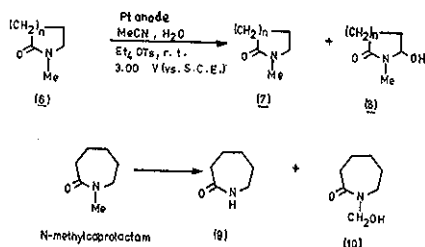


2. The anodic oxidation of some lactams

The anodic oxidation of N-methylactams (6, $n = 1,2$) in acetonitrile with Et_4NOtF 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.



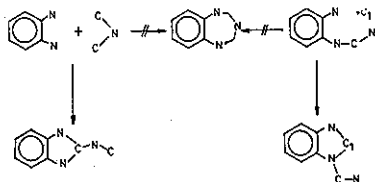
LE 15

NOVEL 1,3,5-BENZOTRIAZEPINE SYNTHESIS

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

LE 16

SOME SUBSTITUTION DERIVATIVES OF ERGOLINE-1 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-1 and 6-norfestuclavine, respectively, prepared by a series of reactions from D-dihydroergotamine, the corresponding D-6-alkyl-8-cyanomethylergolines-1 and 6-alkyl analogues of festuclavine were prepared. Some D-6-alkyl-8-cyanomethylergolines-1 were also prepared by reacting sodium cyanide with D-6-alkyl-8-chloromethylergolines-1, obtained from D-6-alkyl-8-hydroxymethylergolines-1.

Some D-6-alkyl-8-cyanomethylergolines-1 were converted to D-6-alkyl-8-ergolin-1-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 pyridine-aqueous medium in the presence of tetraalkylammonium bases.

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

The 6-alkyl analogues of festuclavine, D-8-cyanomethylergoline-1, and D-8-ergolin-1-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.

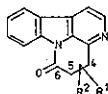
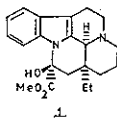
LE 17

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

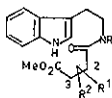
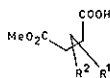
J. Trojáněk*, J. Hájíček

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-



- 2 R¹ = 4-Et, R² = 4-Pr
3 R¹ = 4-Et, R² = 4-Me
4 R¹ = 5-Et, R² = 5-Pr
5 R¹ = 5-Et, R² = 5-Me



- 6 R¹ = 2-Et, R² = 2-Pr
7 R¹ = 2-Et, R² = 2-Me
8 R¹ = 3-Et, R² = 3-Pr
9 R¹ = 3-Et, R² = 3-Me
10 R¹ = 3-Et, R² = 3-Pr
11 R¹ = 3-Et, R² = 3-Me
12 R¹ = 2-Et, R² = 2-Pr
13 R¹ = 2-Et, R² = 2-Me

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

Starting from racemic and optically active 2,2' and 3,3-disubstituted 3-methoxycarbonylpropionic acids 6—9 the appropriate amid-esters 10—13 were prepared, which on Bischler-Napieralski cyclization followed by selenium dehydrogenation afforded the desired 4,5-dihydrocannabin-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 cannabin-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 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

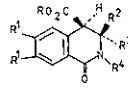
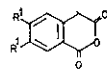
University of Sofia, Department of Chemistry, Sofia 1126, Bulgaria

Recently we reported that the reaction of 1,3-isochromandiones (homophthalic 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-hexadehydrochimbane^{1,2}.

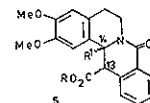
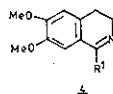
Homophthalic anhydrides 1 react analogously with azomethines of aromatic, heteroaromatic and aliphatic aldehydes and ketones, and aliphatic amines 2, as well as with 1-alkyl(aryl)-6,7-dimethoxy-3,4-dihydroisoquinolines 4 (refluxing of 1 and 2, resp. 4 in benzene or dichloroethane, extraction of 3, resp. 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 (R¹ = H or MeO) and ethoxymethylaniline (2, R² = H, R³ = EtO, R⁴ = Ph) 4-anilinoethylene-1,3-isochromandiones 6 (R¹ = H or MeO) are obtained. In conditions of alkaline hydrolysis they are converted into 4-carboxy-1(2H)-isoquinolinones 7 (R = H, R¹ = H or MeO, R² = Ph). The NMR-spectra of their methyl esters show a great similarity with the spectrum of the ester 7 (R = R² = Me, R¹ = 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.

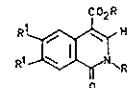
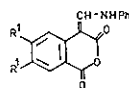
1. M. A. Haimova, N. M. Mollov, S. C. Ivanova, A. J. Dimitrova and V. I. Ognyanov, Tetrahedron 33, 331 (1977);
2. M. Haimova, E. Stanoeva and A. Dimitrova, Compt. rend. 285C, 353 (1977);
3. V. H. Belgaukar, R. N. Usgaonkar, Tetrahedron Letters 1975, 3849.



- R = H or Me; R¹ = H or MeO; R² = H or Me;
R³ = Ph, 2-furyl, Me, Et, iso-Pr etc;
R⁴ = PhCH₂, PhCH₂CH₂, (MeO)₂CHCH₂, Me, Et, n-Pr, iso-Pr, cyclohexyl etc.



- R = H or Me
R¹ = Me, Et,
PhCH₂, Ph



6

7

- R = H or Me
R¹ = H or MeO
R² = Me or Ph

LE 19

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

Andrzej Rykowski*, Poweł 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-[4-¹⁵N]-1,2,4-triazine that amination goes for about 93% via a ring opening - ring closure sequence (S_NANORC-mechanism)¹ (see Scheme)

