structures produced must be checked *a posteriori*. Despite the similarity of the concentric coding of the primitives, as in DARC[7] and the identity, at the structural level, of the principle of progressive assembly of the primitives with that of EPIOS, our work was not cited in the article published.[6]

The three principle "innovations" proposed in SpecSolv are

- −assembly of the substructures using an innovative approach that takes advantage of overlapping substructure information,
- −redundancy in structural description is the key to the new assembly process,
- −this instant validation of intermediate structures is one main difference from other generation programs, which typically validate structures only after generation of an entire molecule.

This approach based on the concept of overlap is termed "innovative" when this concept is in fact at the origin of the EPIOS method and even its name. The fundamental principles of the EPIOS system are not cited. Nonetheless, it appears from the presentation of SpecSolv that the assembly operation corresponds to a repetition of elementary overlaps as defined in EPIOS.

Although one of the authors of the present article (W. Fachinger) previously contributed to the ACCESS system, there is no explicit reference to this system, and SpecSolv is presented as original and without analogy to EPIOS or any relationship to ACCESS. It would, however, have been desirable to do a comparative analysis of this system, also presented as an innovation, with SpecSolv, in order to give readers an idea of the disadvantages of the predecessor and the real merits of the second.

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SpecSolv−An Innovation at Work

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In response to our recent article,[1] Carabédian discusses above the innovative character of our structure elucidation system SpecSolv. This is a response to this discussion.

SpecSolv is a self-learning system based exclusively on ^{13}C-NMR chemical shift, intensity, and multiplicity information. Unlike earlier structure generation programs,[2,3] including the DARC/EPIOS[4] approach. SpecSolv requires neither the molecular formula of the unknown or additional input from other spectroscopic techniques. This is why we regard SpecSolv as a "true innovation" in the field of structure elucidation.

Automatic elucidation of chemical structures by SpecSolv entails four steps:

1. Acquisition of experimental ^{13}C- and DEPT-NMR spectra and extraction of chemical shift, intensity, and multiplicity information.
2. Subspectra search in a dedicated subspectra-substructure correlation (SSC) library and generation of a hit list.
3. Assembly of the retrieved substructures using a new approach that employs a flexible overlap (0−3 atomic spheres) of substructure information.
4. Rigorous validation steps for the intermediate substructures and the final result.

In their EPIOS system, Dubois et al.[5] also utilize overlapping substructure information, as had been done previously by others.[6] Overlapping of substructures during assembly is a fundamental procedure used by many algorithms, but the flexible overlap of substructures over 0−3 atomic spheres[7] is unique to SpecSolv. This feature even allows assembly and validation of substructures containing up to five adjacent heteroatoms as well as handling of systems in the database that lack a 1-sphere SSC (Figure 1 (parts e and f)). Figure 1 summarizes the conceivable types of overlaps used by SpecSolv.

Other systems which use overlapping information have been developed. These include GENOA,[6] CASE,[8,9] ACCESS,[10] and EPIOS.[4,5] Some of the reasons for their inability to elucidate more complex organic structures were (1) the small size of the substructures in their knowledge bases, which lead to combinatorial explosions with larger structures,

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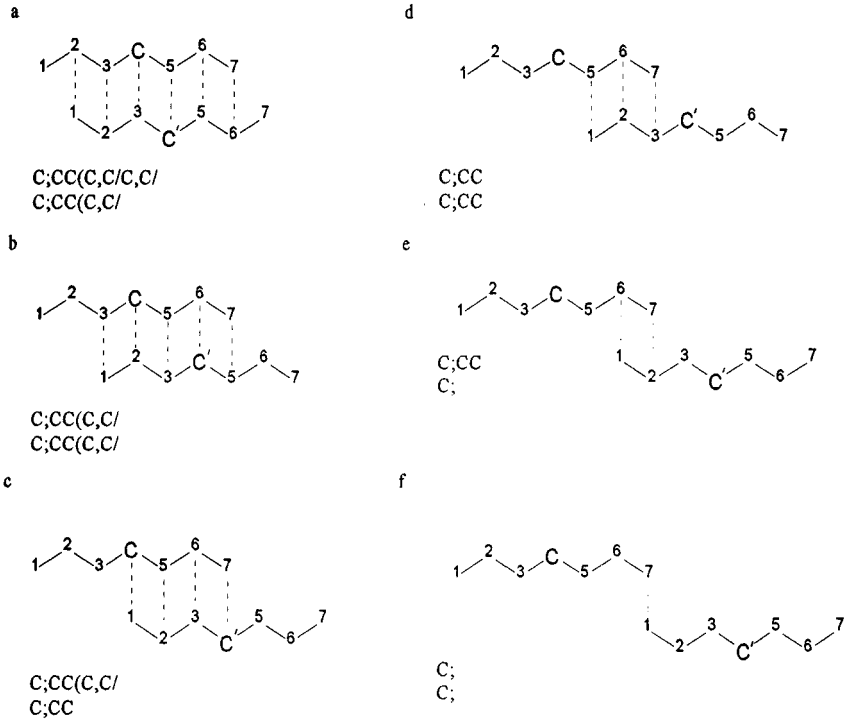

Figure 1. Classes of substructure overlaps in SpecSolv.

(2) the small overlap between substructures, typically only 1 or $1^1/_2$ spheres, as is used by EPIOS with its $ELCO_b$ coding,[4,5] and (3) the most critical deficiency, the lack of stringent verification tools for intermediate and final substructures. Likewise small structures and small overlaps lead to severe permutational problems, especially when one is confronted with the spectra of structures that contain several acyclic nitrogen atoms.[1] Further, most of these earlier systems neglected intensity information[4] which allows automated identification of symmetrical substructures or coincidentally identical chemical shifts.

In our original paper,[1] while referencing prior efforts[2,3] to automate the structure elucidation process including the EPIOS approach, we omitted explicit references to the work of Dubois et al., and we regret this omission. This nothwithstanding, we believe that SpecSolv is an innovative tool for the spectroscopist. It is the only system published to date which allows structure elucidation based only upon ^{13}C-NMR and which does not require knowledge of a molecular formula. It permits unsupervised operation and appears to be the fastest system currently available. It allows automated operation, accepting data at the spectrometer level, and, with no intervention, developing a final structure proposal which can be made available to the spectroscopist or a client of an analytical laboratory. SpecSolv contains an AI assembly algorithm as well as a self-learning database. With respect to the types of substructural overlap shown in Figure 1, it can be seen that the system is capable of generating news SSCs—those associated with the atoms between the two central atoms (C and C′) of the two overlapped structures. New SSCs can be extracted from the assigned experimental data and stored in the SpecSolv knowledge base, which is thus a self-learning database.

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