FT-IR Spectroscopic Investigations Adsorption of Pyrazinamide and 4-Aminopyrimidine by Clays

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Abstract

The adsorption of pyrazinamide (PZA) and 4-aminopyrimidine (4APM) on natural sepiolite, loughlinite (Na-sepiolite), natural and ion-exchanged montmorillonite (Co- or Cu-montmorillonite) has been investigated using FT-IR spectroscopy. The intercalation of pyrazinamide and 4-aminopyrimidine within natural and ion-exchanged montmorillonites has been shown by X-ray diffraction to increase the interlayer spacing. PZA and 4APM interacted with montmorillonites by direct or indirect coordination (through water molecules) to the exchangeable cations. The spectroscopic results indicate that PZA or 4APM molecules adsorbed on sepiolite and loughlinite are coordinated to Lewis acidic centers or surface hydroxyls by H-bonding interaction through either one of the pyrimidine ring nitrogen lone pairs (in the case of 4APM) or carbonyl group (in the case of PZA).

Introduction

Sepiolite and loughlinite belong to the phyllosilicates class of clay minerals. Loughlinite is virtually identical in appearance to sepiolite, both in a hand specimen and microscopically [1] and known as natural Na-sepiolite. However, field observations and mineralogical determinations indicate that sepiolite and loughlinite are formed authigenically and independently in different physicochemical environments rather than being the product of transformation of one to the other [2]. The theoretical formula of loughlinite is $(Mg_6 Na_2) Si_{12} Na_2 O_{30} (OH)_4 (OH_2)_4. 8H_2O$ and that of sepiolite is $Mg_8 Si_{12} O_{30} (OH)_4 (OH_2)_4. 8H_2O$ [1, 3]. They both have a fibrous structure consisting of talc-like ribbons parallel to the fibre axis assembled in such a way that the tetrahedral sheet is continuous throughout but inverts apical directions in adjacent ribbons, each ribbon alternating with channels along the fibre axis (c-axis) [1, 4]. Structurally they consist of blocks and channels extending in the c-axis direction. They have the ability of selectively sorbing polar and non-polar molecules on the external surfaces and for small polar molecules, inside the channels. It is known that surface hydroxyl groups play an important role in the selective sorption on the external surfaces of the sepiolite [4].

Montmorillonite is an expanding layer silicate mineral; composed of aluminosilicate layers stacked one above the other. Each layer has a small net negative charge because of isomorphous substitution of ions in the framework. The charge is compensated by interlayer hydrated cations, which are known as exchangeable cations. Montmorillonite is capable of intercalating many organic compounds [5–8].

Pyrazinamide (pyrazine carboxamide), is a well-known anti tubercle bacillus drug [9]. The parent molecule and its complexes are widely used due to their antimycobacterial properties [9, 10]. On the other hand pyrimidine is the parent heterocycle of very important group of compounds that have been extensively studied due to their occurrence in living systems [11]. Pyrimidine moieties are reported to have antibacterial antifungal and anti-HIV activities [12]. The aim of this work is to contribute to the explanation of the host–guest interaction through the study of the IR spectra of the original and adsorbed species, as well as to investigate the clays as drug carriers. In a previous study, adsorption of pyrazinamide on bentonite was reported but in this study only $\nu(C=O)$ vibrational mode was given [13]. To the best of our knowledge no complete IR spectroscopic investigation on adsorption of PZA or 4APM by clays have been reported in the literature. In our previous studies the sorption of bipyridyls, amino pyridines, biquinoline, pyrimidine and 2-aminopyrimidine by clays were reported [7, 8, 14–19]. Continuing our studies on the adsorption of organics on the clay surfaces, in this study sorption of 4APM and PZA onto natural sepiolite, loughlinite and natural and ion exchanged (Co- and Cu-) montmorillonites have been investigated using FT-IR Spectrometry.

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Experimental

The natural montmorillonite sample was from Cankiri and sepiolite and loughlinite samples used were from Mihalliccik-Eskisehir regions of Anatolia (Turkey). Loughlinite is green and sepiolite is beige claystones. Loughlinite and sepiolite are identified by d(110) reflections at 12.9 Å and 12.3 Å, respectively [2]. The clay samples studied were first identified by X-ray diffraction, differential thermal and IR spectroscopic analyses. The results indicate that loughlinite is associated with analcime (app. 8%) and Al_2O_3 (app. 6%), and has detectable calcite impurity (IR; 1435 cm^{-1}). The IR spectrum of natural montmorillonite indicated a moderate Fe^{3+} content (885 cm^{-1}) with the presence of detectable quartz (697 cm^{-1}) and silica phase (797 cm^{-1}) impurities. The chemical compositions of starting clays are as follows: Sepiolite: 58.0% SiO_2, 25.5% MgO, 0.5% Al_2O_3, 0.5% K_2O, 0.5% CaO, 0.05% TiO_2, 0.05% Na_2O, 0.01% P_2O_5, 0.01% MnO, 0.05% (($FeO+Fe_2O_3$), 14.5% loss on ignition, loughlinite: 55.0% SiO_2, 12.5% MgO, 7.0% Na_2O, 6.5% Al_2O_3, 2.8% ($FeO+Fe_2O_3$), 1.1% K_2O, 1.0% CaO, 0.30% TiO_2, 0.1% P_2O_5, 0.05% MnO, 14.0% loss on ignition, montmorillonite; 58.3% SiO_2, 2.5% MgO, 16.0% Al_2O_3, 1.1% K_2O, 3.5% CaO, 0.6% TiO_2, 2.1% Na_2O, 0.1% P_2O_5, 3.0% (($FeO+Fe_2O_3$), 13.1% loss on ignition.

The homoionic Co- or Cu-montmorillonites were prepared according to Ogawa *et al.* [20]. The CEC values of montmorillonites studied were given in our previous paper [8].

The clays were ground to approximately 200-mesh size powder. The adsorbates (PZA or 4APM) were reagent grade and were used as received. PZA or 4APM treated clays were prepared by methods analogous to those given in the literature [8] by immersing air-dried clays in ethyl alcohol or aqueous solution of PZA or 4APM in sealed bottles at room temperature for 24 hours, or by solid–solid reactions between clays and PZA or 4APM analogous to those of Co-montmorillonite and 2,2′-bipyridine [20]. Solid–solid reactions are known as useful ways to introduce organic guest species into the interlayer species of layered silicates [20, 21]. Products were washed with solution several times to remove excess organic molecules, then dried. The FT-IR spectra of self-supporting films (∼2 mg cm^{-2}), oriented films supported onto CaF_2 window or KBr discs of samples were recorded on a Jasco 300E FT-IR spectrometer.

Results and discussion

The structural formula of PZA and 4APM are given in Figure 1. Treatment of natural or ion-exchanged montmorillonites with PZA or 4APM resulted in an increase in the basal spacing indicating formation of intercalates. The basal spacings of PZA treated natural and Co- or Cu treated montmorillonite are 15.8, 15.9 and 15.7Å, respectively, and those of 4APM treated montmorillonites are ca.16.1Å, compared with the value of ca. 12.0 Å for the basal spacing of untreated clays. These observations suggest that PZA or 4APM mo-
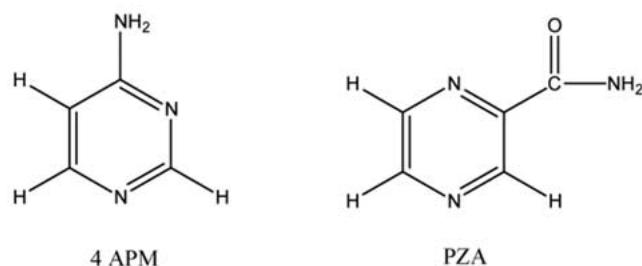

Figure 1. Structural formula of 4-aminopyrimidine ($C_4H_5N_3$) and pyrazinamide ($C_5H_5N_3O$).
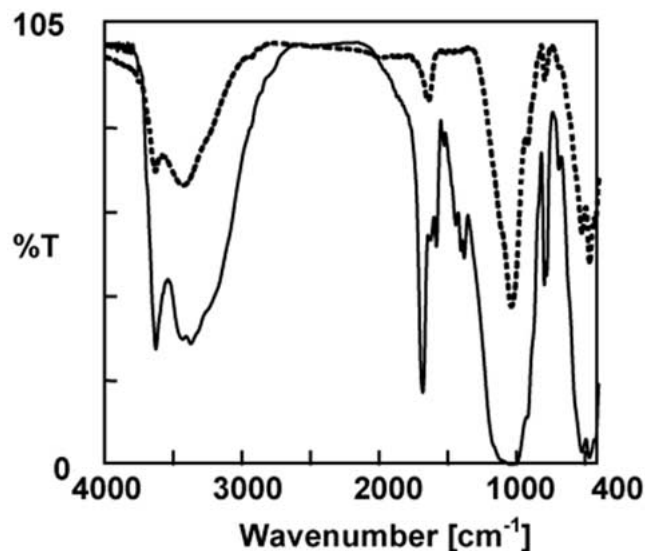

Figure 2. FT-IR spectra of PZA treated (solid line) and untreated Co-montmorillonite (doted line).

lecules intercalate into the interlayers of montmorillonites with a monolayer arrangement.

It is well known that the adsorption of the organic molecule onto clay surface or formation of intercalates gives
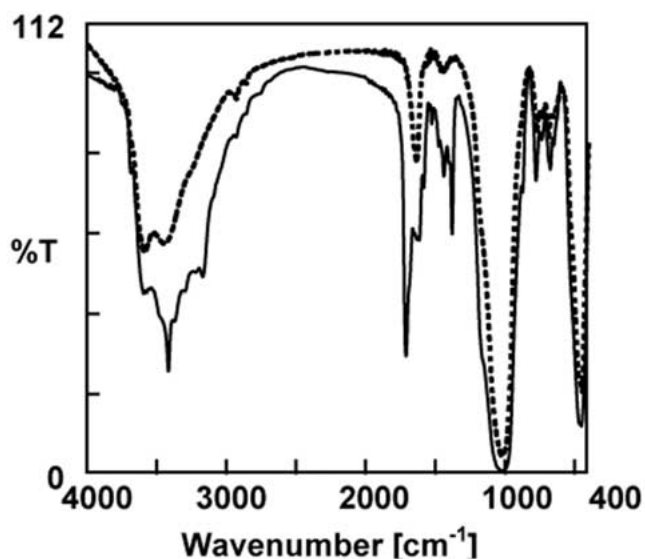

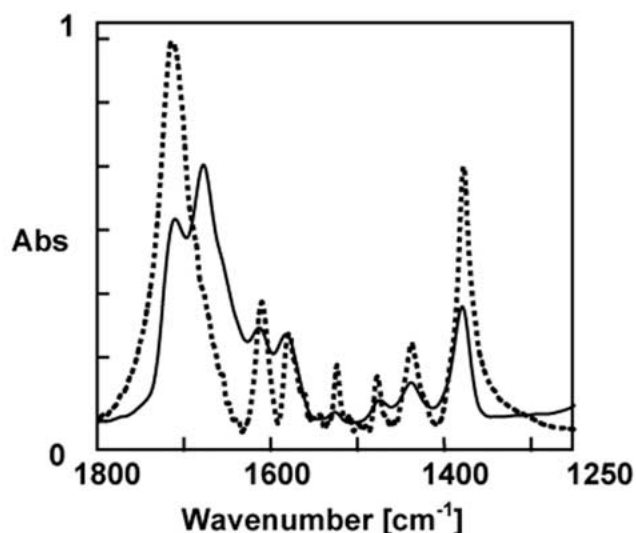*Figure 3.* FT-IR spectra of PZA treated (solid line) and untreated loughlmite (doted line).

Figure 4. 1250–1800 cm^{-1} region ofthe FT-IR spectra of KBr discs of PZA treated sepiolite (solid line) and PZA (dotted line).
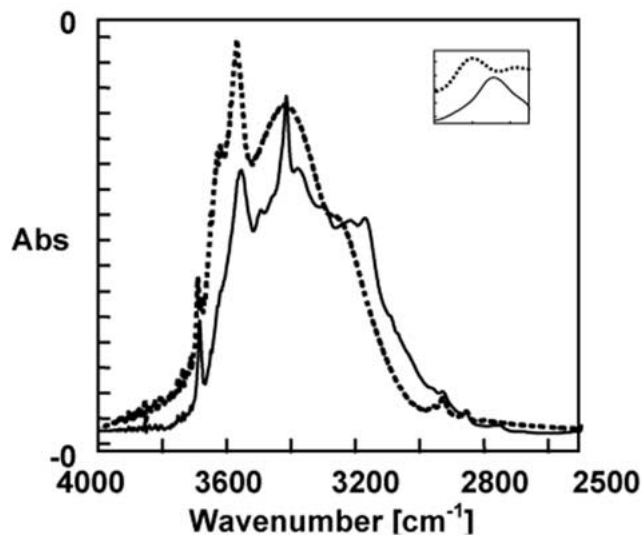

Figure 5. 4000–2500 cm^{-1} region of the FT-IR spectra of natural sepiolite (doted line) and PZA treated sepiolite (solid line). The 3700–3675 cm^{-1} region of both samples is shown comparatively in the small frame given above.

rise to the changes in the IR spectra of the interacting species. In order to determine the interaction mechanism of adsorbed PZA or 4APM molecules by clays, the vibrational wavenumbers of adsorbed molecules are carefully investigated, by taking into account the coordination effects through the ring, through the NH_2 group and in the case of PZA, additionally through the >C=O group. The IR spectroscopic studies of adsorption of pyridine and pyridine derivatives by clays indicated that if the aromatic ring nitrogen involves in direct or indirect coordination (through water molecules), certain ring modes, particularly the ring breathing mode and the two ring stretching modes around 1400–1600 cm^{-1} increase in value [7, 8]). On the other hand, if the coordination occurs through the amino nitrogen atom, it is expected that a great reduction would take place in the NH_2 stretching NH_2 bending and C-NH_2 stretching wavenumbers (e.g. Akalin and Akyuz [22]), and when coordination occurs through the oxygen of carbonyl group, negative shift at (νC=O) mode of coordinated molecule with respect to the free ligand is expected.

The coordination sensitive modes of PZA are tabulated in Table 1. The FT-IR spectra of PZA treated and untreated Co-montmorillonite and loughlinite are illustrated in Figures 2 and 3, respectively. The 1250–1800 cm^{-1} region of the FT-IR spectra of KBr discs of PZA treated sepiolite and microcrystalline PZA are given in Figure 4, and the OH stretching region of PZA treated sepiolite together with natural sepiolite are given in Figure 5. The FT-IR spectra of 4APM treated sepiolite and montmorillonite are given in Figures 6 and 7, respectively. Spectral subtraction and the band component analysis are found to be very useful in order to pick up the overlapping bands, in particularly the vibrational modes of the organic molecule under strong absorption bands of the clay framework.

We could clearly detect the strong NH_2 group stretching vibrations of adsorbed PZA on the H_2O vibrational bands of the clay framework after subtracting the vibrational bands
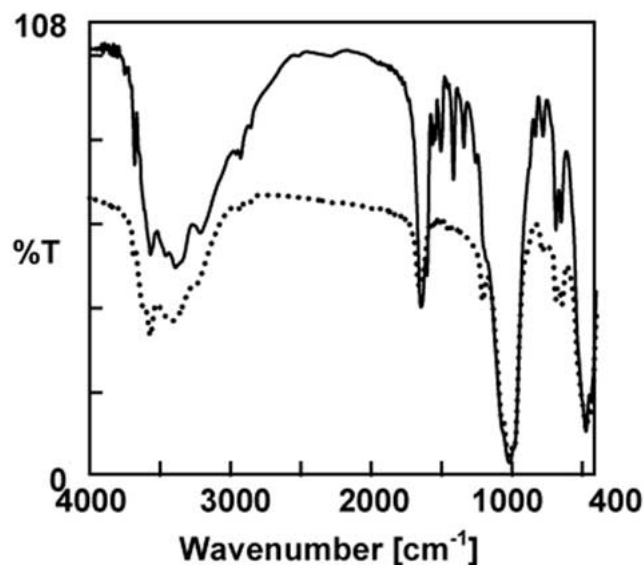

Figure 6. FT-IR spectra of 4APM treated (solid line) and untreated sepiolite (doted line).

of the natural clay. In contrast to the IR spectra of coordinated amino group containing compounds (e.g. [22]) we do not observe wavenumber reductions either in NH_2 group stretching vibrations or C-NH_2 stretching vibrational mode, in comparison to those of microcrystalline PZA (see Table 1). Contrarily these vibrational wavenumbers are found to be higher in wavenumber than the microcrystalline PZA. It must be noted that in the case of microcrystalline PZA H-bonding interaction between the neighbouring molecules through the NH_2 groups are well known [23]. On the other hand, as is clearly seen in Figure 4, we do not observe any blue shift in certain ring modes due to adsorption of PZA by clays (see Table 1), which are known to be very sensitive on coordination through the ring nitrogen. But the IR spectra of the adsorbed PZA show a negative shift of ν(C=O).

Table 1. The vibrational wavenumbers of adsorbed pyrazinamide (PZA)

Assignment[a]	PZA[b]	PZA on sepiolite	PZA on loughlinite	PZA on Mont.	PZA on Co-mont.	PZA on Cu-mont.
$\upsilon a(NH_2)$	3412 vs	3495[c] m	3478[c] m	–	–	–
		3463[c] w	3415[c] s	3448[c] m	3453[c] m	3452[c] m
$\upsilon s(NH_2)$	3368 sh	3416[c] s	3363[c] m	3365[c]	3364[c] m	3365[c] s
	3290 m	3391[c] m			3309[c] m	
$\upsilon(C=O)$ amide	1714 vs	1708 vs	1709 vs	–	–	–
		1681 s	1689 s	1689 vs	1686 vs	1686 vs
υ_{ring}	1581 s	1582 s	1582 m	1583 m	1582 m	1582 m
υ_{ring}	1525 m	1524 m	1524 m	1524 w	1525 w	1525 w
υ_{ring}	1479 m	1474 m	1475 m	1475 m	1475 m	1475 m
υ_{ring}	1437 m	1438 m	1437 m	1437 w	1438 m	1438 m
$\upsilon(C–N)$ (amide)	1378 vs	1378 s	1381 s	1382 s	1382 s	1381 s
Ring breath.	1025 s	1025[d] m	1024[d] s	1024[d] m	1025[d] m	1024[d] m

[a]Taken from Kalkar *et al.* [23].
[b]KBr disc of microcrystalline PZA taken from Akyuz [25].
[c]Obtained by subtraction of the clay bands.
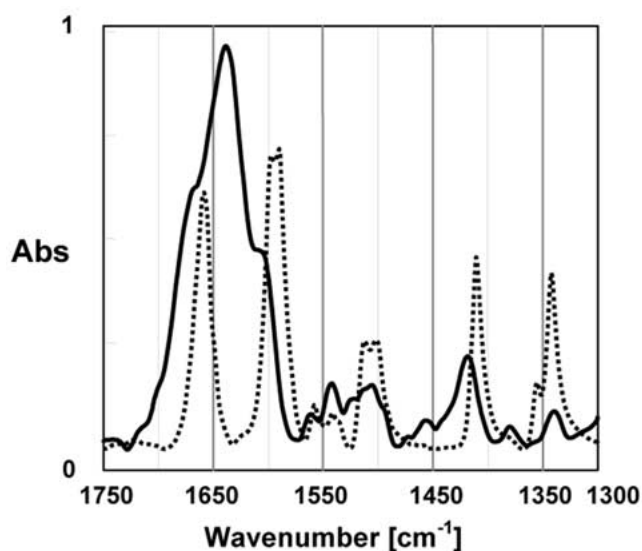[d]Obtained by band component analysis.

Figure 7. 1300–1750 cm^{-1} region ofthe FT-IR spectra of KBr discs of4APM treated montmorillonite (solid line) and polycrystalline 4APM (doted line).

The $\upsilon(C=O)$ mode was observed at 1714 cm^{-1} in the FT-IR spectrum of the KBr disk of PZA. In the IR spectra of PZA treated clays the $\upsilon(C=O)$ mode is observed around 1681–1709 cm^{-1}. Since due to the presence of intra hydrogen bonding interaction between the carbonyl oxygen and adjacent amino hydrogen in solid phase of PZA [23], the $\upsilon(C=O)$ mode of the free molecule is expected at higher wavenumber than that of solid phase, thus the real shift on the $\upsilon(C=O)$ vibration should be higher. Thus, we may conclude that coordination through the >C=O groups in the clay-organic complexes is implied by the FT-IR spectra.

In the case of adsorption of 4APM by clays, contrary to the vibrational results of adsorbed PZA, we observed upward shifts in frequency, on coordination sensitive ring modes of adsorbed 4APM, compared to the IR spectrum of microcrystalline 4APM (see Figure 7). The coordination-sensitive ring stretching modes of 4APM are observed 1604, 1563 and 1420 cm^{-1} in the IR spectra of 4APM-treated clays, whereas the corresponding modes are observed at 1594, 1558 and 1411 cm^{-1}, respectively, in the IR spectrum of polycrystalline 4APM $\{\Delta(\upsilon_{ads} - \upsilon_{solid}) = 10, 5$ and 9 cm^{-1}, respectively$\}$. On the other hand we also observed blue shift on the ring breathing mode of 4APM, which was observed at 988 cm^{-1} as a strong band, in the IR spectrum of polycrystalline 4APM: This mode was unfortunately obscured by the host vibrational modes of the clay structure, $[\upsilon(Si–O)]$, in the IR spectra of clays, however by band component analysis of the 940–1200 cm^{-1} region of the IR spectra of 4PM treated and untreated clays clearly indicated the presence of a ca. 1004 cm^{-1} band in the IR spectra of 4PM treated clays which was not present in those of untreated clays. This band is assigned to the ring breathing mode of adsorbed 4APM, thus the observed upward shift on this mode, due to adsorption, is $\{\Delta(\upsilon_{ads} - \upsilon_{solid})\}$ca. 16 cm^{-1}. In Figure 8, the results of band component analysis of the 940–1200 cm^{-1} region of the FT-IR spectra of untreated and 4APM treated Co-montmorillonites are given. On the other hand, the coordination effects through amino nitrogen on the NH$_2$ group vibrational wavenumbers of adsorbed 4APM were not observed: Although the NH$_2$ group stretching wavenumbers of adsorbed 4APM were obtained after subtracting the H$_2$O vibrational bands of the clay framework of the natural clay, we could clearly detect the C-NH$_2$ stretching mode around 1341 cm^{-1} in the IR spectra of 4APM treated clays, which is observed at 1342 cm^{-1} in the IR spectrum of solid 4APM. Based on the IR spectroscopic results, thus, we can conclude that adsorbed 4APM molecules are coordinated to either exchangeable cations or Levis acidic centers by one of the pyrimidine ring nitrogen lone pairs. The amino group nitrogen of 4APM does not take part in coordination, but amino group hydrogens may include in weak hydrogen bonding interaction, with
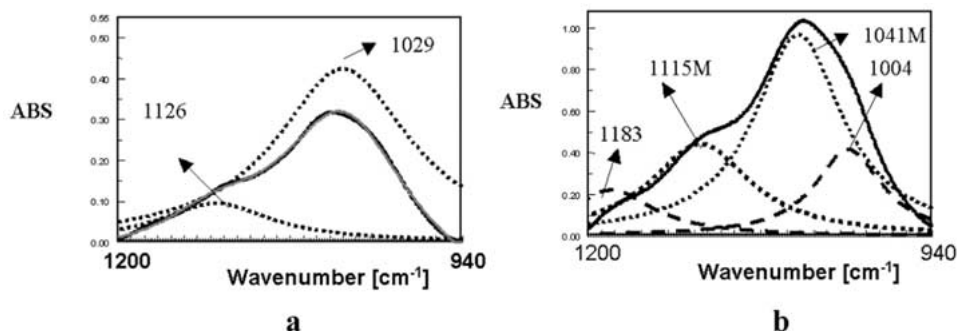
Figure 8. Band component analysis of untreated (a) and 4APM treated (b) Co-montmorillonites; M = vibrational bands belong to montmorillonite.
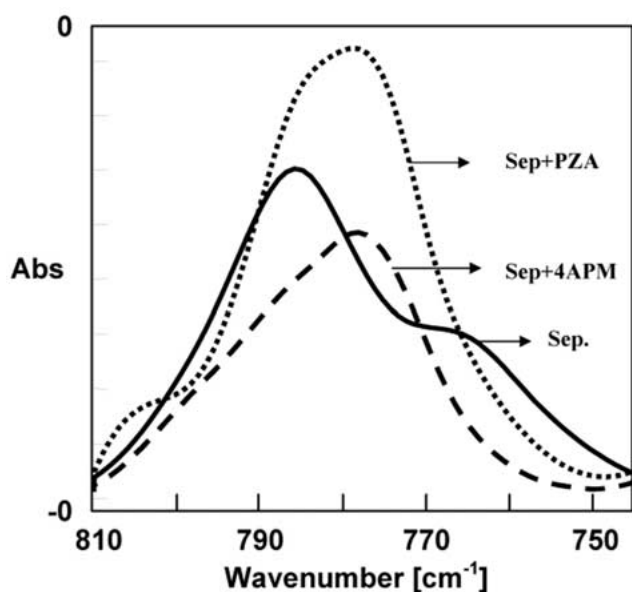

Figure 9. OH deformation region of natural sepiolite (solid line), together with PZA and 4APM treated sepiolites.

Table 2. OH group vibrations of PZA and 4APM treated sepiolites and natural sepiolite, in the IR spectra as obtained band component analysis

	Natural Sepiolite	Sepiolite + PZA	Sepiolite + 4APM
υ (OH) SiOH	3689 w	3684 m	3679 m
υ (OH) dioctahedral system	3627 s	3618 m	3620 m
υ (OH) coordinated water	3569 vs	3556 s	3567 s
υ (OH) zeolitic water	3417 vs br	3390 s br	3333 s br
	3226s br	3199 m br	3209 s br
$\delta(H_2O)$	1660 s	1664 s	1655 s
	1625 ms	1648 s	1638 s
OH deformations	978 vs	976 vs	977
OH deformations	785 m	779 w	778
OH deformations	766 m		
OH translation	690 s	689 s	688 m
OH translation	646 s	648 s	651 m

water molecules. It is worth to mention that ion-exchanged montmorillonites are found to adsorb the organic molecules slightly higher than natural montmorillonite.

In the case of sepiolite, it is well known that the broken Si-O-Si bonds of the terminal silica tetrahedra on the external surfaces compensate their residual charge by accepting a proton or hydroxyl and form Si–OH groups [4, 24]. Therefore the most probably binding sites for PZA or 4APM are surface hydroxyls and Levis acidic centers. The OH stretching mode of the Si–OH bond is observed around 3700 cm^{-1} (ν(OH)) and as a sharp band and OH deformation bands observed as a doubled at 766 and 785 cm^{-1}. If adsorbed organic molecule interacts with surface silanol groups these peaks must be altered. This is what we observed in the FT-IR spectrum of PZA or 4APM treated sepiolite in comparison to that of natural sepiolite. As seen in Figure 5, the Si–OH stretching vibration increased in intensity and decreased in value after adsorption of the organic molecules: This band shifts from 3689 cm^{-1} (for starting sepiolite) to 3679 cm^{-1} (for 4APM treated sepiolite) or 3684 cm^{-1} (for PZA treated sepiolite). The IR spectra of the OH deformation vibrations of natural and PZA and 4APM treated sepiolites are shown in Figure 9. The adsorption of PZA or 4APM shows a considerable alteration on OH deformation peaks of sepiolite structure. Thus, the spectroscopic results indicate that PZA or 4APM molecules adsorbed on sepiolite are coordinated surface hydroxyls by H-bonding interaction. In the case of PZA the interaction takes place through C=O group oxygen, whereas in the case of 4APM, through ring nitrogen lone pairs. In Table 2, the OH group vibrational wavenumbers of natural and PZA or 4APM treated sepiolites, as obtained by band component analysis, are given. Our values of the starting sepiolite are found to be in agreement to those reported absorption bands of sepiolite as obtained by band component analysis [26].

Conclusion

The interpretation of the IR spectral changes of the clays and adsorbents provides information on the nature and characteristics of the formed clay-organic complexes. The intercalation of PZA and 4APM within montmorillonite has been shown by X-ray diffraction to increase the interlayer spacing. IR spectroscopy indicates that sorbed PZA and 4APM molecules on natural and ion-exchanged montmorillonites are coordinated to exchangeable cations directly or indirectly through water bridges. Surface adsorption on sepiolite or loughlinite is resulted. Adsorbate molecules are proposed

to coordinate to surface hydroxyls by H-bonding interaction, either through C=O group oxygen (for PZA) or through pyrimidine ring nitrogen lone pairs (for 4APM).

Acknowledgement

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