

# This Week's Citation Classic

Hinckley C C. Paramagnetic shifts in solutions of cholesterol and the dipyridine adduct of trisdipivalomethanatoeuropium(III). A shift reagent.  
*J. Amer. Chem. Soc.* 91:5160-2, 1969.

[Department of Chemistry, Southern Illinois University, Carbondale, IL.]

Shifts in the nuclear magnetic resonance (NMR) spectrum of cholesterol induced through association with the title lanthanide were shown to be substantial, accompanied by little broadening, and pseudocontact in character. The term 'shift reagent' was introduced. [The SCI® indicates that this paper has been cited in over 545 publications since 1969.]

C.C. Hinckley

Department of Chemistry and Biochemistry  
Southern Illinois University  
Carbondale, IL 62901

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"The experiment described in the cited article grew out of an interest in contact shifts induced in the nuclear resonances of ligands exchanging in solution with paramagnetic centers.<sup>1</sup> Such shifts are also called Fermi contact or Knight shifts, and their magnitudes are dependent upon spin transfer through the electronic structures of the association complexes. In the course of the study I became interested in the closely related phenomenon of pseudocontact shifts, in which the magnitudes of the shifts depend upon the geometry of the complex rather than its electronic structure. Having been introduced to the new lanthanide chelates,<sup>2</sup> prepared by Eisinger and Sievers,<sup>3</sup> I included the new compounds in my work. Eaton had suggested that when the paramagnetic center was a lanthanide, the induced shifts should be pseudocontact in character rather than contact.<sup>4</sup> Though this differed with earlier interpretations,<sup>5</sup> I chose to follow Eaton.

"The research progressed, in about two and a half years, through preparation of complexes of all of the available lanthanides and the study of their association with several exchanging ligands including pyridine, the picolines, dioxane, and other small Lewis bases.

"In the design of the cholesterol experiment, based upon this work, the outlines of

my expectations were well formed. I could confidently expect association, accompanying shifts, and little broadening. What I did not know was how large the pseudocontact interaction would be relative to the contact. In the event, the pseudocontact shifts were spectacular.

"If the above description suggests the flight of an arrow, the execution of the research was anything but. The chemistry I found was complex and confusing. Dimers of the lanthanide chelates seemed to come and go. The association phenomena obscured temperature effects. Though useful in examining acid-base association chemistry, pyridine and the other small molecules studied are particularly inappropriate choices for the examination of pseudocontact shifts. I was at sea on a number of occasions, and had to wait nervously for ideas to come. Looking back on it, I made a lot of wrong choices, and became so embroiled in petty complexities that I forgot for a time what my original purpose had been. The cholesterol experiment was a return to my earlier aims.

"The term shift reagent was devised in response to the felt need for a descriptor which conveyed a sense of generality. The effect is transparently general, stretching right through the heart of organic chemistry. Furthermore, the ability to move magnetic resonances around in a spectrum, so as to avoid interesting overlaps, is extremely useful. Lanthanide shift reagents are still employed for this purpose routinely by some, in spite of the dramatic advances in instrumentation of the last decade.

"One of the reasons for frequent citation of the article was the generality with which shift reagents could be applied.<sup>6</sup> There were many things to do. But most of all, I think that the technique attracted so many practitioners because the experiments were fun, they were easy to do, and were filled with pleasant surprises.

"I was given the Kaplan Research Award by my colleagues on my campus in 1972. I was an A.P. Sloan Foundation Fellow in 1973-1975."

1. Hinckley C C. Contact shifts of acetonitrile solutions of cupric chloride and titanium trichloride. *Inorg. Chem.* 7:396-7, 1968.

2. Green D M & Well J A. Private communications. 1967.

3. Eisinger K V & Sievers R E. Volatile rare earth chelates. *J. Amer. Chem. Soc.* 87:5254-6, 1965.

4. Eaton D R. The nuclear magnetic resonance of some paramagnetic transition metal acetylacetones. *J. Amer. Chem. Soc.* 87:3097-102, 1965.

[The SCI indicates that this paper has been cited in over 135 publications since 1965.]

5. Lewis W B, Jackson J A, Lemons J F & Taube H. Oxygen-17 NMR shifts in aqueous solutions of rare-earth ions. *J. Chem. Phys.* 36:694-701, 1962.

6. Williams R J P. The chemistry of lanthanide ions in solution and in biological systems. *Struct. Bond.* 50:79-119, 1982.