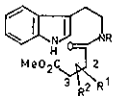
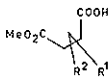


- 2 R<sup>1</sup> = 4-Et, R<sup>2</sup> = 4-Pr  
 3 R<sup>1</sup> = 4-Et, R<sup>2</sup> = 4-Me  
 4 R<sup>1</sup> = 5-Et, R<sup>2</sup> = 5-Pr  
 5 R<sup>1</sup> = 5-Et, R<sup>2</sup> = 5-Me



- 6 R<sup>1</sup> = 2-Et, R<sup>2</sup> = 2-Pr  
 7 R<sup>1</sup> = 2-Et, R<sup>2</sup> = 2-Me  
 8 R<sup>1</sup> = 3-Et, R<sup>2</sup> = 3-Pr  
 9 R<sup>1</sup> = 3-Et, R<sup>2</sup> = 3-Me  
 10 R<sup>1</sup> = 3-Et, R<sup>2</sup> = 3-Pr  
 11 R<sup>1</sup> = 3-Et, R<sup>2</sup> = 3-Me  
 12 R<sup>1</sup> = 2-Et, R<sup>2</sup> = 2-Pr  
 13 R<sup>1</sup> = 2-Et, R<sup>2</sup> = 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-Napieralskii 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**.

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LE 1 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

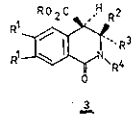
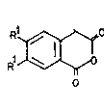
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Recently we reported that the reaction of 1,3-isochromandiones (homophthalic anhydrides) with acyclic and cyclic azomethines can be used as a method for synthesis of 4-carboxy-1(2H)-isoquinolinones, 13-carboxy-8-oxoberbines and 14-carboxy-hexadehydrochimbanes<sup>1,2</sup>.

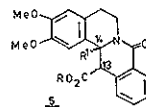
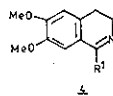
Homophthalic anhydrides **1** react analogously with azomethines of aromatic, heteroaromatic and aliphatic aldehydes and ketones, and aliphatic amines **2**, as well as with 1-alkyl(aryl)-6,7-dimethoxy-3,4-dihydroisoquinolines **4** (refluxing of **1** and **2**, resp. **4** in benzene or dichloroethane, 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)<sup>1,2</sup>. 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<sup>1</sup> = H or MeO) and ethoxymethyleneaniline (**2**, R<sup>2</sup> = H, R<sup>3</sup> = EtO, R<sup>4</sup> = Ph) 4-anilinoethylene-1,3-isochromandiones **6** (R<sup>1</sup> = H or MeO) are obtained. In conditions of alkaline hydrolysis they are converted into 4-carboxy-1(2H)-isoquinolinones **7** (R = H, R<sup>1</sup> = H or MeO, R<sup>2</sup> = Ph). The NMR-spectra of their methyl esters show a great similarity with the spectrum of the ester **7** (R = R<sup>2</sup> = Me, R<sup>1</sup> = H), which was obtained by us from the known

acid **7** (R = H)<sup>3</sup>. In these two cases an aldol condensation between the CH-acidic anhydrides and the azomethine takes place.

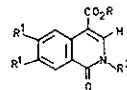
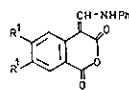
1. M. A. Haimova, N. M. Mollov, S. C. Ivanova, A. J. Dimitrova and V. I. Ognyanov, Tetrahedron **33**, 331 (1977);  
 2. M. Haimova, E. Stanoeva and A. Dimitrova, Compt. rend. **285C**, 353 (1977);  
 3. V. H. Belgaonkar, R. N. Usgaonkar, Tetrahedron Letters **1975**, 3849.



- R = H or Me; R<sup>1</sup> = H or MeO; R<sup>2</sup> = H or Me;  
 R<sup>3</sup> = Ph, 2-furyl, Me, Et, iso-Pr etc;  
 R<sup>4</sup> = PhCH<sub>2</sub>, PhCH<sub>2</sub>CH<sub>2</sub>, (MeO)<sub>2</sub>CHCH<sub>2</sub>, Me, Et, n-Pr, iso-Pr, cyclohexyl etc.



- R = H or Me  
 R<sup>1</sup> = Me, Et,  
 PhCH<sub>2</sub>, Ph



- R = H or Me  
 R<sup>1</sup> = H or MeO  
 R<sup>2</sup> = Me or Ph

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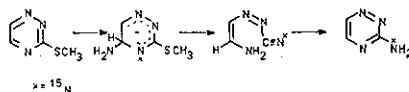
### ON THE MECHANISM OF THE AMINATION OF 3-SUBSTITUTED DERIVATIVES OF 1,2,4-TRIAZINE WITH POTASSIUM AMIDE IN LIQUID AMMONIA

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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-<sup>15</sup>N]-1,2,4-triazine that amination goes for about 93% via a ring opening - ring closure sequence (S<sub>N</sub>ANRORC-mechanism)<sup>1</sup> (see Scheme)



In order to investigate the generality of this mechanism in the 1,2,4-triazine series, we extended our amination studies to some derivatives containing different leaving groups at C-3 and various substituents at C-5 or C-6 of the triazine ring (see Figure).



- |                 |           |        |                  |           |         |
|-----------------|-----------|--------|------------------|-----------|---------|
| 1. X = F        | R1 = Ph   | R2 = H | 11. X = SCH3     | R1 = t-Bu | R2 = H  |
| 2. X = Cl       | R1 = Ph   | R2 = H | 12. X = SO2CH3   | R1 = t-Bu | R2 = H  |
| 3. X = Br       | R1 = Ph   | R2 = H | 13. X = -N(CH3)2 | R1 = t-Bu | R2 = H  |
| 4. X = J        | R1 = Ph   | R2 = H | 14. X = Cl       | R1 = H    | R2 = Ph |
| 5. X = OCH3     | R1 = Ph   | R2 = H | 15. X = SCH3     | R1 = H    | R2 = Ph |
| 6. X = SCH3     | R1 = Ph   | R2 = H | 16. X = Cl       | R1 = Ph   | R2 = Ph |
| 7. X = SO2CH3   | R1 = Ph   | R2 = H | 17. X = OCH3     | R1 = Ph   | R2 = Ph |
| 8. X = +N(CH3)2 | R1 = Ph   | R2 = H | 18. X = SCH3     | R1 = Ph   | R2 = Ph |
| 9. X = Cl       | R1 = t-Bu | R2 = H | 19. X = SO2CH3   | R1 = Ph   | R2 = Ph |
| 10. X = OCH3    | R1 = t-Bu | R2 = H | 20. X = -N(CH3)2 | R1 = Ph   | R2 = Ph |

It was found that besides the corresponding 3-amino compounds as main product, several by-products are formed depending on the nature of the substituents on positions 3 and 5.

With the compounds 2, 3 and 4 a considerable amount of 2,4-diphenyl-1,3,5-triazine is obtained as by-product together with some of the dehalogenated product 5-phenyl-1,2,4-triazine.

With compound 6, ring contraction into 3-methylthio-5-phenyl-1,2,4-triazole takes place as side reaction.

It has been proved using the corresponding [4-<sup>15</sup>N]triazines that the formation of the 3-amino compounds occurs by a ring opening - ring closure sequence (S<sub>N</sub>ANRORC) and/or by the more classical addition-elimination mechanism (S<sub>N</sub>AE). As proved by nmr spectroscopy the addition of the amide ion to C-5 in 3-X-triazines is more favoured than addition to C-3. However, in cases where a substituent is present at C-3 which has highly electron-attracting properties [ +N(CH<sub>3</sub>)<sub>2</sub>, SO<sub>2</sub>CH<sub>3</sub>], the addition to C-3 is the favourite process. The mechanism of the amination and the ring modifying process will be discussed.

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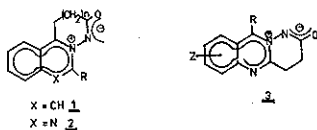
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SOME NOVEL TYPE ELECTRON DEFICIENT HETEROAROMATIC AMMONIOAMIDATES

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Dept. of Organic Chem. TU BUDAPEST

We wish to report on the synthesis of novel type electron deficient heteroaromatic ammonioamidates derived by incorporation of the amidate nitrogen and carbon and of the ammonio nitrogen atoms into a second ring (Compounds 1, 2, 3).

The key step of the syntheses is based on neighboring-group participation of the nitrogen atom of the starting heteroaromatic system in the cleavage of acyl azide groups.



The structures of 1, 2 and 3 were proved by spectroscopical means and by unambiguous syntheses.

The tautomerism and photochemical behaviour of 1-3 were also investigated.

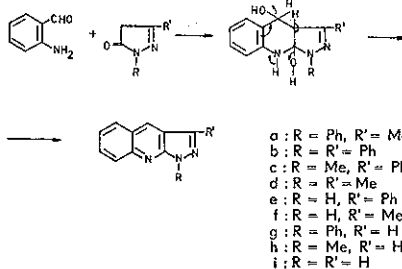
LE I 21

THE CONDENSATION OF o-AMINO BENZALDEHYDE WITH PYRAZOLE-5-ONES

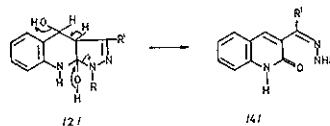
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Department of Chemistry and Geology, Clemson University, Clemson S.C. 29631, USA.

Department of Organic Chemistry, Pedagogical University, 42-201 Częstochowa, Poland.

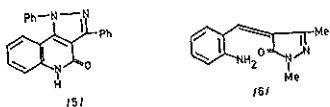
The Friedländer quinoline synthesis was extended to the condensation of o-aminobenzaldehyde with pyrazole-5-one and its derivatives (1a - 1i) in order to obtain pyrazoloquinolines (3)



This could be achieved only in few cases. The behavior of the intermediary compound (2) depends on the electronic properties of both the R and R' substituents. When the pyrazole-5-one is not stabilized by R' = Ph the pyrazole moiety in the intermediary compound (2) is cleaved and corresponding hydrazones of 1-H-3-acylquinoline-2-one (4) are formed apart from other products.



In the case of 1,3-diphenylpyrazole-5-one (1b) pyrazoloquinoline(5) is also formed by the intramolecular Michael-type addition and subsequent oxidation. 1,3-Dimethylpyrazole-5-one (1d) is much more resistant towards condensation and the major product formed was 1,3-dimethyl-4-(o-aminobenzylidene) pyrazole-5-one (6).



Moreover, both hydrazones (4a) and (4d) undergo condensation with o-aminobenzaldehyde yielding 3-(2-quinolyl)quinolin-2-one (7). Also benzylidenepyrazole-5-one (6) turns into both pyrazoloquinoline (3d) and quinolylquinoline-2-one (7). 1-H-Pyrazole-5-ones (1f) and (1i) which are not stabilized with R' = Ph can be a source of hydrazine. The latest is formally liberated from pyrazole-5-ones yielding with o-aminobenzaldehyde 2,2'-diaminobenzaldazine (8).

