SYNTHESIS OF ELLIPTICINE : REVIEW AND COMPUTER SUGGESTIONS

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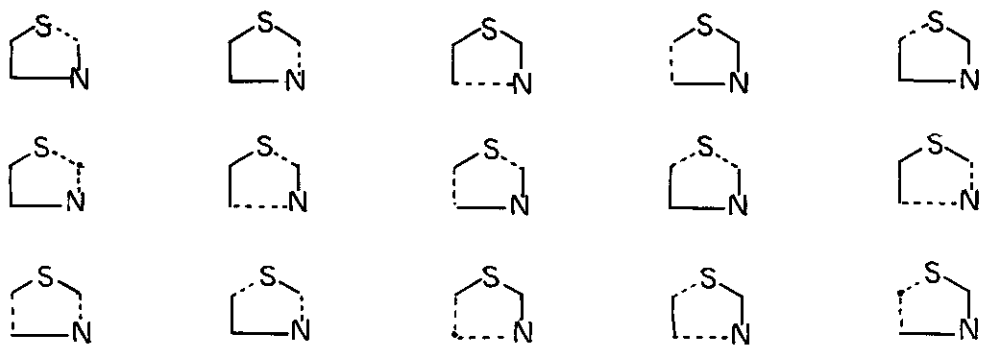
Abstract - A review of recent syntheses of ellipticine is presented and some suggestions of a computer assisted organic synthesis program are given.

INTRODUCTION

Corey[1] and recently Hamon and Young[2] have shown the utility of the analytical approach in organic synthesis. We wrote a computer program using this method[3]. The principle of this computer program is to delete successively the bonds of the target compound. The program delete one bond, then two bonds, and so on, up to a limit given by the user. Only the skeleton of the target compound is represented, the nature of the bonds are not displayed, since the aim of the program is to give ideas of synthesis without preconception.

Scheme 1 shows the simple example of thiazole where the program deleted one and two bonds. From the schemes given by the computer, the chemist has to invent syntheses which build up the broken bonds in one or several steps.

This very simple approach may suggest new syntheses by breaking the target compound in new fragments. We used this method to examine the synthesis of ellipticine known for its interesting antitumor activity[4].



SCHEME 1

RESULTS

Since a recent review[4] synthetic interest is yet shown in synthesis of ellipticine and analogs[5-24] because most of these approaches do not allow easy access to a wide variety of derivatives, and the need for a general synthetic approach is still present.

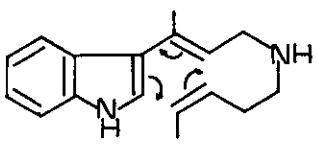
The starting materials of these last syntheses are listed in scheme 2.

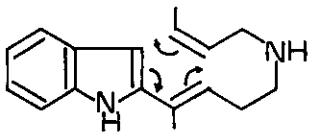
We ordered the program to break only two bonds which leads to 253 solutions. We cannot give here all the possibilities (they are available upon request). We show in scheme 3 the solutions which cover the already known synthesis. The dotted bonds indicate the last step (s) of the ring synthesis.

Some of the 253 computer suggestions are listed in scheme 4. These solutions have been selected because i) they suggest a well known reaction such as Diels-Alder reaction or ii) they involve a simple or an interesting starting skeleton.

Several solutions suggest the possibility of intramolecular Diels-Alder reaction (solutions 1-9).

Syntheses (3) and (4) seem particularly attractive :





A recent review showed that the intramolecular Diels-Alder reaction can be used to synthesize a variety of polycyclic species[58 a,b] and Diels-Alder reactions with vinyl indoles have been tried successfully[59-62].

Solutions (10) and (11) suggest an 1,3-dipolar intramolecular cycloaddition[58b].

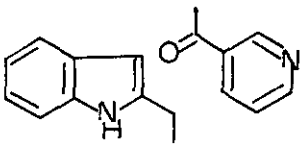
Most of the known syntheses start with the indole nucleus formed by rings A + B (scheme 3), but none try to start with the indole nucleus made by rings B + C as suggested by solutions (20)-(23).

Other solutions involve more complicated skeletons but some may suggest new ideas of synthesis and reaction.

Solutions (28) and (29) have been planned[63-64].

CONCLUSION

This program is simpler than the classical approach of the computer assisted organic synthesis[65-67] but it may however suggest new syntheses such as solutions (3) and (4).



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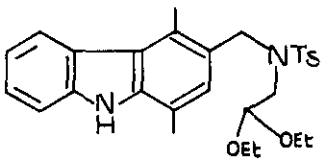

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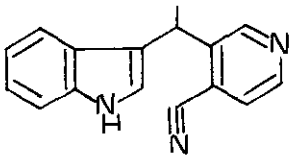

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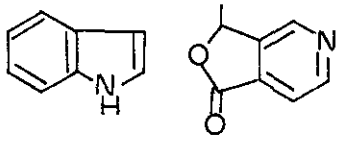

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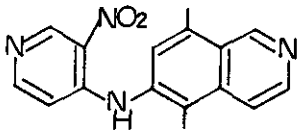

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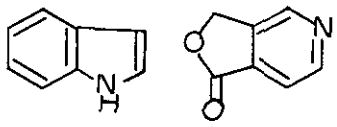

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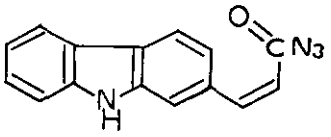

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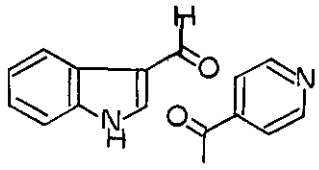

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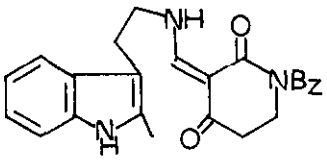

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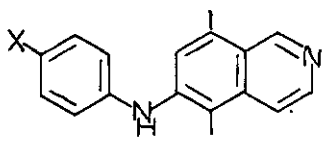

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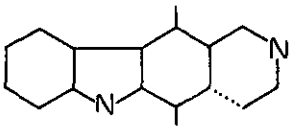

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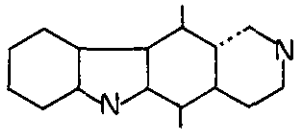

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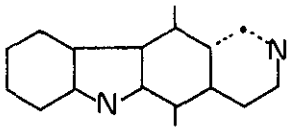

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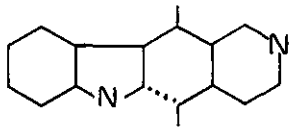

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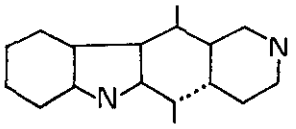

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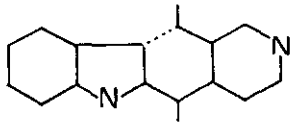

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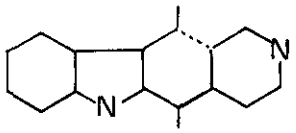

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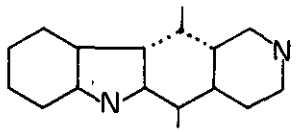

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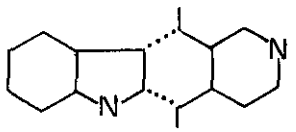

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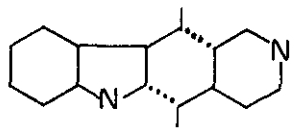

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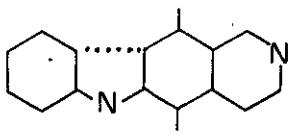

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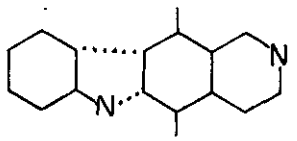

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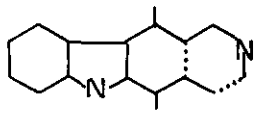

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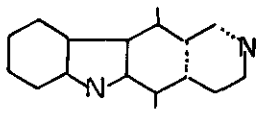

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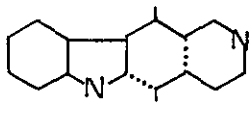

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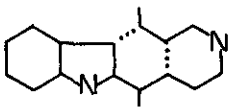

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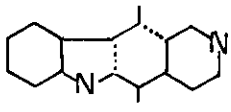

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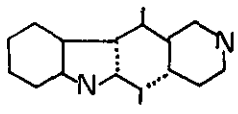

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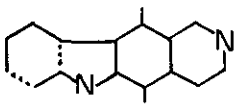

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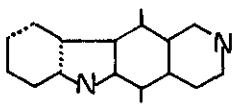

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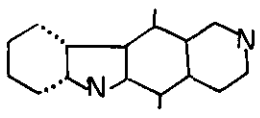

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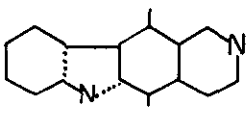

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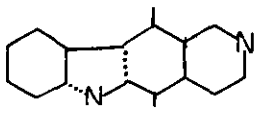

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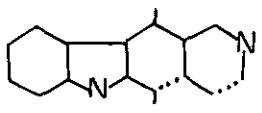

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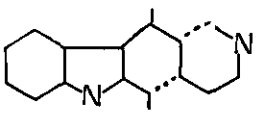

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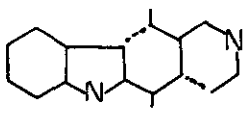

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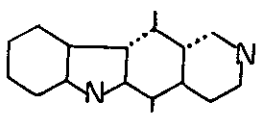

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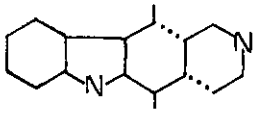

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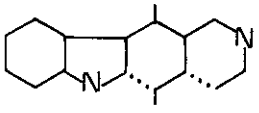

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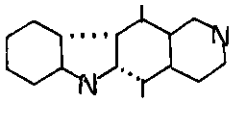

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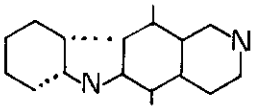

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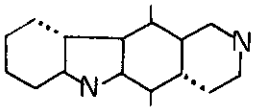

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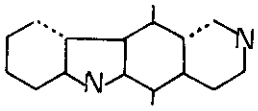

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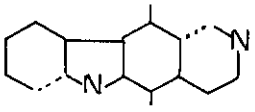

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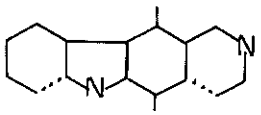

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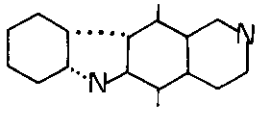

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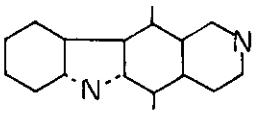

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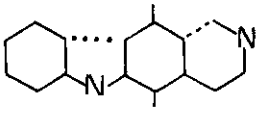

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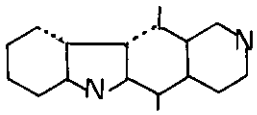

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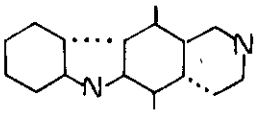

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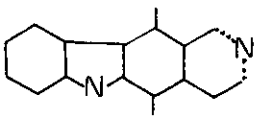

29

SCHEME 4

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