manufacturers of equipment/technical products such as agricultural equipments, fisheries, instruments, biology–biotechnology instruments/chemicals, food and scientific appliances, etc., need to be developed.

Usage of the databases can be encouraged by providing translation facility from English to vernacular language and vice-versa. In fact, in the Indian situation this is the most important and appropriate solution towards spreading biological knowledge to the community at the grass-roots level.

Our national networking agencies should start developing databases in areas which have not been touched so far and for which an in-depth treatment is lacking in global databases. Some of these areas are biostatistics, local living resources and chemistry, medicinal and aromatic plants, traditional systems of medicine, etc. CSIR's recent collaboration with the IDRC, Canada, to develop Asian Information on Health and Environment is a step towards this. These conventional STI programmes should extend their activities to areas of business and financial information as well, by promoting generation of a whole new set of databases and services that the business people also require.

India has emerged as the frontier nation among the Third World countries having its own effective, efficient information network. With the setting up of NICNET (Network of the National Informatics Centre, New Delhi) and its reaching to Taluka level by the end of the Eighth Five Year Plan, it would be possible to disseminate biological knowledge practically to every nook and school of the country. In fact, the success of biomedical information dissemination using NICNET is highly encouraging and databases and databanks related to other fields of biology developed within the country can also be put on the network. It has been felt that NICNET or NICNET-supported BTISNET can play a major role in disseminating the information of current interest.

However, decentralized delivery options such as floppy disks, CD ROM and magnetic tapes are still of significance in our situation. These would minimize the use of telecom services, thereby saving the expenditure on online communications.

Conclusion

It has been felt that more and more subject-specific, textual, numeric, multimedia and interactive databases addressing the local, national as well as global needs must be developed. Though we need to use online media to disseminate these databases, decentralized delivery options can also be utilized with advantage in our situation. It has become evident from our past experience that more and more participation of subject experts and collaboration with international database-developing houses are a must. Uniform formats for acquisition, storage, retrieval and dissemination need to be developed. India has great potential in developing more informative and interactive subject-specific and broad-ranged databases in biology and biotechnology which needs to be tapped.

ACKNOWLEDGEMENTS. We thank the Department of Biotechnology, New Delhi, for sponsoring the Biotechnology Information System (BTIS) facility at NIO, Goa. Thanks are also due to our colleague Dr T G. Jagtap for his suggestions We are grateful to the Director, NIO, and Dr A H Parulekar for constant support and encouragement.

REVIEW ARTICLES

The chemistry of a non-natural product: Tröger's base*

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Tröger's base was the first amine to be resolved where the chirality was solely due to very high inversion barrier around nitrogen atom(s). Though the molecule was known over a century, work done during the past one decade has shown that Tröger's base and its analogues could be used as chiral solvating agents, DNA-binding ligands and for the construction of biomimetic molecular receptors and clathrate hosts. Asymmetric synthesis of Tröger's base analogues has also been achieved recently. Because of the rigid, 'V'-shaped chiral nature of this molecule, there is a growing interest for use of this unit in the design of potential host systems. This review article focuses on the chemistry of Tröger's base along with the possible future utilities.

OVER the centuries chemists have tried to understand nature. Synthetic organic chemists took it as a challenge to synthesize natural products in the laboratory. The

*This paper is dedicated to Dr Tarasankar Pal and Dr Anjali Pal, IIT Kharagpur, India

last five decades have witnessed the success achieved in synthesizing not only natural products with intricate structures but also many unnatural or non-natural compounds. But chemists have not stopped just at synthesizing the compounds in the laboratory; they have also designed molecules to 'perform' specific tasks. The *rational design of molecules* with defined properties has led to the development of *supramolecular structures* to perform *chemistry beyond the molecule*[1]. The development of supramolecular chemistry has been made possible by synthesis of highly organized complex structures with predictable functions. This has found applications in analytical chemistry, medicinal chemistry, drug design, crystal engineering, photoelectronic devices, etc., and this aims at understanding the biological processes at a molecular level.

For the design of synthetic receptor molecules with predictable three-dimensional structures, many simple structural units have been chosen as building blocks. Quite often in organic chemistry, molecules or phenomena that are known for many years offer new opportunities and renewed interest when employed with new concepts in mind. Bile acids, Kemp's triacid, Tröger's base, etc., some of which were known over a century, find new interests for applications. The first two templates have been reviewed in recent literature[2,3]. The purpose of this article is to review briefly the chemistry of Tröger's base which has developed over a century and the possible future utilities employing it.

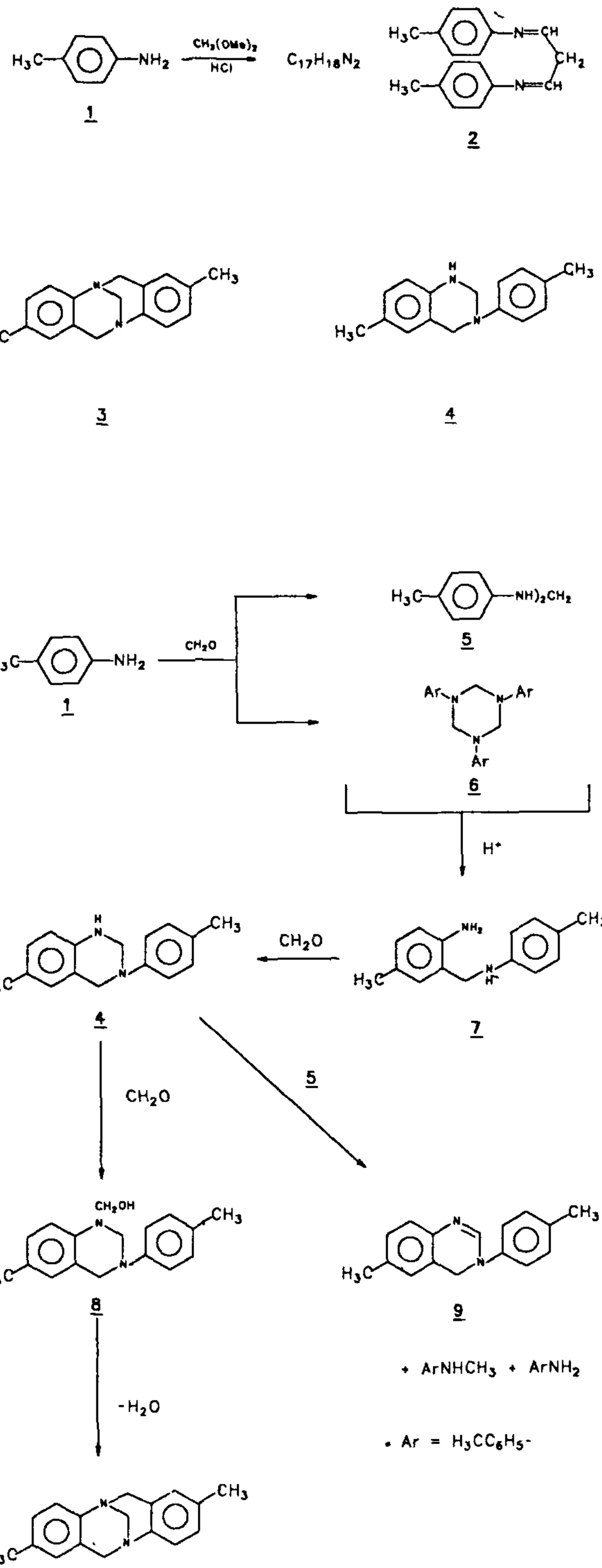
Synthesis and structure

In 1887, Julius Tröger[4], while reinvestigating the condensation reactions of formaldehyde with aromatic amines, found that *p*-toluidine **1** on condensation with methylal in the presence of hydrochloric acid gave a product of the molecular formula $C_{17}H_{18}N_2$. He proposed a structure of the type **2**. However, the structure of this compound remained controversial for decades. The correct connectivity was established by Spielman[5] only in 1935. After careful analysis of the reactivity of the product he proposed the structure **3**.

Spielman confirmed the structure by synthesizing it from the cyclic precursor **4** by condensing with formaldehyde and HCl. This particular compound **3** has become known as Tröger's base after the name of the discoverer of this reaction. Later, the reaction condition has been modified by various workers over a century[6–8].

Mechanism of formation

The mechanism of formation of Tröger's base was first investigated by Wagner and coworkers[9] and by Farrer[10]. The reaction goes via various intermediates (see Scheme 1). Intermediates **5** and **6** form acyclic intermediate **7** in the presence of an acid, which on con-

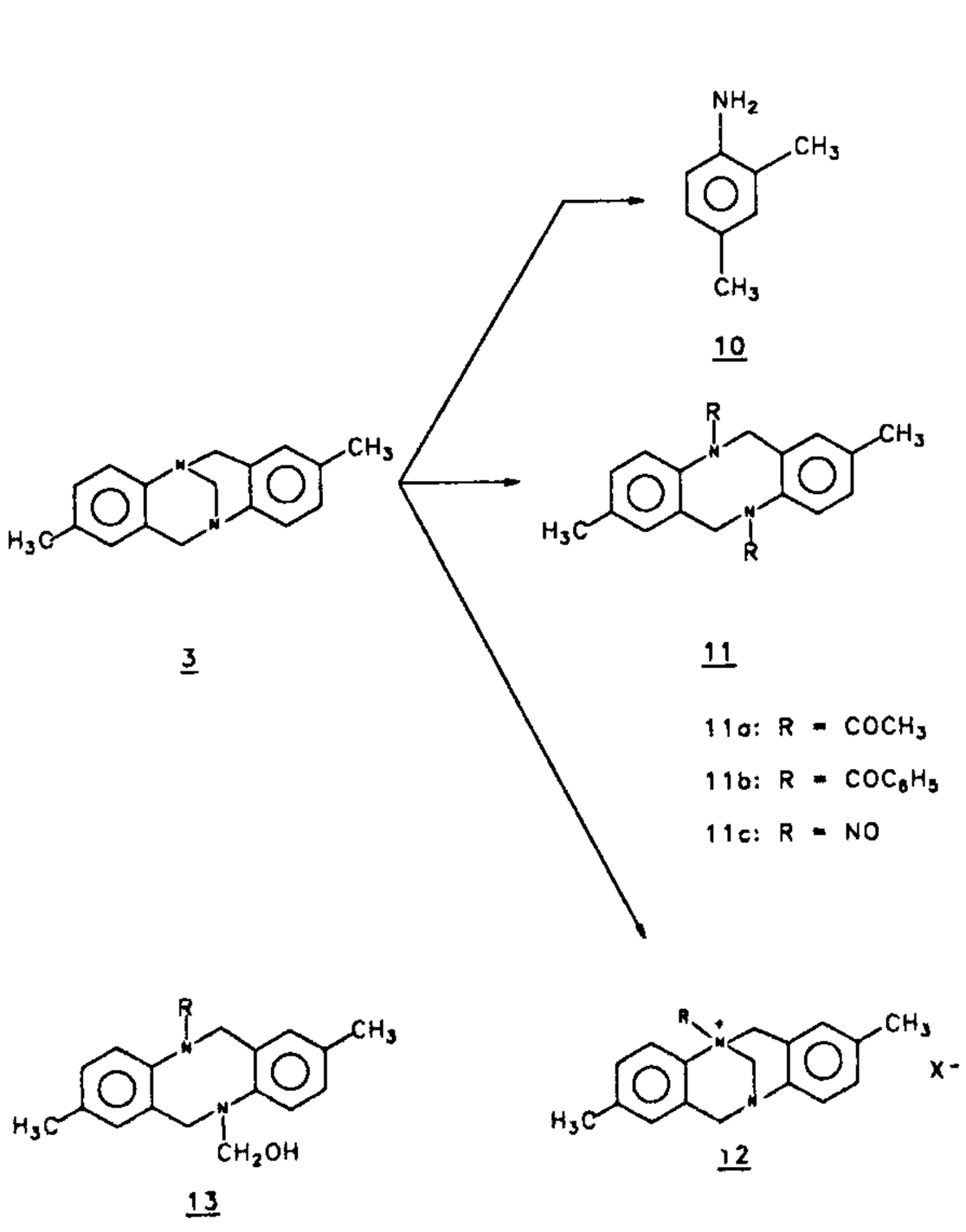


Scheme 1.

densation with formalin gives **8** via the intermediate **4**. Compound **9** is formed as a by-product by dehydrogenation of **4** and this becomes the major product in the case of electron- withdrawing *p*-substituents (e.g. halide instead of Me). This might be because of the reduction of the nucleophilic reactivity of the imino nitrogen[9–11] and hence dehydrogenation of **4** to the dihydroquinazoline **9** becomes the principal reaction. Tröger's base **3** is formed by the elimination of water from **8**.

Reactions of Tröger's base

Even though the name implies that the compound **3** is basic (indeed, it is a tertiary base), this has not found any application as a base in chemical transformations! The pK_a of the monoprotonated salt has been determined to be 3.2 in 50% aqueous alcohol[12]. The reactions of Tröger's base have been thoroughly investigated by Spielman[5] during his structural studies. It does not react with sodium and boiling ethanol or with Sn/HCl. It is not oxidized by mercuric oxide in ether. Degradation with HI/red-P at 200°C gives 4-amino-1,3-xylene (**10**) as the single isolable product. Initial refluxing with HI followed by reduction with Sn/HCl gives a better yield of the reduced product. Reaction with acetic anhydride gives diacetyl derivative **11a** with the loss of one carbon atom in the form of formaldehyde (Scheme 2). Benzoylation with benzoyl chloride gives the corresponding dibenzoylated derivative **11b** with a similar loss of CH_2O. A solution of the hydrochloride salt in dilute hydrochloric acid gives the dinitroso derivative **11c** by reaction with sodium nitrite. Alkylation with common alkylating agents (e.g. iodomethane, dimethyl sulphate, allyl halides, benzyl halides, etc.) gives the mono-N-alkylated product **12** (refs. 13, 14). Interestingly, no bis-quaternized product is formed even with the use of an excess of the alkylating agent. Salt **12** opens up in alkaline media to give **13**.



Scheme 2.

Identification of the first N-containing chiral centre to be resolved: Resolution and acidic equilibria

The substituents at a sp^3-hybridized trivalent N-atom do not lie in the same plane. But in spite of numerous efforts, the enantiomers of an asymmetrically substituted N-containing compound could not be resolved. This was due to the rapid interconversion of the enantiomers at room temperature. It was Prelog and Wieland[15] who thought that the inversion through N would be made difficult or impossible under certain circumstances, e.g. by imposing ring strain to the inversion process. They thought that Tröger's base, having two asymmetrically substituted nitrogen atoms at the branching points of the tetracyclic structure, could exist in two different spatial forms having mirror image relationships (see Figure 1). The vibrations of the N-atoms through the plane of the substituents would be hindered for steric reasons. One of the rational approaches for the resolution was diastereomeric salt formation with chiral acids, e.g., 10-camphorsulphonic acid. But the partially resolved salts were found to racemize in acidic media. Thus, attempts made by Prelog and Wieland to separate the enantiomers by diastereomeric salt formation were unsuccessful. The first success came only by chromtographic technique using chiral d-lactose column in 1944 (ref. 15). Thus, Tröger's base appears to be the first example of an amine to be resolved, where the chirality is solely due to stereogenic N-atom(s) with very high inversion barrier around it. The optically pure isomer was found to be stable at room temperature and could be sublimed without any racemization.

Racemization of Tröger's base, however, takes place in dilute acid solution. It was postulated by Prelog and

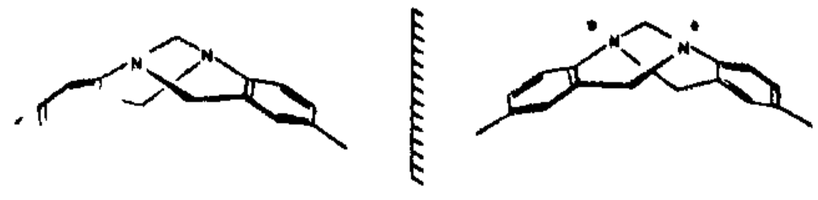


Figure 1.

Wieland that racemization proceeds through the intermediacy of the iminium ion **14** (see Figure 2). From the crude racemization data[15] the $\Delta G^{\#}$ of racemization was estimated to be in the range of 18.9–22.6 kcal/mol (ref. 16). This inversion barrier falls in the range of the inversion barrier of 5,11-diacetyl-5,6,11,12-tetrahydro-2,8-dimethyldibenzo-[b,f][1,5]diazocine **15** (ref. 17) which is a reasonable model for the iminium species **14**, and hence supports the above postulate.

Recently, Greenberg *et al.*[6] have investigated the mechanism of acidic equilibria by spectroscopic methods[16]. They could not detect the presence of the iminium species **14** and found evidence for the monoprotonated 'closed' structure **16** in the conditions used by Prelog and Wieland. They proposed that **14** might be an intermediate present in undetectable amounts. Their investigation also implied that racemization would be more facile in dilute acid rather than in concentrated acid.

Formation of inclusion compounds and molecular recognition

Tröger's base has a sharply folded geometry. The heterocyclic rings are not flat, but each of them with an annealated benzene ring approaches the configuration of 'trans-tetralin'[18]. The crystal structure of Tröger's base was solved only recently by Larson and Wilcox[19] though the structures of Tröger's base analogues were known[13]. Sucholeiki *et al.*[6] had reported the structures of a number of Tröger's base analogues. From these studies it is obvious that the planes of the two phenyl rings are oriented at approximately right angle (see Figure 3). Tröger's base, with its C_2-symmetry, rigidity and sharply folded geometry forming a roof-like appearance seems favourable for inclusion complex formation. Its 'V'-shape and conformationally restricted nature also makes it useful as an armature for the construction of biomimetic molecular systems.

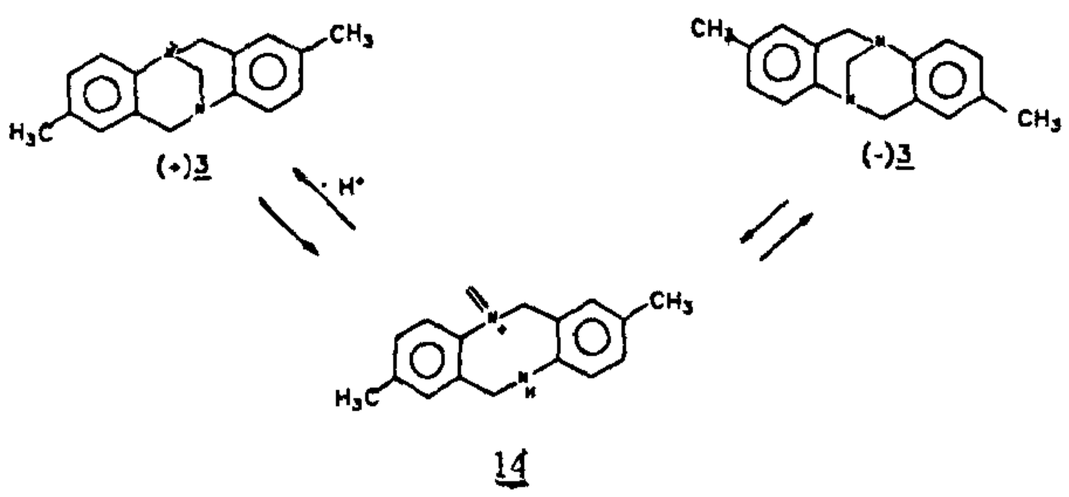


Figure 2.

Inclusion compounds

Even though Tröger's base (and its analogues) with rigid, concave, C_2-symmetric structure is expected to form inclusion compounds[20], there are not many reports in the literature for free Tröger's base analogues forming inclusion compounds[21]. Interestingly enough, the mono-N-alkylated salts of Tröger's base and its analogues form inclusion compounds. Häring[14], in the course of his studies with various N-alkylated derivatives of Tröger's base, encountered difficulties in the purification of N-methyl Tröger's base salt. Weber *et al.*[13] showed that this difficulty in purification was due to the formation of clathrate compounds. They synthesized a number of N-alkylated salts (**12a–12c** etc, Figure 4) and showed that all the quaternary Tröger's base salts studied had inclusion properties. These salts have remarkable preference for aromatic guest solvents. They also showed that alkylation did not alter the basic skeleton much except that the angle at the bridging methylene changed from 112° to 109°. The crystal packing diagram of **12b** $(dioxane)_{0.5}$ is shown in Figure 5, which clearly reflects the clathrate type of inclusion[22]. The layer of host molecules is composed of pairs of quaternary Tröger's base units, forming a void for the inclusion of the guest. Dioxane molecules are embedded into quasi-channels of the host matrix. The guest molecules are free of any significant interaction, except dispersion forces, with the host environment.

Bond and Scott[23] recently reported clathrate formation of a few other alkylated Tröger's base and its derivatives (**12a**, **12d–12f**, etc.) and showed that the stoichiometry of inclusion varies with increasing chain length. The stoichiometry of inclusion with respect to *p*-xylene is shown in Table 1. Increment of the chain length by one methylene unit has a larger effect on the inclusion capacity.

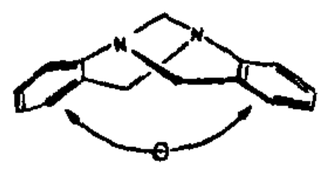
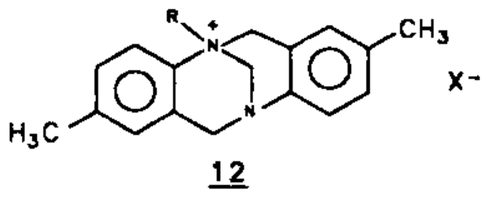


Figure 3.



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12a· R = Me, X = $MeSO_4^-$

12b· R = Me; X = I^-

12c: R = $-CH_2-CH=CH2$; X = Br^-

12d· R = CH_2CH_3; X = I^-

12e: R = $CH_2CH_2CH_3$; X = I^-

12f· R = $(CH_2)_4$ (bridging butyl group); X = I

Fig. 4

Figure 4.

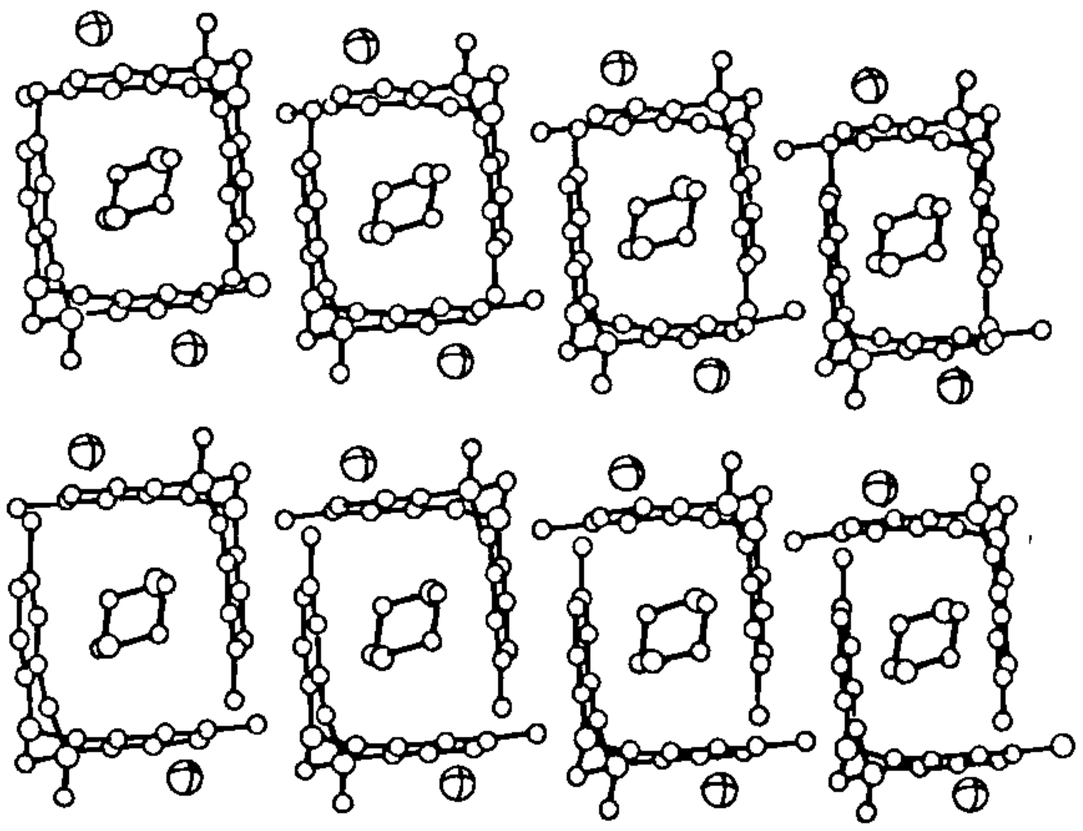


Figure 5. Perspective view of the molecular packing in **12b** $(dioxane)_{0.5}$ clathrate. H atoms are not shown. Dioxane molecules are embedded in the void formed by the pairs of quaternary Tröger's base units. Reproduced with permission of the Royal Society of Chemistry.

Table 1. Stoichiometry of inclusion of *p*-xylene by the *N*-alkylated Tröger's base **12b**

R	H : G
Me–	1 : 0.5
CH_3CH_2–	1 : 1
$CH_3(CH_2)_2$–	1 · 1 25
$-(CH_2)_4$–	1 : 0 75

H stands for host and G for guest for the inclusion complexs.

The studies of these groups have established the potentiality of the monoalkylated Tröger's base analogues to be a new class of clathrate hosts. Tröger's base and its derivatives being chiral, enantioselective guest inclusion[24] by chiral N-alkylated derivatives is yet to be explored.

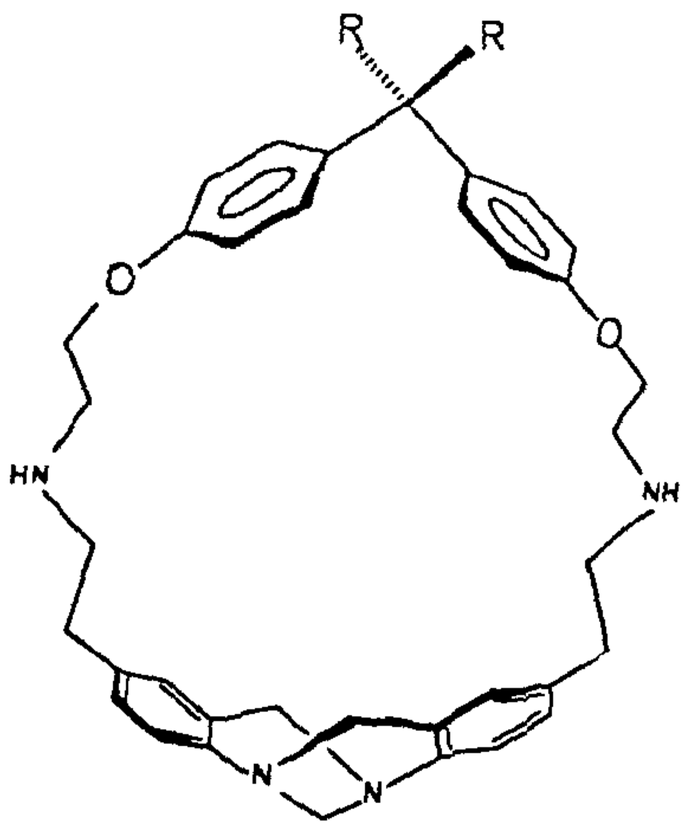
Molecular recognition

In the recent years, mimicry of biological processes using simpler molecules has been a major area of research[25]. The gradual drift of organic chemists into more bio-oriented research has given rise to sophisticated model systems to study the recognition process of substrates by enzymes, antigens by antibodies or messengers by their receptors. To design enzyme mimics, initial attempts were made towards the synthesis of molecular receptors analogous to the substrate-binding site of an enzyme. The design of receptors capable of binding guest molecules in a predictable way and in a particular environment is a challenge. First of all, the designed receptor molecule should be easily synthesizable and secondly the interacting groups in the host should be preorganized[26]. The first evidence that enantiopure Tröger's base can act as a chiral solvating agent was shown by Wilen *et al.* Wilcox *et al.* have shown that Tröger's base with its unique structural features (see above) could be used for the construction of novel molecular receptors. The achievement made towards the use of this particular 'V'-shaped structural unit is described in the following three sections.

Chiral solvating agent. Wilen *et al.*[27] showed that enantiopure (+)-3 can act as a chiral solvating agent. When a $CDCl_3$ solution of racemic aromatic alcohols of the type ϕ-CR′R″OH was treated with (+)-3 then at least one set of peaks showed anisochrony. This was because enantiopure **3** generated intrinsically nonidentical chemical shifts in some of the sensor nuclei of the diastereomeric complexes that were formed between **3** and the racemic alcohols.

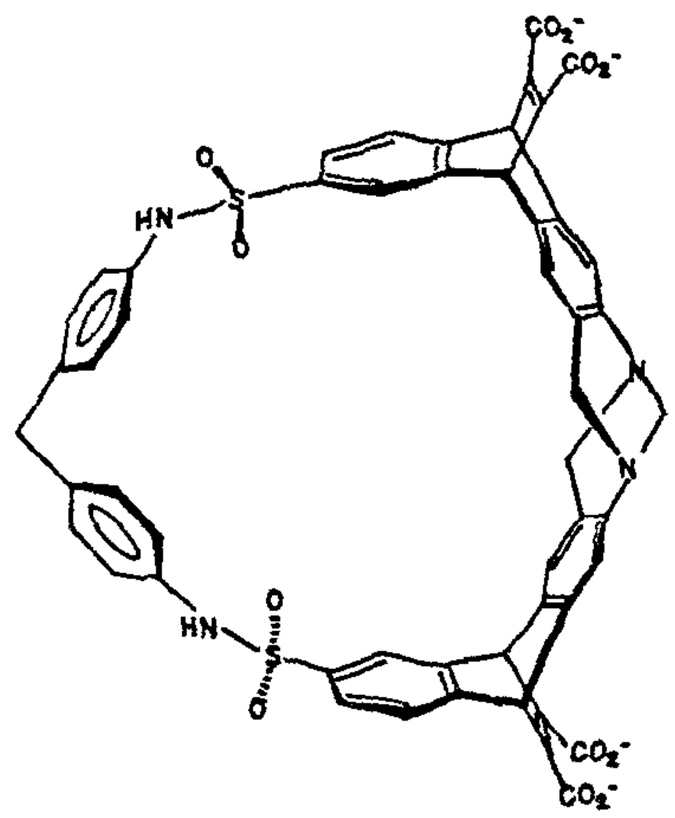
Water-soluble cyclophanes. The Tröger's base unit has been incorporated into the macrocyclic structures (see Figure 6 *a,b*). The rigidity of the dibenzodiazocine structural unit imparts rigidity to the cavity defined by the macrocycles. Hosts **17a** and **17b** are soluble in acidic solution and form a lipophilic cavity. Complexation studies at pD 1.9± 0.1 in D_2O showed that ΔG of association of these hosts for aromatic guests was in the range of 2.1–3.4 kcal/mol (ref. 28).

For diastereoselective complexation a water-soluble chiral cyclophane **18** has been designed[29]. The tetracarboxylate host, with a hydrophobic pocket inside the



17a: R = H

17b: R = CH_3



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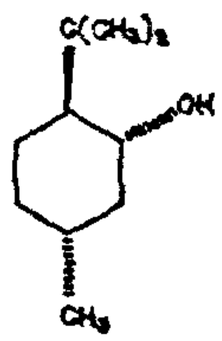

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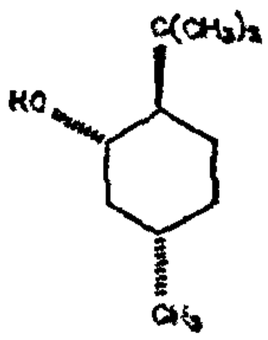

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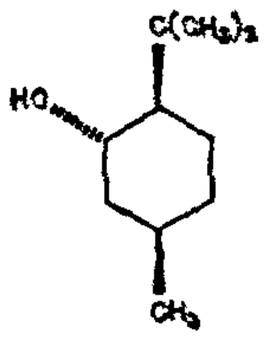

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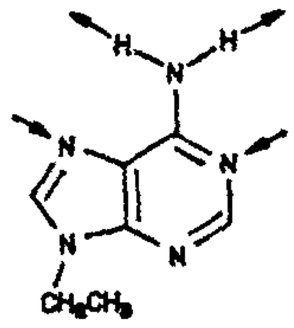
Figure 6.

cavity, is soluble in alkaline solution. Complexation constant measurements in an alkaline buffer solution (pD 9.0) showed association constants of $2500 \pm 200\ M^{-1}$ for (–)-menthol **19** and $2000 \pm 200\ M^{-1}$ for (+)-menthol **20**. The observed differences in binding for enantiomeric guests, though small, are unprecedented for small, alicyclic, sparingly soluble guests in aqueous media. This is indicative of intimate receptor–substrate contacts. Isomenthol **21**, with an axial methyl group, was found to complex with comparatively less affinity ($1000 \pm 200\ M^{-1}$) for steric reasons.

Hydrogen bonding receptor. Adenine derivatives (e.g. **22**) and cyclic derivatives such as biotin **23** possess two hydrogen bond donor–acceptor pairs (Figure 7). A host that would be able to interact *simultaneously* with these donor–acceptor pairs is expected to bind these guests very strongly. Wilcox[30] and his coworkers have designed a receptor **24** based on the Tröger's base moiety. The two carboxyl groups intersect at an angle of ca. 120°. The functional groups are well arranged to bind 9-alkyl adenine and several cyclic urea derivatives by multiple hydrogen bonding. Binding-constant measurements in deuteriochloroform by ^{1}H-NMR titration showed that the host **24** binds with both 9-ethyladenine ($K_a = 4.5 \pm 1.7 \times 10^4\ M^{-1}$ and biotin methyl ester ($K_a = 1.7 \pm 0.3 \times 10^4\ M^{-1}$) and several other guest molecules by multiple hydrogen bonding. The two carboxylic acid groups were preorganized for the complexation.

Thus, based on the unique molecular architecture of the Tröger's base unit, host molecules have been designed to complex with simpler aliphatic and aromatic molecules, including nucleotide bases. This success in receptor design would help in extending further the idea for the development of artificial enzymes and to develop new supramolecular architectures.



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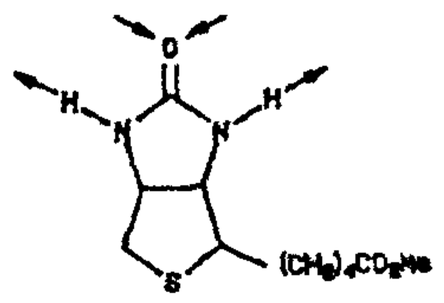

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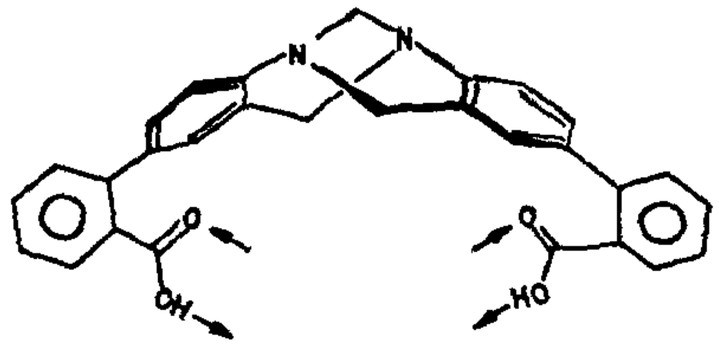

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Figure 7.

First asymmetric synthesis of the Tröger's base unit

Though resolution of racemic Tröger's base has been achieved by chiral column chromatography in 1944 and recently by diastereomeric salt formation using strongly acidic resolving agent (formally by a second-order asymmetric transformation)[27], a general method for the asymmetric synthesis of Tröger's base analogues was unknown[31]. Two *p*-substituted aniline units on cyclization gives the Tröger's base skeleton. We thought that if the aniline units are attached to a suitable chiral template then during the coupling process there might be some chiral induction. We chose deoxycholic acid (**25**), a naturally occurring, chiral, bile acid having two hydroxyl groups at the **3** and **12** positions with different reactivities. Computer modelling studies suggested the feasibility of the coupling (see Figure 8). Our strategy is schematically shown in Figure 9.

Though attempted cyclization on the compound **26a** was unsuccessful in the conventional reaction condition (aq. formalin, HCl, alc.), success was achieved in a newer reaction condition ($CH_2(OMe)_2$, CH_3SO_3H, reflux) affording a mixture of diastereomers **27a** and **28a** (Scheme 3) in 40% diastereomeric excess (de). Though the selectivity was modest, we could demonstrate that our design was working. The Tröger's base part could

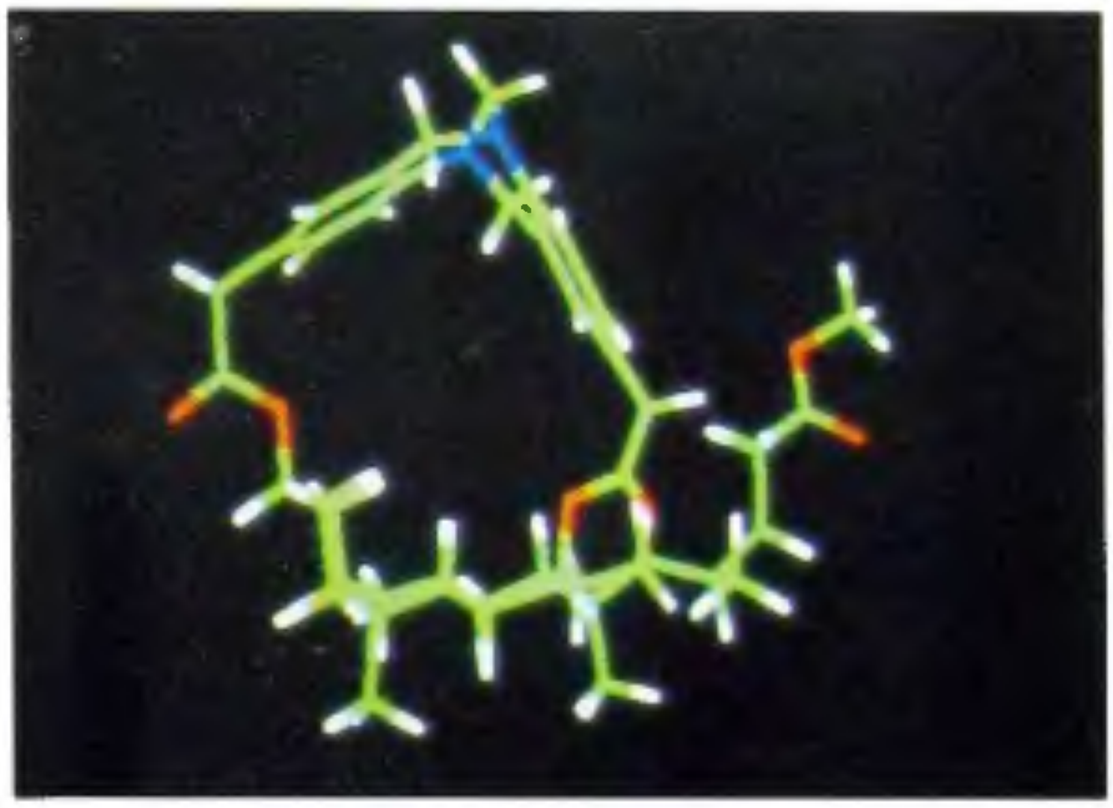
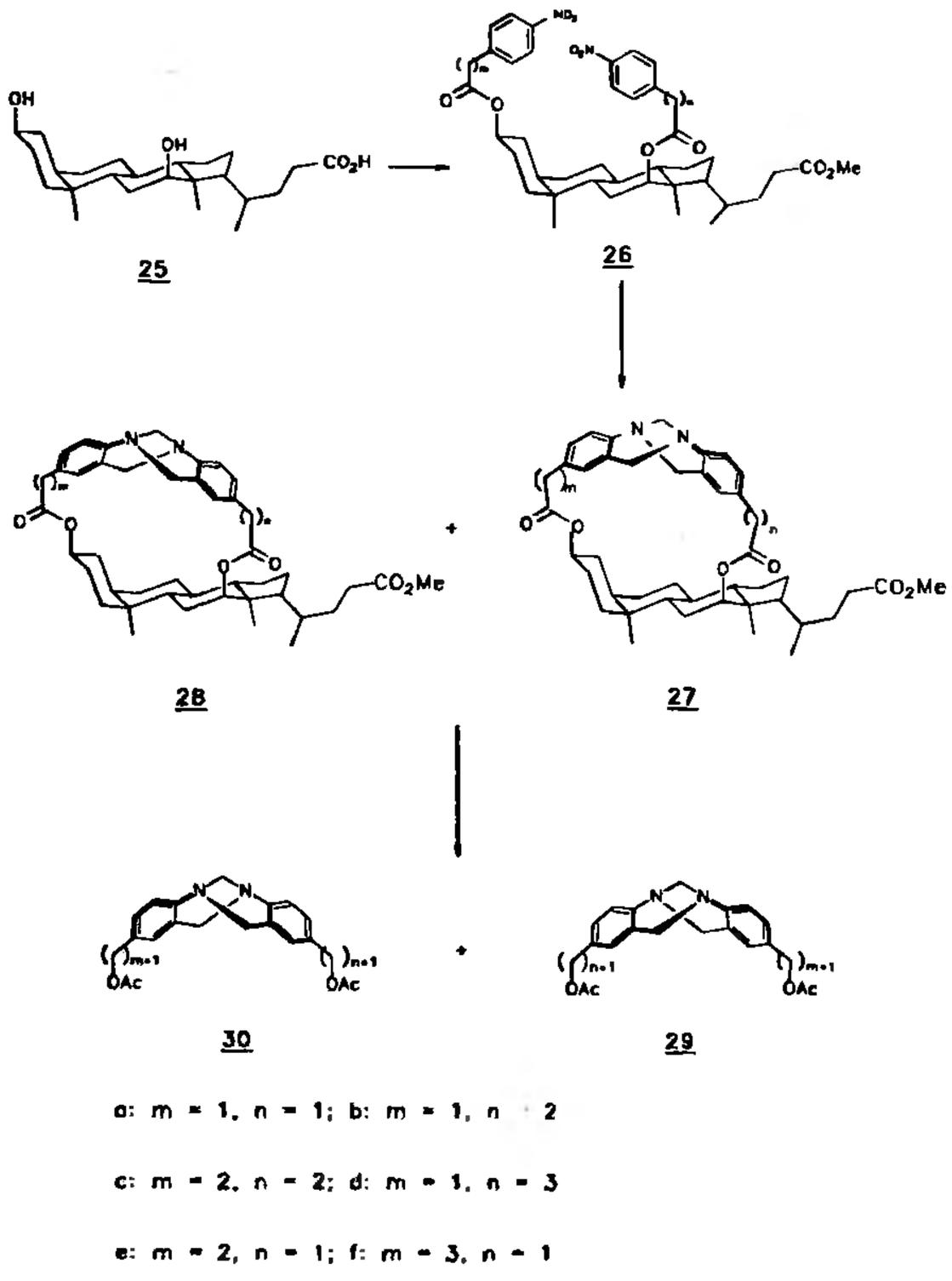


Figure 8. DTMM modelled structure for the Tröger's base unit (S,S at N) on the steroid template.



Scheme 3.

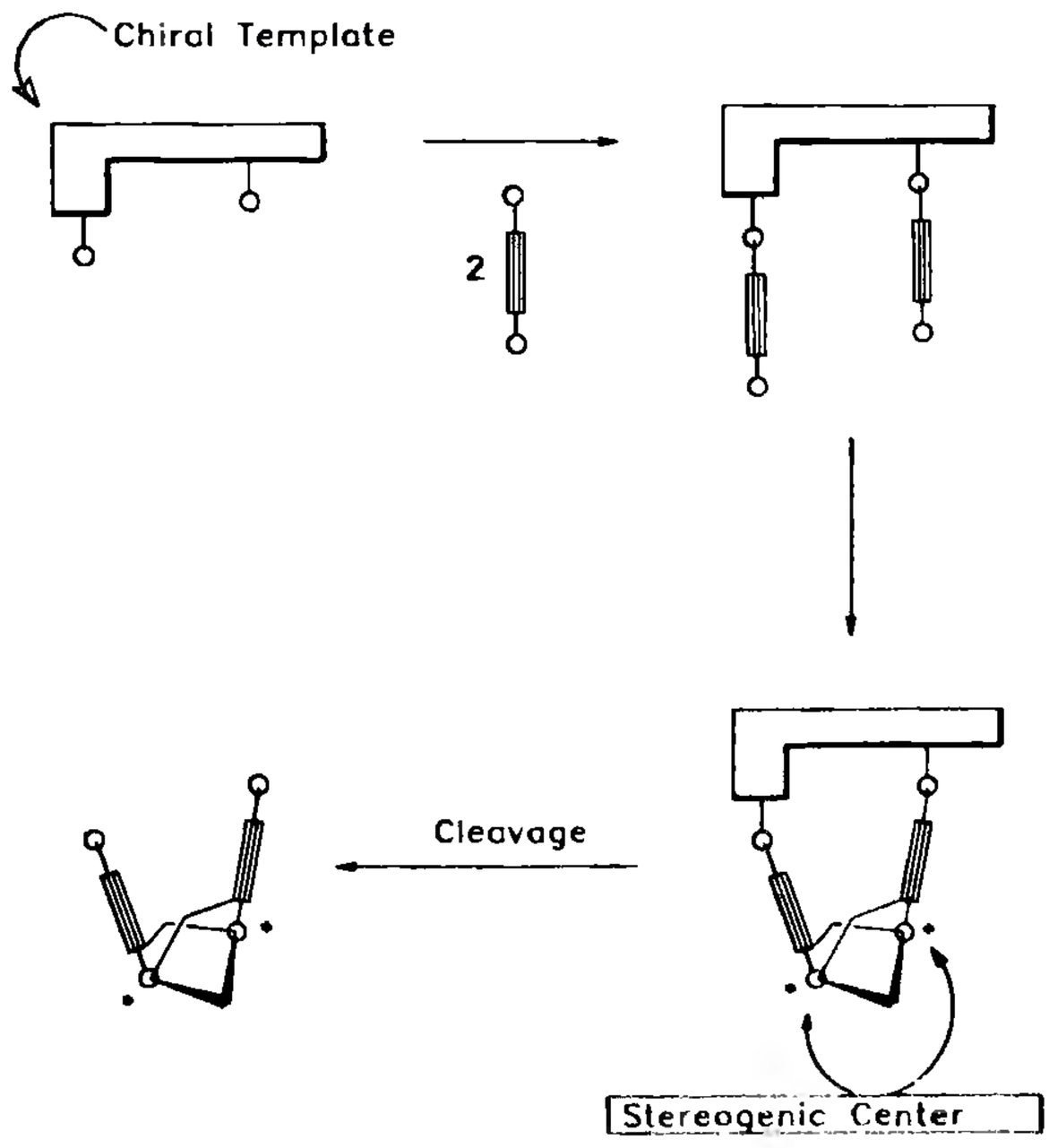


Figure 9. Schematic representation of coupling on a template

be reductively cleaved from the template affording the Troger's base analogues **29a** and **30a** (ref. 8).

One interesting observation was that the *minor diastereomer could be crystallized out* in pure form, thus enriching the major isomer in the mother liquor. The absolute configuration, determined by spectroscopic methods for the pure isomer (**R, R** at **N**) obtained by reductive cleavage of the pure diastereomer **28a**, was later on shown to be correct by X-ray crystallographic studies.

Storage of optical enrichment

Another very interesting observation was that, diastereomers did not equilibrate in the acidic reaction condition though the cleaved isomers did so. This proved that the selectivity obtained was under kinetic rather than thermodynamic control. Tröger's base is expected to be protonated in acidic reaction medium. Based on the studies of Prelog and Wieland[15], and Greenberg *et al.*[16] we can postulate that even though the monoprotonated species **31** obtained from **27a** can open up to give the iminium species **32**, equilibration with **28a** in the reaction condition is not feasible because of the steric constrains of the template unit (see Figure 10). This observation is also interesting from the fact that optical enrichment would remain unaltered in the protic nonnucleophilic environment when the Tröger's base moiety is attached with the steroid template!

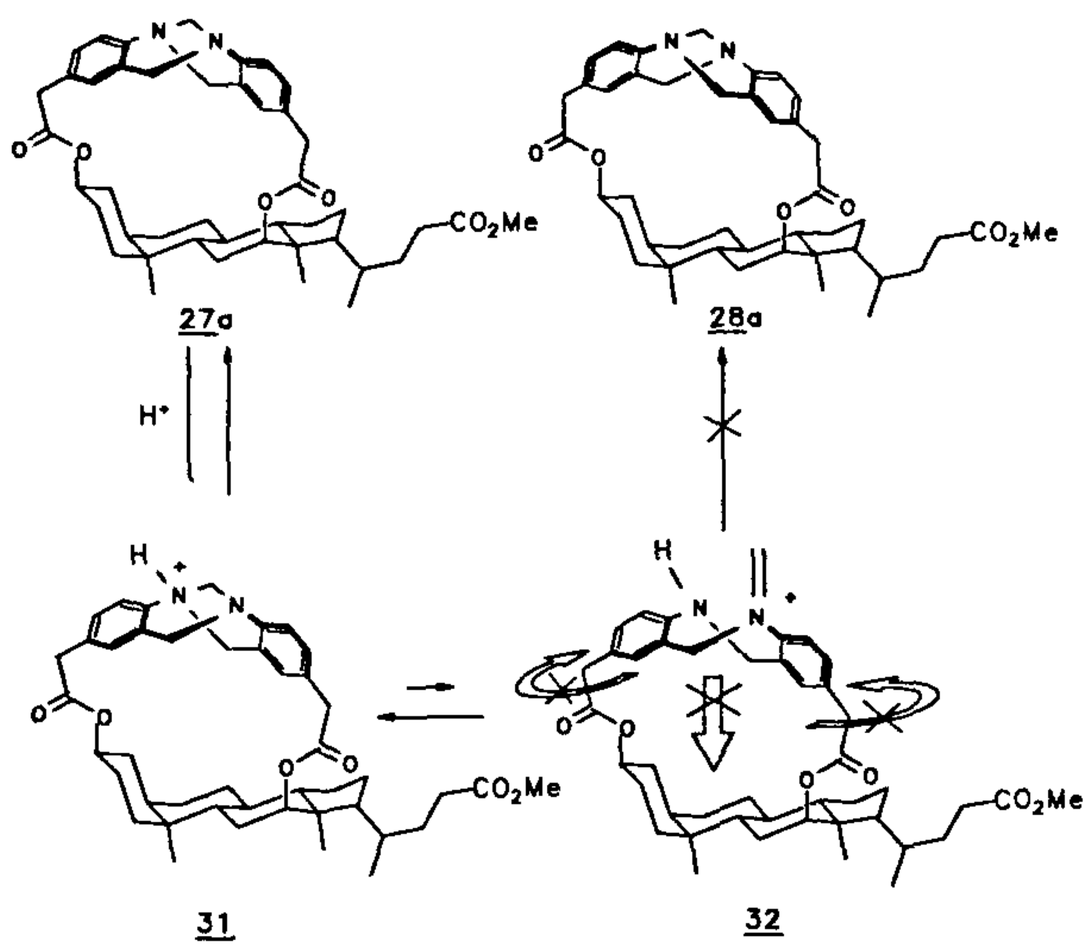


Figure 10.

Asymmetric synthesis of symmetrical/ unsymmetrical Tröger's base analogues

The **3** and **12** hydroxyl groups of the template deoxycholic acid have different reactivity (3 > 12)[32]. This opened up a possibility of synthesizing both symmetrical and unsymmetrical Tröger's base analogues **29b–f, 30b–f** (Scheme 3). As the two diastereomers have different orientations in space, the stereoselectivity is expected to vary with varying spacer lengths. Indeed, by systematic variation of the spacer lengths from the steroid template it has recently been shown that with a CH_2 spacer from the C-3 side and CH_2CH_2 spacer from the C-12 side, the unsymmetrical Tröger's base **29b/30b** could be obtained in high yield and stereoselectivity (75% yield and 70% de using yet another method of Tröger's base cyclization: hexamethylenetetramine, TFA/heat). As before, this also could be reductively cleaved from the template without any loss of optical enrichment (unpublished results from this laboratory).

Thus, asymmetric synthesis of Tröger's base using a chiral template is promising for the synthesis of symmetrical/unsymmetrical analogues. As the two diastereomers **27a/28a** have different spatial demands, the selectivity could be altered by creating a steric bulk from one side. Cholic acid having three suitably positioned hydroxyl groups offers an opportunity to study this behaviour (see Figure 11 for a schematic representation). Preliminary investigations indicate that with a pivaloate group at the C-7 position the selectivity could be changed (unpublished results from this laboratory).

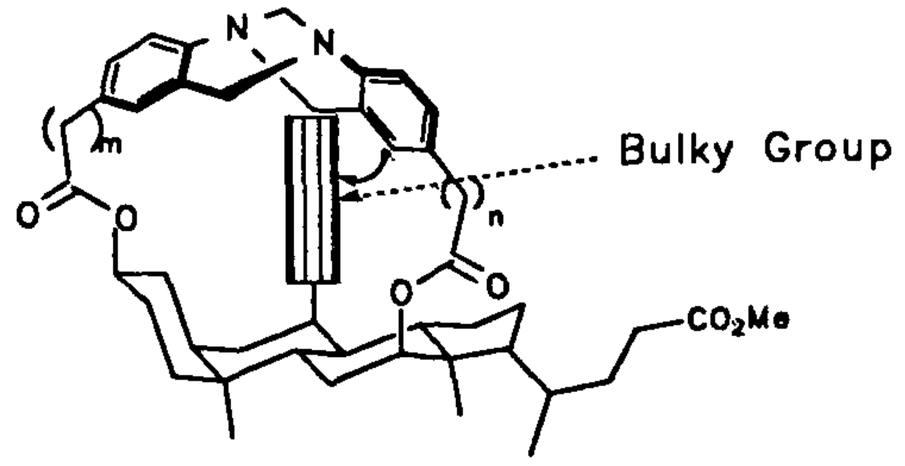
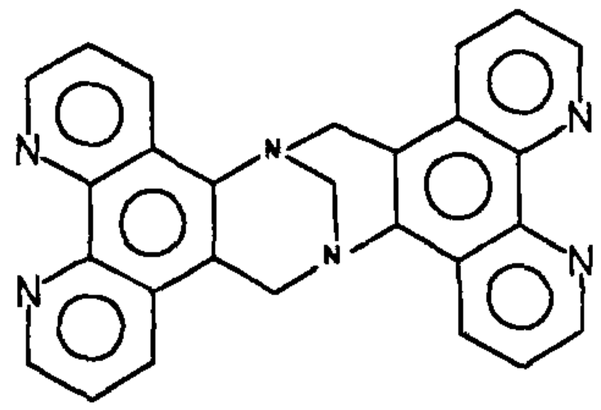


Figure 11.

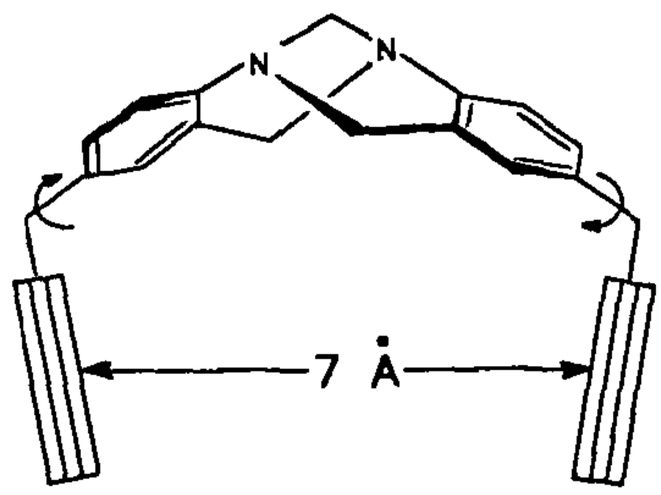
Future prospects

Though Tröger's base was known for over a century, the chemistry of it has flourished mostly during the last one decade. A recent preliminary report has shown that a phenanthroline-derived Tröger's base (**33**) could intercalate DNA[33]. Computer-aided design showed that the type of compound **34** would have a distance of separation between the two suspended aromatic units of about 7 Å in the close conformation. An aromatic guest could be easily incorporated in the host keeping a distance of separation of about 3.5 Å with the aromatic units (as found in DNA double helix)[34]. This seems promising

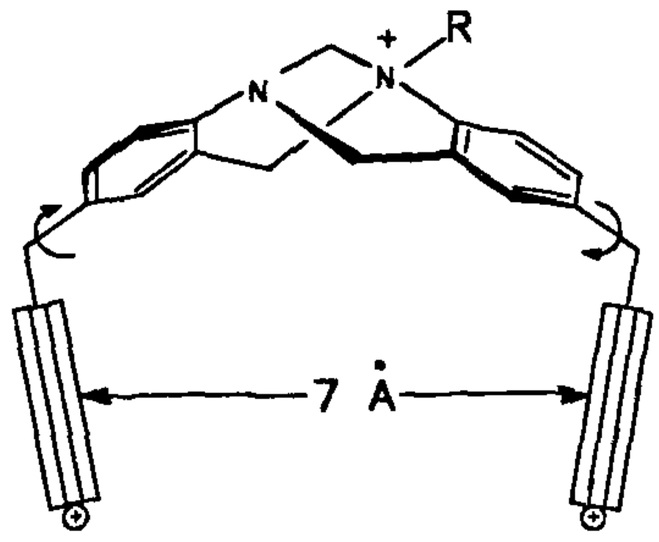
not only for the design of newer host molecules capable of binding aromatic guest molecules but also for potential



33



34



35

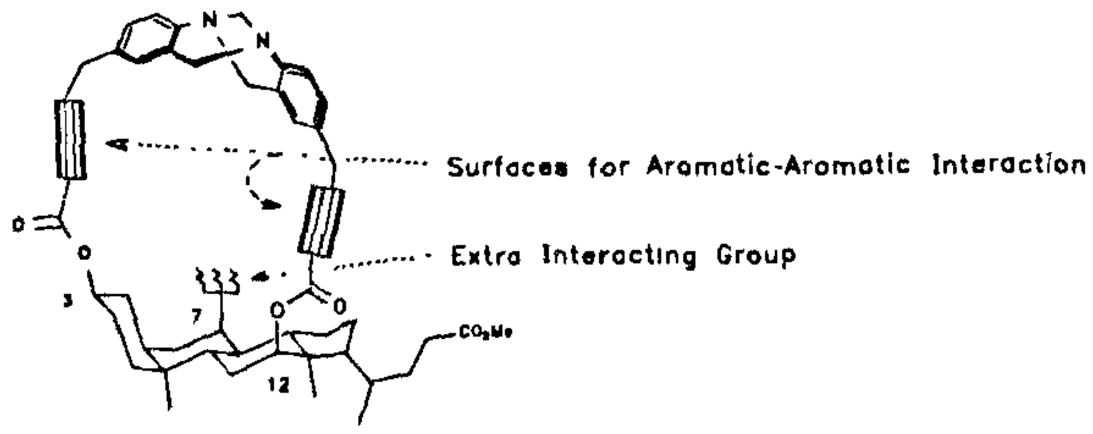


Figure 12.

ligands capable of intercalating with DNA.

Monoprotonated Tröger's base salt along with two suspended positively charged aromatic units of the type **35** is speculated to bind electron-rich aromatic guest molecules because of solvophobic effect and electrostatic interaction.

Tröger's base unit, when attached to the steroid template with appropriate spacers, would have multiple binding sites (see Figure 12). The chiral host could be speculated to have enantiodifferentiation during complexation. Studies along these lines are in progress in this laboratory.

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Lathyrus sativus: A future pulse crop free of neurotoxin

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***Lathyrus sativus* is popular among farmers due to its ease of cultivation and high climatic adaptability. However, full potential of this crop has not been realized due to the presence of a toxin, β-*N*-oxalyl-L-α,β-diaminopropionic acid (ODAP) which causes a paralytic disorder known as neurolathyrism in humans. Conventional breeding and selection methods have failed to produce varieties free of the neurotoxin. Research utilizing recombinant DNA technology and tissue culture has been initiated in the recent years to produce *Lathyrus sativus* plants free of neurotoxin. The progress in this area of research includes isolation and characterization of ODAP-degrading gene from pure cultures of bacteria. It offers the scope for introducing this gene into *L. sativus* by *Agrobacterium*-mediated transformation. As part of the second approach, oxalyl-CoA (coenzyme A) synthetase, which is a key enzyme in the biosynthesis of ODAP, has been purified and monoclonal antibodies raised against it. This can be used to construct antisense gene of this enzyme for introducing into *L. sativus*. Somaclones having very low toxin contents have also been developed. All these results show the potential of producing neurotoxin-free *L. sativus* plants in the near future.**

LATHYRUS SATIVUS L., commonly called the chickling vetch, is an exceptionally hardy, protein-rich (28–40%) legume crop cultivated in many parts of the world. It is popular among the farmers due to its ease of cultivation and high climatic adaptability that permits growth even under such extreme conditions as drought or water logging. All these factors make *L. sativus* a potentially valuable food crop for arid regions ot the world. In India, it occupies nearly 5,000,000 acres under cultivation, which is 4% of the total area under pulse crops and constitutes 3% of the total pulse production. Madhya Pradesh produces more than 50% of the total produce in the country[1]. Besides, it is also cultivated in eastern Uttar Pradesh, Maharashtra, Bihar, West Bengal and Assam. However, the full potential of *L. sativus* has not been realized since prolonged or excessive consumption of this pulse leads to a paralytic disorder known as neurolathyrism or human lathyrism[2], caused by a neurotoxin. The disease has been documented in a number of countries in Europe, Africa and Asia. Human lathyrism continues to be a public health problem in parts of Bangladesh, China, Ethiopia and India.

The present article reviews the biochemical nature and the mode of action of *Lathyrus* neurotoxin, its occurrence and synthesis in different plant parts and the methods for removal of the toxin. Finally, the use of recombinant DNA technology and tissue culture methods in producing the neurotoxin-free *L. sativus* plants has been highlighted.