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NMR SPECTRAL STUDIES X - ARSENIC TRICHLORIDE AS A CONVENIENT SOLVENT FOR C-13 NMR SPECTROSCOPY[1,2]

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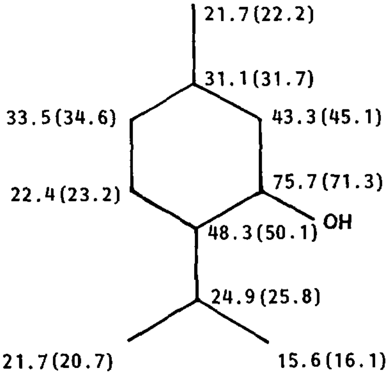
For compounds of low solubility in $CDCl_3$, other nmr solvents such as DMSO-d_6, acetone-d_6, CD_3OD, CD_3CN, CD_3CO_2D, etc., are commonly used. These solvents do not usually interfere with pmr spectroscopy except for removal of exchangeable protons; however, they give rise to intense multiplets in C-13 nmr spectra and often submerge some of the cmr signals of the compounds under study. A few years ago Szymanski and coworkers[3-5] and Brame and coworkers[6] reported the successful use of $AsCl_3$ and $SbCl_3$ as solvents for pmr spectroscopy of organic compounds and polymers which are sparingly soluble in $CDCl_3$ or CCl_4. These and other reports[7] suggested the possibility that $AsCl_3$ (and $SbCl_3$) might be useful for obtaining cmr spectra of various compounds with poor solubility in $CDCl_3$ or CCl_4. We present here the results of our preliminary investigation on the suitability of $AsCl_3$ as a solvent for cmr spectroscopy.

We have examined the cmr spectra of several classes of organic compounds such as hydrocarbons, alcohols, ethers, ketones, acids, esters, amides, hydantoins and β-lactams in a 2:1 (v/v) mixture of $AsCl_3$ and $CDCl_3$[8] and compared the chemical shifts with those for the same compounds in $CDCl_3$ or DMSO-d_6. Scheme I shows the chemical shifts of the various carbon atoms for a few of these compounds. It is seen that in almost all cases with the exception of alcohols the chemical shift differences (≤ 1 ppm) are negligible on the cmr scale.

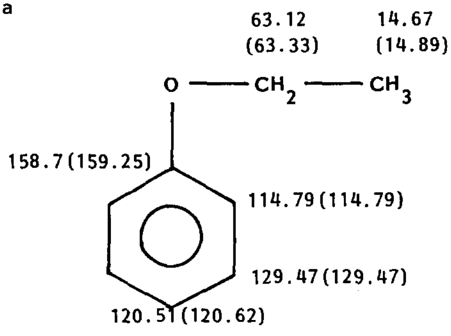
Alcohols show a downfield shift of about 2-4 ppm for the hydroxyl bearing carbon and upfield shift of about 2 ppm for the immediately adjacent carbons. However, the alcohols employed by us were recovered unchanged upon addition of water to the solution and extracting with a suitable organic solvent. Several amino compounds reacted vigorously with $AsCl_3$ forming solid products and hence these were not studied further.

From these observations it may be concluded that $AsCl_3$ or $AsCl_3 + CDCl_3$ is a superior solvent for recording cmr spectra of sparingly soluble compounds without hydroxy and amino groups. Apparently $AsCl_3$ behaves as a shift reagent for carbon carrying a hydroxy group and adjacent carbons. Comparison of spectra run under identical conditions in $CDCl_3$ and $AsCl_3 - CDCl_3$ shows that there is no appreciable difference in peak intensities or line widths between the two sets of spectra.

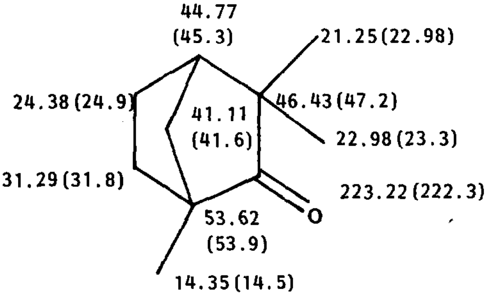
SCHEME I[a]



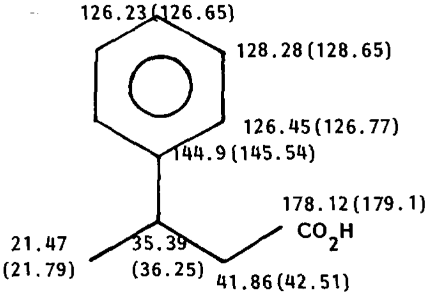
1-MENTHOL



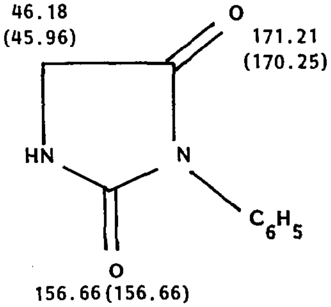
PHENETOLE



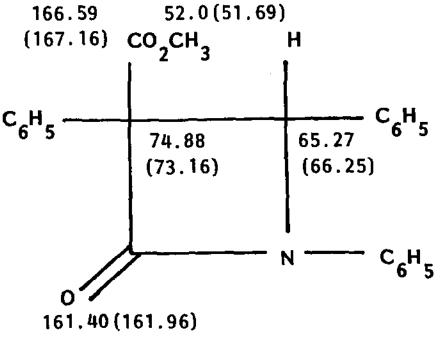
FENCHONE



3-PHENYLBUTYRIC ACID



3-PHENYLHYDANTOIN[b]



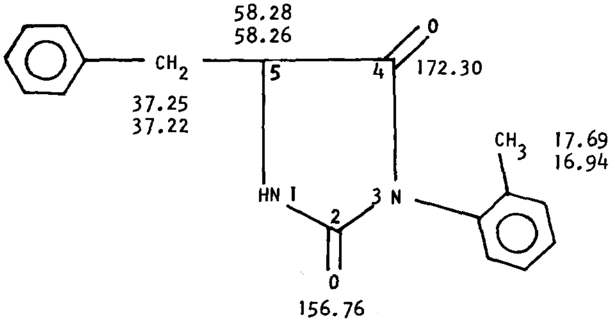
1,3,4-TRIPHENYL-3-CARBOMETHOXY-2-AZETIDINONE

a. The numbers correspond to C-13 chemical shifts (in ppm downfield from TMS) for the compound in $AsCl_3$-$CDCl_3$ solution; numbers in parentheses are for $CDCl_3$ solution

b. The numbers in parentheses are for the compound in DMSO-d_6 solution.

Table I

Lanthanide Induced Shift (LIS) Studies[a] on 3-*o*-Tolyl-5-benzylhydantoin[b]



Shift Reagent	Solvent	LIS (in ppm[c])		
		C_2	C_4	C_5
$Eu(fod)_3$	$CDC\ell_3$	+2.16 +1.73	0.00	+0.76 +0.65
$Eu(fod)_3$	$AsC\ell_3$ - $CDC\ell_3$	-2.15	-0.35 -1.08	-0.10 -0.11
$Pr(fod)_3$	$CDC\ell_3$	-4.53 -5.28	-1.83 -1.19	-2.15 -1.83
$Pr(fod)_3$	$AsC\ell_3$ - $CDC\ell_3$	+1.84 +1.41	-0.11	+0.11 +0.10

a. In all cases, 300 mg of compound and 85 mg of the lanthanide were employed.

b. Chemical shifts in ppm for $CDCl_3$ solution with TMS as internal reference; two resonances are shown by most of the carbon atoms becasue the tolyl group exists in two different orientations, H. Fujiwara, Ph.D. Thesis, Stevens Institute of Technology, 1974.

c. + denotes shift to lower magnetic field.

Lanthanide shift reagents are very widely used now for nmr spectral studies. Therefore, we examined the compatibility of the $AsCl_3$ - $CDCl_3$ system with these shift reagents. 3-*o*-Tolyl-5-benzylhydantoin was chosen for this study and the shifts induced on its carbon atoms by both $Eu(fod)_3$ and $Pr(fod)_3$ in the above solvent mixture as well as in $CDCl_3$ solution were measured (see Table 1). Interestingly, the direction of shifts in $AsCl_3$ were the opposite of those observed in $CDCl_3$ and the magnitudes of the shifts also varied. The reasons for this behaviour are not yet clear but once a pattern of shifts for different kinds of carbon atoms in this solvent mixture is recognized, useful information could be derived for compounds of unknown structural features. Some line-broadening and drop in peak intensities are noticed upon addition of the lanthanide shift reagents to $AsCl_3$ - $CDCl_3$ solutions; similar effects are noticed in $CDCl_3$ solutions also.

It may be noted that lanthanide shift reagents cannot be used in DMSO-d_6, acetone-d_6, CD_3CN, CD_3OD, or CD_3CO_2D. The $AsCl_3$ or $AsCl_3$ - $CDCl_3$ system therefore has a major advantage over these solvents. Since $AsCl_3$ is cheap (cheaper than even $CDCl_3$) and readily available, it may be used in a routine fashion for ^{13}C nmr spectroscopy. Caution must be exercised in working with $AsCl_3$ and in disposing off of the solution because of the toxic nature of arsenic compounds. During recovery of sample, which is best effected by adding a desirable organic solvent and water to the $AsCl_3$ - $CDCl_3$ solution, the organic layer is washed once or twice with cold 5% aqueous NaOH solution. If recovery is not desired, the solution is dispensed into a large bottle containing 10% aqueous NaOH solution.

Acknowledgment

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8. $CDCL_3$ was used to provide the source of ^2H for the deuterium lock of the Bruker HX-90 NMR Spectrometer; this also made the solutions less viscous. (However, if necessary, spectra could be taken in neat $AsCl_3$ with a central 5 mm capillary containing D_2O for the ^2H lock). TMS was used as internal reference and C-13 spectra were recorded by PFT on the above instrument using an internal ^2H lock (13.815 MHz) with an operating frequency of 22.628 MHz for ^{13}C and employing broad-band proton (90 MHz) decoupling. A mixture of $AsCl_3$: $CDCl_3$ (2:1, v/v) could be stored for several weeks in a tightly stoppered bottle. Care was exercised in handling this solution to avoid contact with skin. $AsCl_3$ (Anhydrous, 99%) purchased from Research Organic/Inorganic Chemical Corp., Sun Valley, Calif., was used directly for these experiments. This reagent is also available from Ventron Corporation and PCR Incorporated.