FORMATION OF A NEW RING SYSTEM VIA ADDITION OF ACRYLONITRILE TO BENZOQUINOLIZINES

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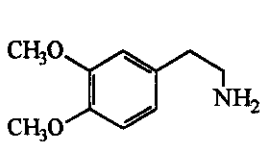
Abstract-The reaction of enamine (**4**) with acrylonitrile gave rise to compound (**6**) in addition to four (**7-10**) stereoisomeric derivatives of a new ring system.

As reported earlier[1] the so called Wenkert enamine[2] can be easily alkylated by electrophilic olefins at position 1. The presence of a methyl group attached to the indolic nitrogen prevents this alkylation and an addition reaction occurs instead.[3] It was an intriguing question to be answered: what is the outcome of a similar reaction using the benzoquinolizidine ring system having no indole nitrogen at all ?
The already known enamine (**4a**)[4] was alkylated by acrylate esters at position 1 as expected.[5,6] However, compound (**4b**) having an ethyl group at position 1 behaved quite differently.

Scheme 1.



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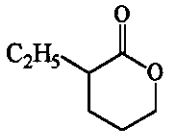

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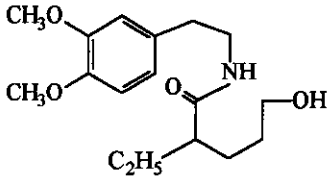

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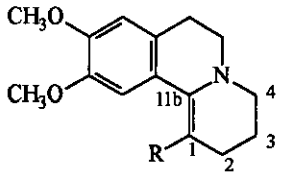
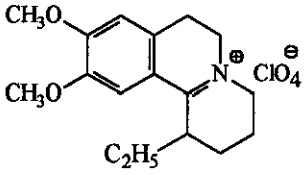


4a R = H
4b R = C_2H_5



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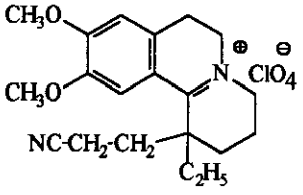

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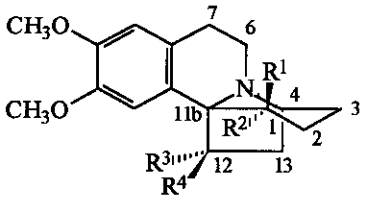
Compound (**4b**) was prepared by reacting homoveratrylamine (**1**) with 2-ethylpentanolide (**2**)[7] in boiling chlorobenzene followed by treatment of the product (**3**)[8] with phosphoryl chloride. The new product was isolated and characterised as its perchlorate salt (**5**)[9] (Scheme l).

When the solution of the latter salt in dichloromethane was treated with aqueous sodium hydroxide it was not entirely transformed into the enamine (**4b**), thus in the course of the Michael addition both **4b** and its salt were present. The latter mixture was allowed to react with acrylonitrile in dichloromethane - methanol at ambient temperature. After work up the following products were isolated: the iminium perchlorate (**6**)[10] (17%), and four additional products (**7-10**), which proved to be stereoisomers of a new heterocyclic ring system (Scheme 2).

Scheme 2.



	R^1	R^2	R^3	R^4
7	$(CH_2)_2CN$	CH_2CH_3	CN	H
8	CH_2CH_3	$(CH_2)_2CN$	CN	H
9	$(CH_2)_2CN$	CH_2CH_3	H	CN
10	CH_2CH_3	$(CH_2)_2CN$	H	CN

7 - 10

According to the nmr studies **7**[11] and **8**[12] differ in the stereoposition of the ethyl group. The relation between **9**[13] and **10**[14] is similar On the other hand compounds (**7**) and (**9**) as well as (**8**) and (**10**) differ in the configuration at C-12.

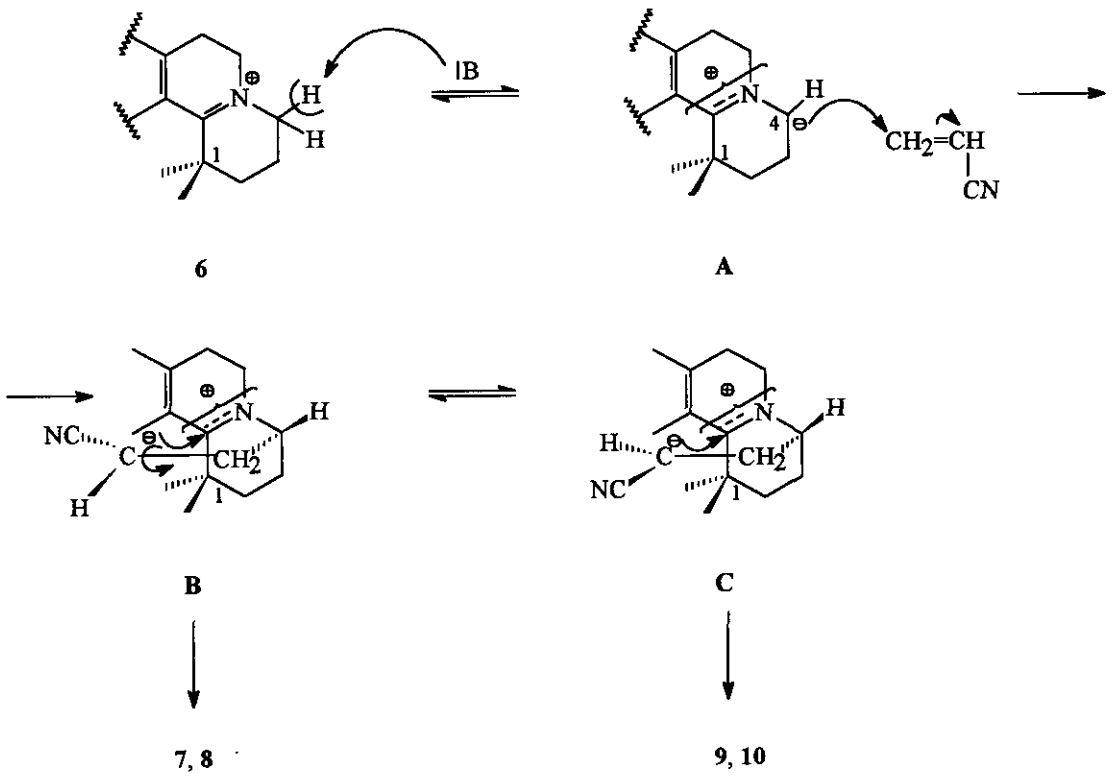
The X-ray studies substantiated the depicted structures unambiguously, e.g., the bridging of C-4 and C-11b by an ethano group. In **7** and **8** the cyano group at C-12 can be found in the "syn" (12 S*), while in **9** and **10** in the "anti" (12R*) position.

Compounds (**7**) and (**8**) are formed in 53% combined yield, while (**9**) and (**10**) stereoisomers only in 5.5%. All these compounds can be regarded as combinations of the tropane and benzoquinolizidine skeleton. Their formation can be rationalised as follows

The acidic proton of **6** in the α position with respect to the charged nitrogen is removed by base. The subsequent attack on the zwitter-ion (**A**) by electrophilic acrylonitrile yields the intermediate 1,5-dipole **B** from which **7** and **8** can be deduced. It can be safely supposed that **B** is in equilibrium with **C** formed by rotation of the side-chain at C-4. The minor products (**9**) and (**10**) can be derived from dipole **C** (Scheme 3).

From the stereoselectivity (10: l) of the reaction one may conclude a concerted pathway as well, instead of the step-by-step mechanism [15,16]

Scheme 3



The above discussed reaction can be generalised. Compound (**4a**) reacts with other electrophilic olefins (e.g., methyl acrylate) in a similar way. Related benzoquinolizines having different substituents at the aromatic ring gave analogous products.

ACKNOWLEDGEMENT

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8. **3**: mp: 91 °C (1,2-dichloroethane). Y: 77 %.

9. **5**: mp: 185 °C (methanol). Y: 62 %.

10. **6**: mp: 2l6-217 °C (methanol) Y.: 7 %.

11. **7**: mp: 160-162 °C (methanol). Y.: 20.8 %.

12. **8**: mp: 225-227 °C (methanol).Y.: 32.5%.

13. **9**: mp: 180 °C (methanol).Y.: 2.6 %.

14. **10**. mp: 164-165 °C (methanol). Y.. 2.9 %.

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17. All the products gave satisfactory elemental analyses and the ir and nmr spectra were in harmony with the given structures.

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