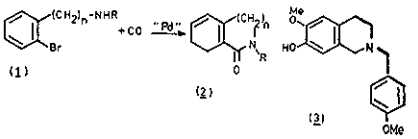
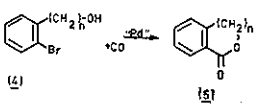
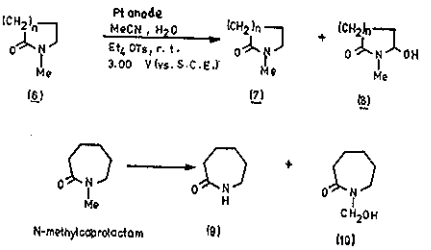




2. The anodic oxidation of some lactams

The anodic oxidation of N-methyllactams (6, n = 1,2) in acetonitrile with Et_4NOTs as an electrolyte gave N-methylimides (7, n = 1,2) and N-methylhydroxylactams (8, n = 1,2) in moderate yields. In a similar manner, the oxidation of N-methylcaprolactam (6, n = 3) afforded caprolactam (9) and N-hydroxymethylcaprolactam (10) in 22 and 19% yields, respectively. The last reaction is now being applied to a new synthesis of some aldehydes.



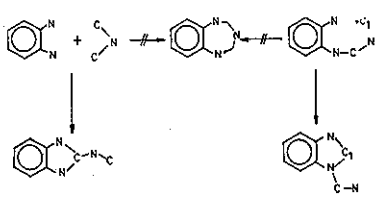
LE I 15

NOVEL 1,3,5-BENZOTRIAZEPINE SYNTHESES

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

Research Group for Alkaloid Chemistry, Hungarian Academy of Sciences, Budapest

Seven-membered heterocycles such as 1,4-diazepines and triazepines are of great pharmacological interest. During the past several years, we have investigated the possibility of devising novel syntheses of the 1,3,5-benzotriazepine skeleton[1,2]. This heterocyclic system has yet scarcely been explored and only a very few authenticated derivatives of this system have been described. This is probably due to the fact that, the most obvious syntheses of benzotriazepines may alternatively lead to substituted benzimidazoles:



In order to minimize the danger of the formation of isomeric benzimidazole derivatives, an auxiliary ring was fused to the seven-membered ring.

Two simple, rational syntheses of condensed 1,3,5-benzotriazepines will be discussed. Some of the obtained products displayed CNS activity.

1) G. Doleschall, Gy. Hornyák, B. Ágai, Gy. Simig, J. Fetter and K. Lempert: Tetrahedron 32, 57 (1976).
2) B. Ágai, G. Doleschall, Gy. Hornyák, K. Lempert and Gy. Simig: Tetrahedron 32, 839 (1976).

LE I 16

SOME SUBSTITUTION DERIVATIVES OF ERGOLINE-I WITH PROLACTIN-INHIBITING ACTIVITIES

J. Křepelka*, M. Semonský

Research Institute for Pharmacy and Biochemistry, 13060 Prague 3, Czechoslovakia

By introduction of alkyl groups from alkyl halides in the dimethylformamide medium into the molecules of D-8-cyanomethylergoline-I and 6-norfestuclavine, respectively, prepared by a series of reactions from D-dihydroergotamine, the corresponding D-6-alkyl-8-cyanomethylergolines-I and 6-alkyl analogues of festuclavine were prepared. Some D-6-alkyl-8-cyanomethylergolines-I were also prepared by reacting sodium cyanide with D-6-alkyl-8-chlormethylergolines-I, obtained from D-6-alkyl-8-hydroxymethylergolines-I.

Some D-6-alkyl-8-cyanomethylergolines-I were converted to D-6-alkyl-8-ergolin-I-ylacetamides, either via the corresponding 8-carboxymethyl acids, their methyl esters, and their hydrazides, or by direct addition of water to the nitrile groups in the parent compounds in a heterogeneous biphasic pyridinic-aqueous medium in the presence of tetraalkylammonium bases.

1-Nitroso derivatives of D-6-alkyl-8-ergolin-I-ylacetamides were prepared by the action of excess nitrous acid upon the corresponding hydrazides of D-6-alkyl-8-ergolin-I-ylacetic acids and decomposition by aqueous ammonia of the intermediate 1-nitroso derivatives of azides of the acids.

The 6-alkyl analogues of festuclavine, D-8-cyanomethylergoline-I, and D-8-ergolin-I-ylacetamide produced marked antinidation and antilactation effects in biological tests. On introduction of the ethyl, propyl or allyl groups into the position 6 in the ergoline cycle the prolactin-inhibiting activities of the compounds were markedly enhanced in comparison with the activities of the corresponding 6-methyl derivatives.

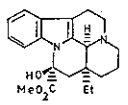
LE I 17

THE SYNTHESIS OF GEMINALLY DISUBSTITUTED 4,5-DIHYDRO-6H-CANTHIN-6-ONES

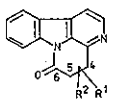
J. Trojánek*, J. Hájíček

Research Institute for Pharmacy and Biochemistry, 19404 Prague 9

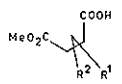
In the past decade some alkaloids of the eburnane group, e.g. vincamine 1, have attracted much interest, especially in view of their known biological activity. In continuation of our bro-

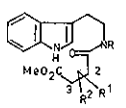


1



2 R^1 = 4-Et, R^2 = 4-Pr
3 R^1 = 4-Et, R^2 = 4-Me
4 R^1 = 5-Et, R^2 = 5-Pr
5 R^1 = 5-Et, R^2 = 5-Me





6 R^1 = 2-Et, R^2 = 2-Pr
7 R^1 = 2-Et, R^2 = 2-Me
8 R^1 = 3-Et, R^2 = 3-Pr
9 R^1 = 3-Et, R^2 = 3-Me
10 R^1 = 3-Et, R^2 = 3-Pr
11 R^1 = 3-Et, R^2 = 3-Me
12 R^1 = 2-Et, R^2 = 2-Pr
13 R^1 = 2-Et, R^2 = 2-Me

ader programme in this field we focused our attention on the synthesis of their degradation products — 4,5-dihydrocanthin-6-ones — particularly on (—)-4-ethyl-4-propyl-4,5-dihydro-6H--canthin-6-one **2**, which was readily obtained by degradation of (+)-vincamine **1**.

Starting from racemic and optically active 2,2[a] and 3,3-disubstituted 3-methoxycarbonylpropionic acids **6**—**9** the appropriate amid-esters **10**—**13** were prepared, which on Bischler-Napieralskii cyclization followed by selenium dehydrogenation afforded the desired 4,5-dihydrocanthin-6-ones **2**—**5**.

The synthesis of succinic acid-esters **6**—**9** will be discussed briefly together with the physico-chemical properties of tryptamides **10**—**13** and especially of canthin-6-ones **2**—**5**.

LITERATURE

1) The Vinca Alkaloids. Botany, Chemistry, and Pharmacology, Ed. Taylor W. I. and Farnsworth N. R., Marcel Dekker, Inc., New York 1973.

LE I 18

SYNTHESIS OF SUBSTITUTED 1(2H)-ISOQUINOLINONES AND 8-OXOBERBINES FROM HOMOPHTALIC ANHYDRIDES AND AZOMETHINES

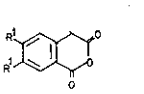
M. A. Haimova*, S. C. Mihovska and E. R. Stanoeva

University of Sofia, Department of Chemistry, Sofia 1126, Bulgaria

Recently we reported that the reaction of 1,3-isochromandiones (homophtalic anhydrides) with acyclic and cyclic azomethines can be used as a method for synthesis of 4-carboxy-1(2H)--isoquinolinones, 13-carboxy-8-oxoberbines and 14-carboxy-hexadehydroyohimbanes[1,2].

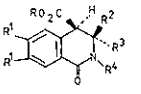
Homophtolic anhydrides **1** react analogously with azomethines of aromatic, heteroaromatic and aliphatic aldehydes and ketones, and aliphatic amines **2**, as well as with 1-alkyl(aryl)-6,7--dimethoxy-3,4-dihydroisoquinolines **4** (refluxing of **1** and **2**, resp. **4** in benzene or dichloroethane, extraction of **3**, resp. **5** with NaOH , aq), where trans-2,3-disubstituted or 2,3,3-trisubstituted-4-carboxy-3,4-dihydro-1(2H)-isoquinolinones **3** (R = H) and 14-alkyl(aryl)-13-carboxy-8-oxoberbines **5** (R = H), resp., are obtained. The relative configuration of **3** is proved chemically and by NMR-investigation of their corresponding methyl esters **3** (R = Me)[1,2]. The spatial structure of C-13 and C-14 can not be established by NMR-analysis of **5** (R = Me).
Only in the case of the reaction between **1** (R^1 = H or MeO) and ethoxymethyleneaniline (**2**, R^2 = H, R^3 = EtO, R^4 = Ph) 4-anilinomethylene-1,3-isochromandiones **6** (R^1 = H or MeO) are obtained. In conditions of alkoline hydrolysis they are converted into 4-carboxy-1(2H)-isoquinolinones **7** (R = H, R^1 = H or MeO, R^2 = Ph). The NMR-spectra of their methyl esters show a great similarity with the spectrum of the ester **7** (R = R^2 = = Me, R^1 = H), which was obtained by us from the known acid **7** (R = H)[3]. In these two cases an aldol condensation between the CH-acidic anhydrides and the azomethine takes place.

1. M. A. Haimova, N. M. Mollov, S. C. Ivanova, A. J. Dimitrova and V. I. Ognyanov, Tetrahedron **33**, 331 (1977);
2. M. Haimova, E. Stanoeva and A. Dimitrova, Compt. rend. **285C**, 353 (1977);
3. V. H. Belgaonkar, R. N. Usgaonkar, Tetrahedron Letters **1975**, 3849.



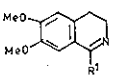
1

2

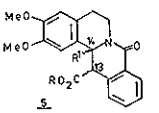


3

R = H or Me; R^1 = H or MeO; R^2 = H or Me;
R^3 = Ph, 2-furyl, Me, Et, iso-Pr etc.
R^4 = $PhCH_2$, $PhCH_2CH_2$, $(MeO)_2CHCH_2$, Me, Et, n-Pr, iso-Pr, cyclohexyl etc.

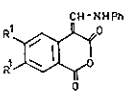


4

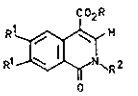


5

R = H or Me
R^1 = Me, Et, $PhCH_2$, Ph



6



7

R = H or Me
R^1 = H or MeO
R^2 = Me or Ph

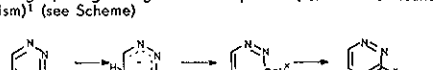
LE I 19

ON THE MECHANISM OF THE AMINATION OF 3-SUBSTITUTED DERIVATIVES OF 1,2,4-TRIAZINE WITH POTASSIUM AMIDE IN LIQUID AMMONIA

Andrzej Rykowski*, Paweł Nantka-Namirski
Institute of Organic Chemistry, Polish Academy of Sciences, Poland

Henk van der Plas
Laboratory of Organic Chemistry, Agricultural University, Wageningen, The Netherlands

Amination of 3-methylthio-1,2,4-triazine with potassium amide in liquid ammonia at —75 °C yields the corresponding 3-amino compound and in addition 3,3'-bis(methylthio)-5,5'-bi-1,2,4-triazine. It has been proved using the corresponding 3-methylthio-[4-^{15}N]-1,2,4-triazine that amination goes for about 93% via a ring opening - ring closure sequence ($S_NANRORC$-mechanism)[1] (see Scheme)



* = ^{15}N