

## TOTAL SYNTHESIS OF (U-<sup>13</sup>C) DIELDRIN, ENDRIN, OXYCHLORDANE, AND RELATED POLYCHLORINATED NORBORNENE PESTICIDES

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### Introduction

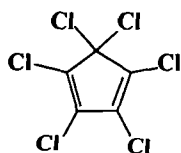
Polychlorinated compounds derived from hexachlorocyclopentadiene, such as chlordane, endrin, dieldrin, mirex, etc, most of which have a norbornene-type structure, have been used for decades as insecticides, although their use has been phased out in the U.S.A. and many other countries. These compounds are slowly degraded in the environment, and hence remain as persistent and toxic environmental contaminants, prompting a need for accurate quantitative analytical methods.

Stable isotope dilution GC/MS analysis has proven to be the most accurate, sensitive method available for such analyses. For this purpose, stable isotope-labeled surrogates of many of the hexachlorocyclopentadiene-derived pesticides have been prepared in a number of laboratories. However, the available labeled standards, having up to four <sup>13</sup>C-enriched positions (eight positions in the case of kepone and mirex), are inadequate for accurate quantitation of pesticide residues due to the natural presence of chlorine isotopes (<sup>35</sup>Cl, 76% and <sup>37</sup>Cl, 24%). The chlorine isotopes make clean distinction of the labeled surrogate from the unlabeled form of the analyte very difficult. There has been a long-standing need for more heavily labeled surrogates for use in accurate quantitative analyses of these important environmental contaminants.

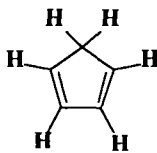
### Results

Syntheses have now been completed of fully-<sup>13</sup>C-labeled forms of these pesticides, carried out in response to this need for better resolution of labeled surrogate molecular ion clusters from those of the unlabeled analytes.

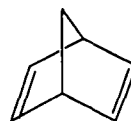
For the synthesis, three labeled primary building components were required in fully <sup>13</sup>C-labeled form: norbornadiene, cyclopentadiene, and hexachlorocyclopentadiene. These were synthesized by adaptation of known methods from the chemical literature, starting with acetylene (<sup>13</sup>C<sub>2</sub>), carbon dioxide (<sup>13</sup>C), carbon monoxide (<sup>13</sup>C), and carbon tetrachloride (<sup>13</sup>C) as the primary initial labeled materials.



Hexachlorocyclopentadiene (<sup>13</sup>C<sub>5</sub>)



Cyclopentadiene (<sup>13</sup>C<sub>5</sub>)



Norbornene (<sup>13</sup>C<sub>7</sub>)

Combination of hexachlorocyclopentadiene ( $^{13}\text{C}_5$ ) and norbornene ( $^{13}\text{C}_7$ ) gave aldrin ( $^{13}\text{C}_{12}$ ) and subsequently dieldrin ( $^{13}\text{C}_{12}$ ). The mass spectra of the labeled products show a complete separation of the molecular ion cluster from the corresponding peaks of the unlabeled analytes, thus yielding labeled surrogates that allow much greater sensitivity and accuracy for analysis of environmental samples.

Similarly, reaction of vinyl chloride ( $^{13}\text{C}_2$ ) (from acetylene ( $^{13}\text{C}_2$ )) with hexachlorocyclopentadiene ( $^{13}\text{C}_5$ ), followed by reaction with cyclopentadiene ( $^{13}\text{C}_5$ ) gave isodrin ( $^{13}\text{C}_{12}$ ), epoxidation of which yielded endrin ( $^{13}\text{C}_{12}$ ). Conversion of endrin into the environmental transformation products, endrin aldehyde and endrin ketone is currently in progress. These oxidation products of endrin are also persistent environmental contaminants, for which stable isotope-labeled surrogates have never before been available. Mass spectrometric data for the isodrin ( $^{13}\text{C}_{12}$ ) and endrin ( $^{13}\text{C}_{12}$ ) also show complete resolution of molecular ion cluster peaks from those of the unlabeled compounds.

In the most complex series of transformations, combination of hexachlorocyclopentadiene ( $^{13}\text{C}_5$ ) with cyclopentadiene ( $^{13}\text{C}_5$ ) gave chlordene ( $^{13}\text{C}_{10}$ ), further chlorination of which gave both the cis- and trans- isomers of chlordane, which have been separated. Allylic chlorination of chlordene ( $^{13}\text{C}_{10}$ ) gave heptachlor ( $^{13}\text{C}_{10}$ ), which was epoxidized to yield its environmental oxidation product, heptachlor epoxide ( $^{13}\text{C}_{10}$ ). Further chlorination of heptachlor ( $^{13}\text{C}_{10}$ ) gives both cis- and trans-nonachlor ( $^{13}\text{C}_{10}$ ), which also have been separated. Finally, further oxidative transformation of trans-nonachlor ( $^{13}\text{C}_{10}$ ) gave another environmental oxidation product, oxychlordane ( $^{13}\text{C}_{10}$ ). Thus, for the first time, essentially all of the most important polychlorinated pesticides related to chlordene have now been made available in fully  $^{13}\text{C}$ -labeled form for use in optimally sensitive environmental analyses.

Preparation of  $^{13}\text{C}$ -labeled endosulfans (Thiodans) I and II and their diol metabolite, and also mirex and kepone are also complete or currently in progress. The structures of the synthesized compounds (not showing isotopic labels) are given below:

