

The results of the reaction of N-(2-chloromethylphenyl)benzimidoyl chloride, a versatile intermediate for preparation of 6-, 7-, 8-, and 9-membered benzannelated heterocyclic compounds, with some acyl hydrazines are presented.

Following the discovery of psychotropic effects of 1,4-benzodiazepines (Diazepam, Oxazepam, Pinazepam, etc.), the quest for novel higher analogues started. Among the most popular analogues were the benzodiazocines and benzodiazonines, besides other heterocycles. Numerous potential tranquilizers were synthesized, among them 1,3- and 2,4-benzodiazepines, 1,3,4-benzotriazepines, 2,1,5-benzothiadiazocines, and 5,1,3-benzothiadiazocines [1-3]. Their testing revealed various kinds of bioactivity, such as CNS depressant, anticonvulsive, muscle relaxant, and antidepressive.

The key intermediates in the synthesis of the above heterocycles are 2-acylanilines (I):

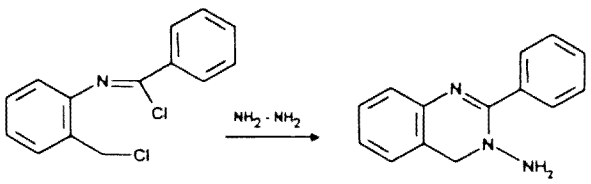


I

We found another useful intermediate, the N-(2-chloromethylphenyl)benzimidoyl chloride (II), a compound with two electrophilic reaction centers. Accordingly, when reacted with suitable bifunctional nucleophiles, novel rings are formed, thus affording benzoazepines, benzoazocines, and benzoazonines, respectively [4, 5].

The starting N-(2-chloromethylphenyl) benzimidoyl chloride was prepared by chlorination of N-(2-methyl-phenyl)benzamide with thionyl chloride, and the arising N-(2-tolyl)benzimidoyl chloride was, after isolation, treated with sulphuryl chloride to give compound II [4].

When II reacted with hydrazine hydrate, only 3-amino-2-phenyl-3,4-dihydroquinazoline (III) was formed:

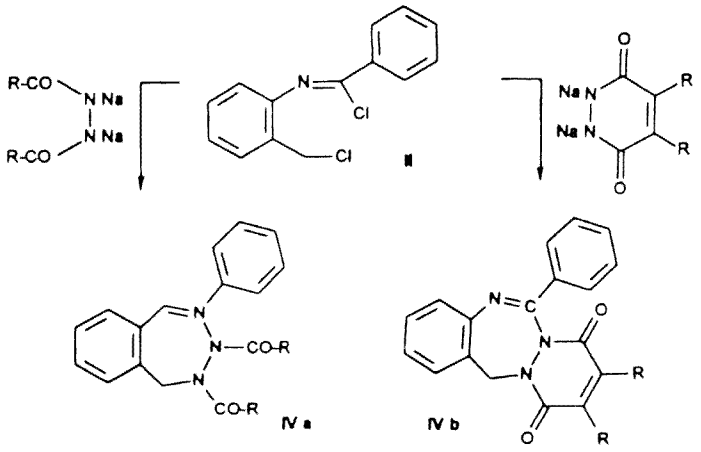


II III

Department of Organic Chemistry, Slovak Technical University, 812 37 Bratislava, Slovak Republic. Published in Khimiya Geterotsiklicheskikh Soedinenii, No. 10, pp. 1383-1384, October, 1995. Original article submitted August 24, 1995.

0009-3122/95/3110-1211$12.50

We have found that the reaction of compound II with some acyl hydrazines leads to benzotriazepines (IVa,b) in low yields.



IV a R = Me, Ph, EtO; IV b R = H; R + R = —CH=CH—CH=CH—

When II was treated with sodium salt of mentioned acyl hydrazines, prepared by reaction of acyl hydrazines with sodium ethoxide, the corresponding 3,4,5-trihydro-1,3,5-benzotriazepines (IVa,b) were formed in a good yield.

The following acyl hydrazines were used: IVa: R = acetyl, benzoyl, carbethoxy; IVb: phthalic hydrazide, maleic hydrazide.

REFERENCES

1. R. Richter and O. Morgenstern, Die Pharmacie, **39**, 301 (1984).
2. D. N. Reinhoudt, Rec. Trav. Chim., **92**, 20 (1973).
3. M. Bodajla, Š. Stankovský, S. Jantová, D. Hudecová, and K. Špirková, Chem. Papers, in press.
4. J. B. Bream and J. Schmutz, Helvetica Chim. Acta, **60**, 2872 (1973).
5. M. Bodajla, Š. Stankovský, and K. Špirková, Collect. Czech. Chem. Commun. (1995), in press.