

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

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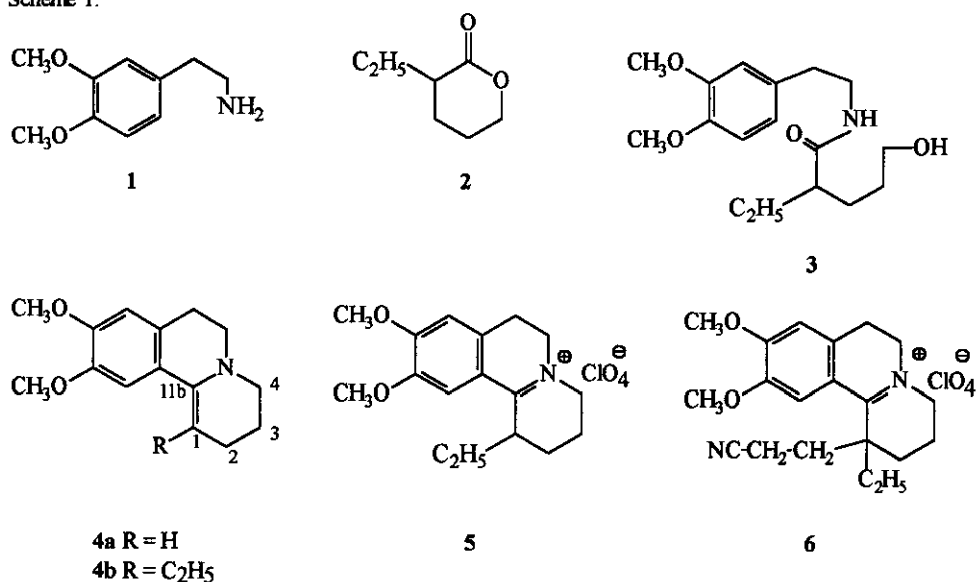
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Abstract-The reaction of enamine (4) with acrylonitrile gave rise to compound (6) in addition to four (7-10) stereoisomeric derivatives of a new ring system.

As reported earlier¹ the so called Wenkert enamine² 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.

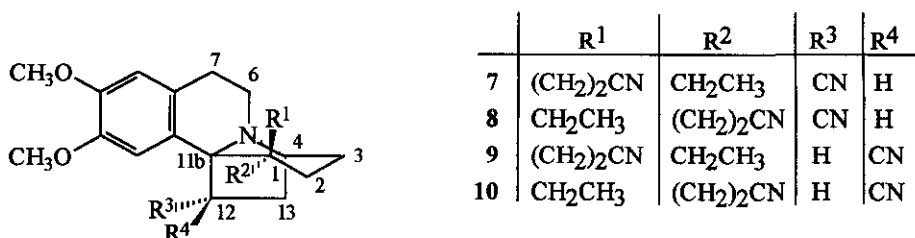
Scheme 1.



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 1).

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.



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.

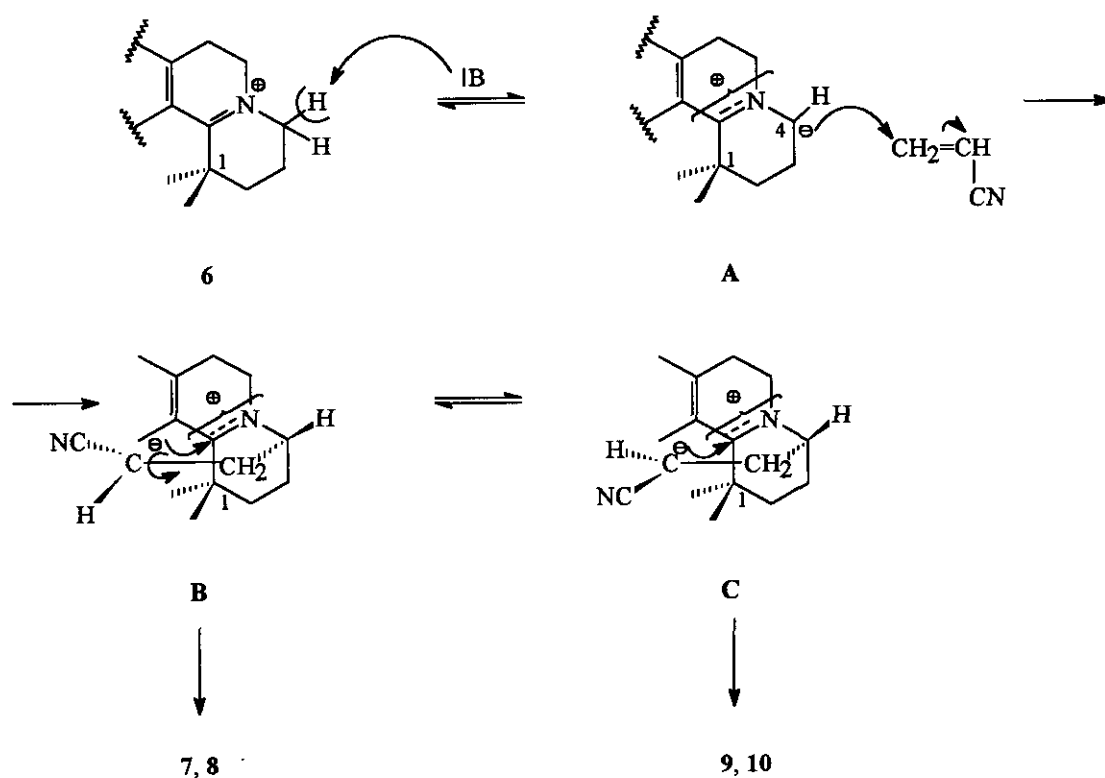
The X-ray studies substantiated the depicted structures unambiguously, e.g., the bridging of C-4 and C-11b by an ethano group. In **7** and **8** the cyano group at C-12 can be found in the "syn" (12 S*), while in **9** and **10** in the "anti" (12 R*) position.

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 (10:1) 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.

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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: 216-217 °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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