APPLICATION OF SHIFT REAGENTS IN ^{1}H- AND ^{19}F-NMR SPECTROSCOPY. INTERACTIONS WITH CHLOROFLUOROALKANOLS C_3, C_4

František Skácel[a], Milan Hájek[b], František Liška[c], Petr Trška[c] and Zbyněk Ksandr[a]

[a]*Department of Analytical Chemistry,*
[b]*Laboratory of Synthetic Fuels, and*
[c]*Department of Organic Chemistry,*
Prague Institute of Chemical Technology, 166 28 Prague 6

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The interaction Eu(FOD)$_3$–substrate was examined in $CDCl_3$ and CCl_4 solutions by the methods of ^{1}H- and ^{19}F-NMR spectroscopy, and the stoichiometry, equilibrium constants, and limiting induced shifts of the adducts substrate–shift reagent were determined. 1-Propanol, 4-chloro-3,3,4-trifluoro-2-methyl-2-butanol, and 2,2,3,3-tetrafluoropropanol were employed as the substrates.

The changes induced in a NMR spectrum by a shift reagent are affected, in addition to the geometrical factors, also by the stoichiometry of the formed complex adduct of the substrate (S) and the shift reagent (L) and by the set of the equilibrium reactions in the system measured. Reactions are also involved which are not directly related with the formation of the complex adduct L_mS_n, particularly substrate[1] or reagent[2–4] self-association or interactions of the substrate with the solvent[2,5] or with impurities[2], if present (traces of water). The relations in a real system are rather complicated and information on them can be obtained from experimental data[6] of the dependences of the induced shifts on the substrate and shift reagent concentrations. The solution of this problem was the concern of several works[1,2,7–11]. A simplification of the spectra can be achieved in some instances by employing ^{19}F-NMR spectroscopy[12]. The complex adducts L_mS_n are determined by the equilibrium constants K_{mn} and the limiting induced shifts ΔL_mS_n, which can be obtained by graphical[1] or numerical methods[4,13–15]. The graphical methods are time consuming and tedious and the results do not always describe the system properly[16]. The numerical methods are based on a fit of the mathematically formed models to the experiment. In this manner it is possible to come to very precise and accurate values of the limiting induced shifts; the values of the equilibrium constants, however, are only approximate[4].

In this work we attempted to solve the equilibrium systems of the shift reagent Eu(FOD)$_3$–substrate. 1-Propanol and two fluoroalkanols served as the substrates; the effect of their self-association on the shift reagent–substrate interaction was investigated. The equilibrium constant values obtained for the two fluoroalkanols from the ^{1}H- and ^{19}F-NMR measurements were compared.

EXPERIMENTAL

The shift reagent $Eu(FOD)_3$ (Merck) was purified by crystallization from methylene chloride[17] and sublimation in vacuum. 1-Propanol (*I*) (Lachema) was subjected to rectification on a Vigreux column, 4-chloro-3,3,4-trifluoro-2-methyl-2-butanol (*II*) was the product of the photochemical addition of 2-propanol to trifluorochloroethylene[18], 2,2,3,3-tetrafluoropropanol (*III*) resulted from the telomerization of tetrafluoroethylene and methanol[19]. The purity of all substrates was checked by gas chromatography and proton and fluorine NMR spectra. The solvents, deuteriochloroform (Merck) and tetrachloromethane reagent grade purity (Lachema), as well as the substrates were dried by molecular sieve 4 A, all substrates and shift reagents were stored over P_2O_5. Tetramethylsilane (Merck) served as the internal standard in all cases.

The self-association of the alcohols *I*–*III* was measured in the concentration region 0.03–1 mol l^{-1} in the volume 0·5 ml. The induced chemical shifts were obtained by the method of successive additions of the reagent into 0·5 ml of 0·5M solution of the substrate in the region of $R_p = 0-2$ ($R_p = c_L/c_S$, where c_L is total concentration of shift reagent and c_S is total concentration of substrate).

The ^{19}F-NMR spectra were measured at 94·1 MHz on a spectrometer Varian XL-100, the proton spectra at 60 MHz on an instrument Tesla BS-467 and at 100 MHz on the spectrometer Varian XL-100 (self-association of the substrate). The working temperature of the instrument Varian was 37°C, that of the instrument Tesla 27°C.

RESULTS AND DISCUSSION

For an examination of the effect of the substrate self-association on the equilibrium formation of the substrate–reagent adduct, the dependence of the chemical shifts on the molar concentration was employed (Fig. 1). Inasmuch as

$$\delta = \delta_1 \cdot f_1 + \delta_2 \cdot f_2 + \ldots + \delta_n \cdot f_n , \qquad (1)$$

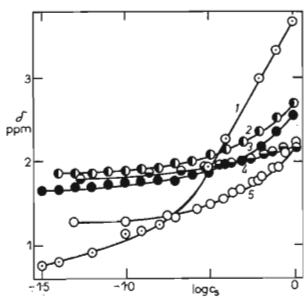

FIG. 1

Chemical Shifts of the Hydroxy Group, Obtained from the ^{1}H-NMR Spectra

1, *2* 1-Propanol, *3*, *4* 4-chloro-3,3,4-trifluoro-2-methyl-2-butanol, *5* 2,2,3,3-tetrafluoropropanol; *1*, *3*, *5* in $CDCl_3$, *2*, *4* in CCl_4.

where δ_1 to δ_n are the shifts of the nucleus of the monomer to n-mer and $f_n = n[S_n]/c_S$, we have

$$c_S = [S_1] + 2[S_1]K_{A2} + \ldots + n[S_1]K_{An}, \quad (2)$$

where $[S_1]$ is concentration of the monomer.

Combining these relations under the assumption that the total concentration of the substrate is

$$c_S = [S_1] + n[S_1]^n K_{An}, \quad (3)$$

we obtain a simple relation for the calculation of the substrate self-association constant

$$\delta = (\delta_1[S_1] + n\delta_n K_{An}[S_1]^n)/c_S. \quad (4)$$

This relation was solved iteratively by using the program[20] based on the nonlinear regression method. The input data were the chemical shifts of the hydroxy group protons, molar concentration of the substrate, and the initial δ_1, δ_n, and K_{An} values found from the primary processing of the data by the SH method[20]. The final self-association constants and the values of the optimization criterion U (defined as $U = \sum(\delta_{obs} - \delta_{calc})^2$, where the subscripts refer to the observed and calculated shifts, respectively) are given in Table I.

From the comparison of the optimization criterion values for the corresponding n-mers it follows that for 1-propanol (*I*) in $CDCl_3$ as well as in CCl_4 the dependence of the chemical shifts on the concentration derived from the trimer formation mechanism fits best the experimental dependence; the constant K_{A3} was therefore used for

TABLE I

Parameters of Self-Association of the Substrates *I*—*III*, Obtained by ^{1}H-NMR Spectroscopy
K_{An} equilibrium constant, in l^{n-1} mol$^{-(n-1)}$, U optimization criterion, in ppm^2.

System		Dimer		Trimer		Tetramer	
		K_{A2}	U	K_{A3}	U	K_{A4}	U
I	$CDCl_3$	0·068	128	0·19	72	1·01	146
I	CCl_4	0·235	631	1·226	124	8·296	572
II	$CDCl_3$	0·182	4·1	1·14	12	4·94	24
II	CCl_4	0·194	3 661	1·191	344	5·315	431
III	$CDCl_3$	0·201	6 188	1·078	222	4·207	292

the subsequent mathematical processing of the dependence of the induced shifts on the shift reagent concentration. For 4-chloro-3,3,4-trifluoro-2-methyl-2-butanol (*II*) in $CDCl_3$, the dimer formation was found to suit best, and the constant K_{A2} was used in the following calculations; in CCl_4, on the other hand, the optimization criterion values are considerably lower for the trimer or tetramer formation than for the dimer formation. The constants K_{A3} and K_{A4} were therefore used simultaneously during the processing, since the two mechanisms are approximately equally probable. Alike is the case with 2,2,3,3-tetrafluoropropanol (*III*) in $CDCl_3$, where the constants K_{A3} and K_{A4} were again employed simultaneously during the successive mathematical treatment of the dependence of the induced shifts on the shift reagent concentration. The values of these self-association equilibrium constants agree by their orders of magnitude with the published data on methanol, ethanol, n-butanol, and tert-butanol[21-25].

The experimental data were processed by using a program based on the nonlinear regression method, whose input data were the induced shifts and the molar concentrations of the reagent and the substrate. The stoichiometric coefficients m and n of the adduct L_mS_n were calculated by the iterative method[11] applicable to any type of equilibrium including the formation of polynuclear complexes.

The various types of the shift reagent–substrate interactions used in the first step of the mathematical treatment of the dependence of the induced shifts on the reagent-to-substrate concentration ratio are summarized in Table II (Fig. 2 a 3).

TABLE II

Equilibria of the Shift Reagent–Substrate Complex Adduct Formation as Employed in the First Step of the Mathematical Processing of the Dependence of the Induced Shifts on the Reagent-to-Substrate Ratio

$K_{11} = [LS]/[L]\,[S]$ in 1 mol^{-1}, $K_{12} = [LS_2]/[L]\,[S]^2$, $K_{21} = [L_2S]/[L]^2\,[S]$, both in 1^2 mol^{-2}.

Complex adduct	Equilibrium constant	Limiting induced shift
LS	K_{11}	Δ^{LS}
LS_2	K_{12}	Δ^{LS_2}
L_2S	K_{21}	Δ^{L_2S}
LS, LS_2	K_{11}, K_{12}	Δ^{LS}, Δ^{LS_2}
LS, L_2S	K_{11}, K_{21}	Δ^{LS}, Δ^{L_2S}
LS_2, L_2S	K_{12}, K_{21}	Δ^{LS_2}, Δ^{L_2S}
LS, LS_2, L_2S	K_{11}, K_{12}, K_{21}	Δ^{LS}, Δ^{LS_2}, Δ^{L_2S}

For random errors to be eliminated during the minimization, the calculations started always from several internal parameter values differing by two orders of magnitude.

In the first step of the mathematical processing of the dependence of the induced shifts on R_p, the internal parameters were calculated for all of the seven substrate–shift reagent equilibrium types, given in Table II. The following conclusions can be drawn based on the values of the optimization criterion U (defined as in the case of the self-association). The alkanol *I* forms predominantly the adduct L_2S *via* the one-step equilibrium. For the alkanol *II*, this comparison indicates the formation of the LS_2 adduct in the two solvents, *via* both the one-step and two-step reactions, as borne out also by agreement of the results of the proton and fluorine resonance techniques. For the alkanol *III* in $CDCl_3$, the two-step formation of the adduct LS_2 and the one-step formation of the adduct L_2S seem to be adequate based on the agreement of the results of the two NMR techniques.

In the second step of the mathematical treatment, the input values of the program[26] were augmented with the substrate self-association constants K_{An} ($n = 2, 3, 4$). The resulting equilibrium constants of the L_mS_n adduct formation and the optimization criterion values were again compared, from which a unique mechanism emerged as the most probable for all the substrates in both solvents, *viz.* the one-step formation of the adduct LS_2.

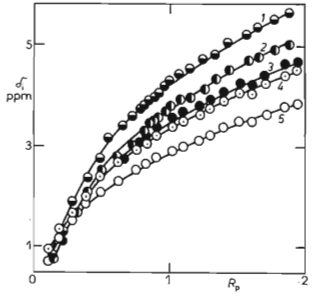

FIG. 2

Induced Shifts of 4-Chloro-3,3,4-trifluoro-2-methyl-2-butanol Obtained from the ^{1}H- and ^{19}F-NMR Spectra

Concentration 0·5 mol l^{-1} in $CDCl_3$; nuclei: *1* HCFCl, *2* CF_2, *3* $^2CH_3$, *4* $^1CH_3$, *5* HCFCl.

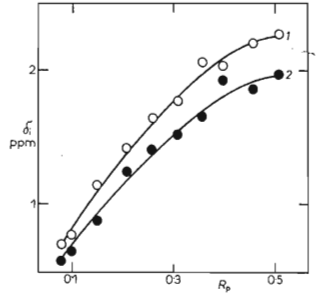

FIG. 3

Induced Shifts of 4-Chloro-3,3,4-trifluoro-2-methyl-2-butanol Obtained from the ^{1}H-NMR Spectra

Concentration 0·5 mol l^{-1} in $CDCl_3$; nuclei: *1* $C(CH_3)_3$, *2* HCFCl.

As follows from Table III, the selection of the optimum equilibrium types reduced to a single mechanism only; also the optimization criterion values lowered and the values of the equilibrium constants as well as of the limiting induced shifts approached each other.

Propanol (*I*) exhibits a good agreement of the K_{12} equilibrium constant values for the individual protons, both in $CDCl_3$ and in CCl_4. The value of the constant decreases from the proton CH_3 to CH_2OH. While the values of the limiting induced shift $_{\Delta}LS_2$ in the two solvents approach each other closely, those of the equilibrium constant K_{12} are one order of magnitude higher in $CDCl_3$ than in CCl_4. This can be explained in terms of the lower tendency of the substrate *I* to form a complex adduct with the $Eu(FOD)_3$ reagent in CCl_4; it rather undergoes self-association. This is borne out by the values of the self-association constant, which in CCl_4 is one order of magnitude higher than in $CDCl_3$ (Table I).

The fluorobutanol *II* in $CDCl_3$ exhibits a good agreement of the values of the equilibrium constant K_{12} for the individual protons; they decrease from the proton CHFCl to CH_3. The K_{12} values obtained by ^{19}F-NMR spectrometry also agree for the individual fluorine atoms, decreasing from the fluorine nucleus CHFCl to CF_2; they are, however, one order of magnitude lower than those obtained from the proton resonance spectra. In CCl_4, the K_{12} values for the individual protons or fluorine nuclei are in a mutual agreement; the results obtained from the two resonance techniques differ, however, their mutual relation being reverse to that observed in $CDCl_3$.

The tetrafluoropropanol *III* was only measured in $CDCl_3$, because in CCl_4 it is low soluble. The results show that the equilibrium constants K_{12} obtained from the proton and fluorine spectra agree by order of magnitude, apart from the high difference found within the fluorine resonance spectra.

Based on the above findings, ^{19}F-NMR spectrometry can be claimed to have proved an efficient method for the determination of the substrate–shift reagent interaction parameters for substrates containing fluorine atoms. From the point of view of the mutual ratios of the L_mS_n adduct formation constants obtained for the individual fluorine nuclei groupings and of the optimization criterion values, this method is roughly comparable with ^{1}H-NMR spectrometry. The fluoroalkanols *II* and *III* form less strong complex adducts with $Eu(FOD)_3$ as compared with 1-propanol (*I*). This can be explained in terms of the higher tendency of the alcohols *II* and *III* to the formation of their n-mers by self-association, high electronegativity of chlorine and fluorine, and possibly also steric factors.

The above results indicate that the self-association of the fluoroalkanols *II* and *III* as well as of 1-propanol has a great effect upon the formation of the substrate – reagent adducts. As follows from Table III, allowance for the substrate self-association made during the calculation of the equilibrium conditions of the reagent – substrate adduct formation brings about not only a considerable improvement of the optimization criteria, but particularly changes in the selection of the optimum types of

the system equilibria. The solvent effect upon the reagent–substrate interaction is related with the formation of the n-mers of substrate as well as of shift reagent by self-association (Table III – 1-propanol for instance). A complex solution of the

TABLE III

Data on the Most Probable Adducts (LS_2) of the Substrates *I*—*III*, obtained by Calculation from the Dependence of the Induced Shifts of the ^1H and ^{19}F Nuclei on the Adduct-to-Reagent Concentration, Taking into Account the Substrate Self-Association

The values obtained by disregarding the self-association are given in parentheses.

Nucleus	K_{12} $l^2\,mol^{-2}$	Δ^{LS_2} ppm	U ppm^2
	I[a] in $CDCl_3$, ^1H-NMR		
CH_3	47·5	11·83	1·5
	(105·2)	(26·30)	(19·09)
CH_2	45	18·18	3·49
	(67·59)	(33·64)	(40·16)
CH_2OH	42	31·87	8·72
	(61·5)	(57·31)	(126·5)
	I[a] in CCl_4, ^1H-NMR		
CH_3	3·32	21·86	1·69
	(81·15)	(21·98)	(20·8)
CH_2	3·17	32·93	3·39
	(120·9)	(84·7)	(17·6)
CH_2OH	3·16	58·4	12·6
	(44·33)	(46·75)	(124·6)
	II[b] in $CDCl_3$, ^1H-NMR		
CHFCl	17·6	6·9	0·1
	(2·63)	(6·72)	(0·1)
$^1CH_3$	17·1	9·09	0·17
	(10·9)	(8·08)	(5·22)
$^2CH_3$	16·7	8·47	0·14
	(12·48)	(8·5)	(6·54)
	II[b] in $CDCl_3$, ^{19}F-NMR		
CHFCl	2·68	11·2	0·08
	(3·72)	(9·27)	(1·18)
CF_2	2·29	10·56	0·2
	(1·88)	(10·99)	(0·21)
	II[c] in CCl_4, ^1H-NMR		
$^1CH_3$	5·02	16·71	5·29
	(3·65)	(14·95)	(0·12)
$^2CH_3$	6·83	14·91	2·07
	(3·30)	(16·03)	(0·17)
	II[c] in CCl_4, ^{19}F-NMR		
CHFCl	11·89	11·28	0·31
	(17·66)	(9·97)	(3·64)
CF_2	10·53	10·28	0·18
	(5·96)	(10·53)	(1·12)
	III[c] in $CDCl_3$, ^1H-NMR		
HCF_2	25·78	6·54	0·11
	(9·87)	(7·39)	(0·31)
CH_2OH	21·5	17·43	0·91
	(9·66)	(18·88)	(2·78)
	III[c] in $CDCl_3$, ^{19}F-NMR		
HCF_2	19·73	11·86	1·5
	(5·86)	(13·35)	(3·11)
CF_2	53·61	7·46	9·73
	(26·19)	(7·94)	(9·84)

[a] With allowance for the substrate trimer formation; [b] with allowance for the substrate dimer formation; [c] with allowance for the simultaneous substrate trimer and tetramer formation.

substrate–shift reagent equilibrium system requires the possibility of the formation of all complex species to be taken into account. At present, experimental difficulties and problems associated with the interpretation of the results obtained are, however, encountered. Open – with respect to the solution of the problem of the reagent–substrate interaction and to the comparison of the methods of the fluorine and proton resonance – remains the evaluation of the magnitude of the contact contribution to the induced shift.

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