Introduction

The information provided from $^{31}$P NMR Spectra can be extremely valuable when trying to elucidate or verify phosphorus containing chemical entities. While understanding the scope may not present the same robust challenges as the interpretation of $^1$H nuclei, the diversity of environments that can surround the $^{31}$P nucleus is enormous. Therefore, a comprehensive knowledge base of $^{31}$P NMR that can be searched could serve as a valuable tool. With both time and quality of the essence for such searches of data, the most obvious approach is to compile an appropriate collection of data into an electronic database and enable the appropriate types of searches.

ACD/XNMR includes collections of such data for $^{15}$N, $^{19}$F, and $^{31}$P. For this discussion, we will focus on the $^{31}$P data. The ACD/XNMR version 8 content database contains over 23,000 chemical structures (over 33,000 chemical shifts). These data are culled from the literature and checked for quality according to a number of stringent criteria prior to adding to the database. The chemical shift reference is homogenized during the process such that all shifts are relative to one reference. The result of five years of effort to construct this database is that it presently represents the largest electronic collection of data available today for $^{31}$P. A record will include the chemical structure, the original literature reference, the chemical shift(s), and, where available, associated coupling constants. These data can be searched by structure, substructure, similarity of structure, chemical shift and chemical shift range, coupling constant and coupling constant range, formula, and many other optional data fields. Add to this the ability to search through the databases by formula and mass (whether nominal, average, or exact mass) and a phosphorus chemist immediately has access to a warehouse of valuable information. This Application Note will highlight the usefulness of structure verification of phosphorus containing compounds using the ACD/Labs $^{31}$P database.

Structure Verification Using Content Databases

For the purpose of structure verification, the common approach is to review the literature for related species and use their chemical shifts and couplings as models to allow estimates of these properties for the new species.

Let’s take, for example, the following analytical data available for an unknown. EI-MS gives a mass of 268 a.m.u and $^{31}$P NMR gives -40 ppm. A search of the database gives 268 hits with a mass of 268 a.m.u. Searching the database for the chemical shift range -38 to -42 ppm (to allow for experimental differences in measuring the shift) gives two hits as shown on the following page.
In general, the knowledge of the basic chemistry would easily confirm the structure. Verifying whether either of these was correct would be easy using $^1$H NMR. In this case, the chemical structure was confirmed to be structure 1.

Another example of a search giving rise to an identified chemical structure could be based on multiple phosphorus resonances. In this case, two resonances are observed at 32.0 and -40.2 ppm. Performing a search of the database using shift ranges of 30-34 ppm and -38 to -42 ppm gives two hits once again as shown below.

Verification of whether it was actually one of these structures would of course be simple. Broadening the search to 25..34—45..-35 still only gives four structures to consider.

As an example of a substructure search, consider a particular molecule that contains a single phosphorus atom connected to a phenyl group. Based on prior information, it is known that a
single silicon atom is located within the molecule. Using a combination of a substructural search (using the fragment below) on a list pre-filtered for Si, produces 195 hits as shown in Figure 1.

![Substructural Search Fragment](image)

**Figure 1**: A tiled display of 15 of the 195 structures extracted from the database using a substructure search defined above. Notice that for ease of viewing, the Si atom is highlighted (red) and the P-Ph moiety is also highlighted (blue).

Consider a more challenging example where the unknown is not contained in the database but where directed searches can lead to useful information regarding potential chemical classes. $^{31}$P NMR gave a single chemical shift of -44 ppm. $^1$H NMR showed a series of resonances and it was easy to distinguish the presence of a phenyl ring connected directly to a phosphorus atom and the presence of an ethyl group. A search of the DB was made using a range of -42 to -46 ppm which gave 260 hits. Using the substructural units shown below as inputs, 12 hits resulted as shown in Figure 2. These could obviously be of value for suggesting potential chemical classes to allow structure verification.
Figure 2: Database hits resulting from a search using two substructure units. Notice that the two substructure search units are highlighted (blue and red).

As a facile method to access a knowledge base of information regarding $^{31}$P NMR spectral properties, an electronic database provides an ideal solution. The ACD/XNMR database is updated on an annual basis with new data extracted from the literature. This database is also the foundation of data used to derive the prediction algorithms which are required to predict NMR spectral properties for chemical structures not contained within the database.
Multinuclear Database Searching to Enable Structure Verification

The full characterization of a phosphorus containing chemical entity commonly uses multiple forms of analytical data and does not depend solely on $^{31}$P NMR spectroscopy. Rather, $^1$H and $^{13}$C NMR data are also commonly obtained in order to determine the chemical structure. With this in mind, it makes sense that the availability of both $^1$H and $^{13}$C databases containing phosphorus containing species could be of value. Also, the ability to predict the $^1$H and $^{13}$C NMR spectra of phosphorus containing species would offer a similar advantage. At the time of writing, the $^1$H and $^{13}$C NMR databases available from ACD/Labs contain over 135,000 structures each, a total of close to 2.5 million chemical shifts. The $^{13}$C database contains ca. 6900 phosphorus containing species while the $^1$H database contains ca. 7800 structures.

Using structure 5,5-dimethyl-2-vinyl-1,3,2-dioxaphosphinane 2-oxide as an example structure for challenging the $^1$H predictions gives the result shown in Figure 3. The $^1$H NMR spectrum is predicted at a resonance frequency of 400 MHz (an option which can be adjusted). 477 individual lines are calculated for the spectrum and these are buried in the natural line width setting of 0.1 Hz.

Examination of the $^1$H calculation protocol shows excellent representative structures which were used in the prediction. Figure 4 shows that 38 substructure fragments were used to generate the chemical shift for the axial and equatorial proton pair for (CH$_2$)-5. This class of chemical structures is obviously well-represented in the database which is the culmination of over a decade of data collection from a series of diverse literature sources and journals.

Figure 3: The $^1$H NMR spectrum for 5,5-dimethyl-2-vinyl-1,3,2-dioxaphosphinane 2-oxide. Note the highlighted proton on the structure which simultaneously highlights the chemical shift (left table) and associated coupling constants (right table). Specifically, the 2J coupling between the phosphorus atom and the H8a is highlighted in the table.

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Notice the similarity between the substructure fragment used for the prediction of the proton chemical shifts associated with the axial and equatorial proton pair for (CH$_2$)$_2$-5. The axial and equatorial protons are selected using the proton mark selection tool highlighted in dark blue.

A $^{13}$C NMR prediction provides similar information regarding the chemical shifts of the species as well as the expected couplings with the phosphorus nucleus. In this case, the investigator may find a substructure search of the database to be of value as an aid to assigning the carbon nuclei within the ring system. Performing a search using the 5,5-dimethyl-1,3,2-dioxaphosphinane 2-oxide fragment as the input produces 31 hits in the database as shown in Figure 5. For completeness, it should be noted that a search for the same substructure gave 30 hits in the $^1$H database and 37 hits in the $^{31}$P database.

Figure 5: A substructure search of the 5,5-dimethyl-1,3,2-dioxaphosphinane 2-oxide fragment in the CNMR DB produces 31 direct hits (shown in Tiled View).
Each hit in the database, as in both the ACD/PNMR and ACD/HNMR databases, contains the chemical shifts and coupling constants extracted from the literature and a reference to the journal from which the data were extracted. An example of the information displayed within the database is shown in Figure 6. With access to the literature source for the data, the investigator may choose to access the original article for further information regarding either the synthesis or the details of the NMR assignment process.

Figure 6: A screenshot of one of the structures identified by the substructure search. The tables list the chemical shifts, $^{31}\text{P}-^{13}\text{C}$ coupling constants and the original reference.

Conclusion

The information in this Application Note provides the user with a reliable and comprehensive approach to interpreting $^{31}\text{P}$ NMR spectra. With a diverse library of over 23,000 phosphorus containing compounds, ACD/PNMR DB offers the most valuable PNMR resource available. Not mentioned in this application note is the software’s ability to estimate $^{31}\text{P}$ NMR chemical shifts. More information on the prediction capabilities of ACD/PNMR DB and the advantages of user training are outlined in the accompanying technical note entitled, “$^{31}\text{P}$ NMR Prediction and Enhancement with User Training”.

References