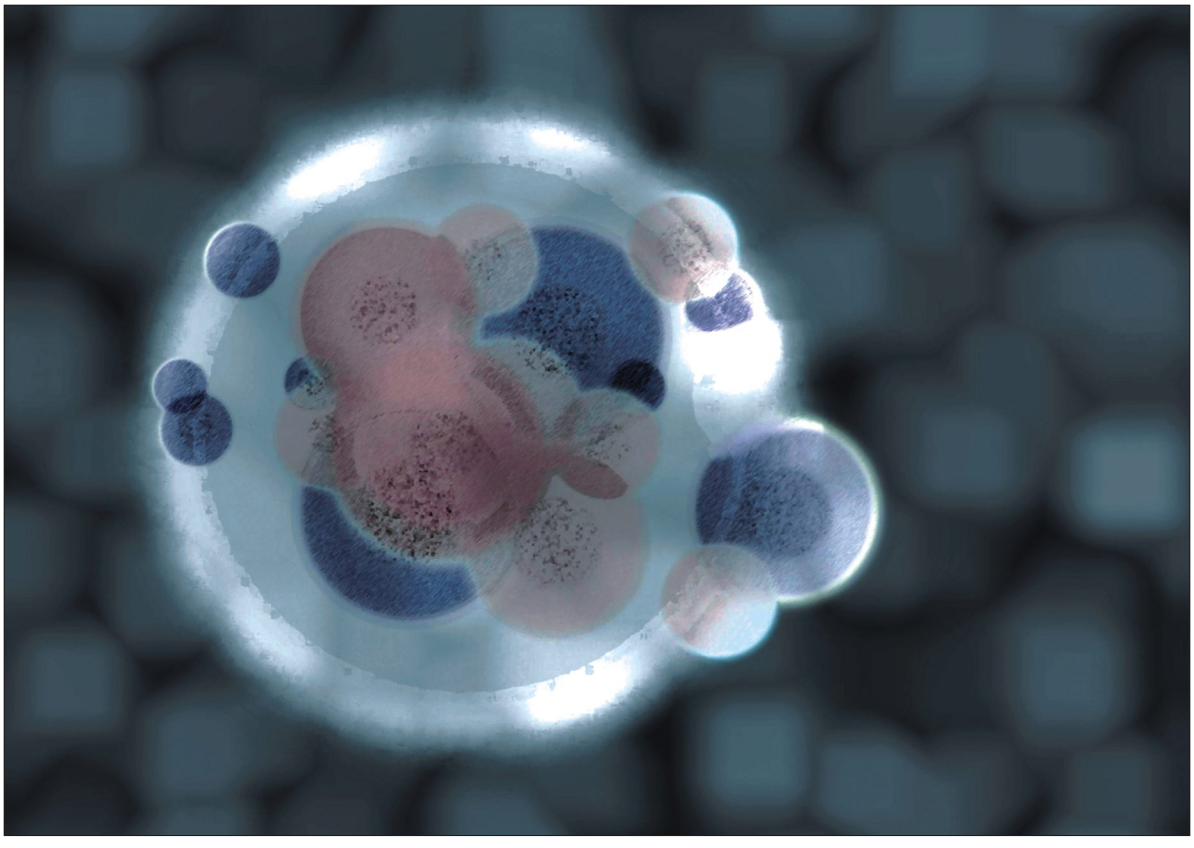

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IR and UV Spectral Investigations of 2-Aminodiphenyldihydropyrimidines

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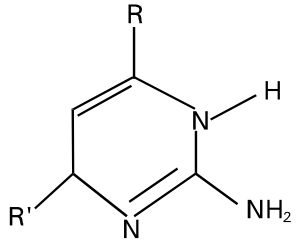
Abstract: The infrared spectroscopic investigations for the =CH and NH vibrations and the effect of substitution at different positions in the phenyl rings of 2-amino-4,6-diphenyl-3,6-dihydropyrimidines have been described. The CH stretchings were observed between 3070-3060 cm^{-1}. The observed frequencies differ for –NH bending and the =CH and –CH stretching vibrations, and the difference between the two frequencies is larger than the predicted differences between scaled frequencies. It has been observed that the substitution of phenyl rings with –OH, $-OCH_3$, $-NO_2$ and –Cl groups, further complicated the elucidation of the spectra. The electronic transitions in the UV spectra were observed to be hypsochromic (blue shift) when a powerful electron donor group is present in the heterocyclic nucleus. Other electronic transitions were observed in the ultraviolet spectra to check the presence of π-π * and n-δ transitions in these compounds.

Key words: Aminopyrimidines, IR, UV absorptions, Solvent shifts

Introduction

An interest in the purine and pyrimidine derivatives has been stimulated by the finding that they form a biologically and pharmacologically important group of compounds (Wang *et al.,* 1999). Several sulfur substituted pyrimidines have been found as clinically useful drugs. The position in which sulfur is introduced, enhances the biological activity, for instance, 2-thiouracil a potential medicine for antithyroid activity (Bandekar and Zundell, 1983). The synthesis and biological evaluation of 5-arylfuro[2,3-*d*]pyrimidines as novel dihydrofolate reductase inhibitors has been reported by Wahid *et al*. (1999). The pyrimidine carbocyclic nucleosides with a hydroxyamino group, are known to show potential antitumor and antiviral activity (Ogawa *et al*., 1999).

The thermoanalytical behavior of 2-amino- and 2-oxo-substituted pyrimidines (Shah *et al*., 2001) has been recently reported by us. In the present paper, we are reporting the infrared and UV spectral investigations of the amino substituted pyrimidines: 2-amino-4,6-(p-methoxy)diphenyl-3,6-dihydropyrimidine (**a**), 2-amino-6-(m-nitro)diphenyl-3,6-dihydropyrimidine (**b**), 2-amino-4-(o-hydroxyphenyl)-6-(o-chlorophenyl)-3,6-dihydropyrimidine (**c**), 2-amino-4-(o-hydroxyphenyl)-6-(p-dimethylaminophenyl)-3,6-dihydropyrimidine (**d**), and 2-amino-4,6-(p-dimethylamino)-diphenyl-3,6-dihydropyrimidine (**e**).



a	R = C_6H_5	R′ = H_3C-O-C_6H_4
b	R = C_6H_5	R′ = O_2N-C_6H_4
c	R = HO-C_6H_4	R′ = Cl-C_6H_4
d	R = HO-C_6H_4	R′ = $(CH_3)_2N$-C_6H_4
e	R = C_6H_5	R′ = $(CH_3)_2N$-C_6H_4

Fig. 1: Structures of 2-aminodiphenyldihydropyrimidines

Materials and Methods

The infrared and UV spectral investigations of the compounds (**a-e**) were undertaken in the laboratories of the Center of Excellence in Analytical Chemistry, University of Sindh, Jamshoro.

Chemicals and Glassware: The spectroscopic and analytical grade reagents were purchased from Merck/ Fluka (Germany). The glassware was obtained from Quick-fit (England) or Brand (Germany).

Synthesis of Compounds: Guanidine hydrochloride and substituted 1,3-diphenyl-2-propen-1-one were mixed in a molar ratio of (2: 1) in dry ethyl alcohol. The mixture was made alkaline using potassium hydroxide pallets, and then heated under reflux on a steam bath for 4-6 h. Alcohol was removed by distillation and residues were taken up in inert solvent (diethyl ether/ benzene), acidified and washed with water and dried with sodium sulfate. The solvent was evaporated to a thick residual mass, which was crystallized with ethanol. The crystallized material was Chromatographed on a silica gel column. The distillation of the eluent gave various yields of crystallized 2-amino-4,6-diphenyl-3,6-dihydropyrimidines (Rahman *et al*., 1994).

Elemental Analyzer: A Yanaco MT-3 CHN corder/analyzer equipped with a built-in printer and a recorder (Philips 8000) were employed to analyze samples for percent carbon, hydrogen and nitrogen. Each sample was analyzed in five replicates and standards (acetanilide and p-nitroaniline) were run before and after samples, in order to check the calibration and detection sensitivity of the instrument.

The results for percent C, H and N in the compounds **a-e** were found in conformity to the theoretical percent of these elements.

IR Spectrophotometer: A Hitachi 260-50 infrared Spectrophotometer was used to record spectra over 4000-250 cm^{-1} range. Polystyrene film was run prior to recording the sample spectra to check the wave number accuracy (± 2 cm^{-1}) of the instrument. Solids were examined

in as KBr pallet and discs were prepared in 1:50 (sample: KBr) ratio using Riken Power Hydraulic Press (Japan), and by applying a pressure of 400 kg/cm^2 for 30 sec.

UV-VIS-NIR Spectrophotometer: A Shimadzu UV-365 double monochromator recording Spectrophotometer with built-in microcomputer were used to record spectra over the range of 185-400 nm. The wavelength accuracy was ± 0.3 nm.

Results and Discussion

Infrared Absorptions

=CH and NH bending: The multifunctional compounds: a-e (Fig. 1) studied here, were elucidated in the infrared and ultraviolet spectra. The aryl group =CH valence oscillation is expected in the infrared spectra. The -CH stretching values for such compounds are observed at 3070-3060 cm^{-1}. The C_5H out-of-plane bending vibration at 680 cm^{-1} and bands observed at 670 and 630 cm^{-1} have been taken to represent this mode. The bands at 735-720 cm^{-1} have been assigned as due to the ring breathing mode (Nishimura *et al.*, 1981). Table 1 lists the infrared spectral bands for the compounds: a-e.

The observed frequencies in Table 1 differ for -NH bending and the =CH and CH$^-$ stretching vibrations in 2-amino-4,6-diphenyl-1,3-dihydropyrimidines. The difference between the two -NH stretching frequencies (ca. 50 cm^{-1}) is larger than the predicted difference between scaled frequencies.

The expected vNH band of 2-amino-4,6-diphenyl-1,3-dihydropyrimidines (in CCl_4) occur at 3335 cm^{-1} and the other at 3202 and 3142 cm^{-1}, involving the overtone of NH_2 bending. These values are both surprisingly low and their separation is very large, when compared with the aliphatic amine, like methylamine (in CCl_4), exhibits vNH asymmetric stretching at 3398 cm^{-1} and vNH_2 stretching at 3344 cm^{-1}. The preferred explanation was due to the fact that the two-NH stretching vibrations in our molecules do not couple, and one of them is substantially lowered in frequency by the intermolecular hydrogen bonding with the lone pair of -NH groups present in structures. It can be argued from the symmetry and band consideration that the N-H stretching region will be different for these conformations. The axis of the lone pair movement would be coincident with either two nitrogen available in the molecule. This will be perpendicular to the ring plane and thus deviated from their directions. Therefore, one can determine the direction of the dipole moment change for the symmetric and anti-symmetric NH_2 stretching relative to principal axis. The anti-symmetric stretching demonstrates that the amino group in our structures (Fig. 1) is orthogonal to the ring plane, with one amine-hydrogen above and below plane.

4,6-phenyl groups: The phenyl ring at 4- and 6-position in our compounds further complicated in the elucidation of spectra, because these rings are also substituted with OH^-, OCH^-_3,NO^-_2 and Cl^- groups. The vibrational assignments were observed in the region 1560-1550 cm^{-1} as absorptions of medium intensity for phenylalkene groups. Bellamy (1980) assigned a band at 1565 cm^{-1} for 1,3-diphenylpropenone which covers the phenylalkene stretching vibrations.

The position of such band is very sensitive to the substitution in the aromatic rings. Such vC=C bonds in the system bring about a Bathochromic shift in this band as expected. The presence of vOH group in 2-position to one of the phenyl ring shows a shift in stretching vibration at 1630 cm^{-1} from 1642 cm^{-1}. The substituent at 2- and 4-position helps the existence of resonance system, thereby shifting the vC=C stretching band to the lower frequency, whereas, a substituent at 3-position is not helpful in this respect. The

Table 1: Infrared spectral bands in 2-aminodiphenyldihydropyrimidines

Absorption band (cm^{-1})
2-amino-4,6-(p-methoxy)diphenyl-3,6-dihydropyrimidine (a)
3330 m –NH_2 group overtone bending, 2900 w asymmetric (CH) stretching, 1610 m 1,4-substituted phenyl ring stretching, 1565 sm aryl =CH vibration, 1540 sm and 1510 m (–N-H), 1460 st (=CH) bending, 1380 st v(CH_3), 1300 m, alkoxyphenyl vibration, 1245 m, 1175 m and 1110 sm v(-CH) stretching, 1030 m, CH_3 group rocking, 830 m (=CH-) out-of-plane deformation, 730 sm ring breathing, 630 sm aryl ring in-plane bending.
2-amino-6-(m-nitro)diphenyl-3,6-dihydropyrimidine (b)
3330 m –NH_2 group overtone bending, 2980 w asymmetric v(CH) stretching, 1685 m v(N-C), 1640 m v(N-C-N) bending, 1600 sm 1,3-substituted phenyl ring stretching, 1540 v(N-H), 1460 m (=CH-), 1365 m, 1040 m substituted aryl ring, 1000 sm and 955 m ring in-plane bending, 755 m out-of-plane deformation, 720 m v(CH) stretching, 640 sm aryl group in-plane bending.
2-amino-4-(o-hydroxyphenyl)-6-(o-chlorophenyl)-3,6-dihydropyrimidine (c)
3553 sm overtone of –NH_2 bending, 3210 m v(N-H), 3070 w asymmetric v(CH) stretching, 2975 sh symmetric v(CH), 1710 St N-C-N bending, 1630 m 1,2-disubstituted aryl group stretching, 1573 m v(=C-H)/ v(N-H), 1450 m ring stretching β(-NH), 1300 m phenyl ring stretching, 1155 m δ(=CH-C), 1070 m and 1055 1,2-disubstituted phenyl ring, 1020 m, 995 m δ(OH), 840 m, 755 m out-of-plane deformation, 720 m v(N-H), 700 m ring out-of-plane deformation, 650 m ring in-plane deformation, 590 m ring in-plane bending.
2-amino-4-(o-hydroxyphenyl)-6-(p-dimethylaminophenyl)-3,6-dihydropyrimidine (d)
3300 m and 3150 sm overtone of –NH_2 bending, 2950 w asymmetric v(-CH), 1605 m 1,2- and 1,4-disubstituted phenyl rings, 1565 m v(=C-H)/ v(N-H), 1460 st ring stretching β-(-NH), 1380 sm v(CH_3) rocking, 1170 m v(CH), 1000 m v(CH_3), 965 sm and 945 m δ(OH), 860 m, 855 m and 815 m δ(CH=CH), out-of-plane deformation, 725 m ring breathing, 645 m and 630 (=CH) out-of-plane bending.
2-amino-4,6-(p-dimethylamino)-diphenyl-3,6-dihydropyrimidine (e),
3265 sm, 3165 sm overtone of –NH_2 bending, 3000 st asymmetric v(-CH) stretching, 1615 m 1,4-disubstituted phenyl ring stretching, 1580 sm v(=C-H)/ v(-NH) stretching, 1460 st ring stretching β(NH), 1380 m v(CH_3) rocking, 1230 sm 1,4-disubstituted phenyl ring, 1110 m CH_3 rocking, 930 m v(CH), 850 m δ(=CH-CH) out-of-plane deformation, 725 sm v(N-H), 700 st ring breathing, 640 m and 625 m ring in-plane bending.

Key: st = strong, m = medium, sm = small, sh = shoulder, b = broad, δ = in-plane bending, β = out-of-plane bending

position of this band is very susceptible to the position and the nature of the substituent groups in the aromatic rings.

A number of medium to intense absorption peaks appear in this range which could be associated with the benzene ring vibrations. The position of these peaks, depends to some extent, upon the substitution. As there are two phenyl groups present at 4- and 6-position in our structures carrying substituents in different ways.

The effect of substitution on various positions of the phenyl ring could be s tudied. A band occurs in the range 1330-1390 cm^{-1} with the vOH deformation vibration of the phenolic group. Two strong peaks occur at 1635 ± 5 cm^{-1} and 1350-1365 cm^{-1}. In most of the cases, the second absorption band could be distinguished from a corresponding band due to the CH_3 symmetric deformation on the basis of its sharpness. An alkoxy group on an aromatic ring is shown to have two correlated bands assigned in 1210-1310 cm^{-1} and 1010-1050 cm^{-1} regions. The latter band however, is often missed on the account of its low intensity and also because this lies in the same absorption range as due to the aromatic vC-H in plane deformation vibration. The vC-H deformation vibration due to alkoxy group coincides with those of the methyl group and so could not be separated from the latter.

Ultraviolet Absorptions: The presence of out-of-plane transitions (n-π*) and π-π*) and in-plane transition (π-π* and n-δ*) is normally observed in various pyrimidines. The in-plane transitions are composed of π-π*, and n-δ* configurations and for lower energies less than 210 nm, the π-π* configuration prevails in such structures. The out-of-plane transitions occur at 295 nm (π-π*) and 255 nm (π-π*) and in-plane transitions are present at 243 nm and 213 nm in the pyrimidine bases. The observations for 270 nm and 240 nm regions are taken to represent the out-of-plane n-π* and π-π* transitions and the area around 220-200 nm corresponds to the in-plane n-π* and n-δ* transitions respectively.

The compounds which contain non bonding electrons having group such as OH^- and SH^-, there occurs a band below 210 nm which corresponds to n-δ* transition. It is interesting to note that during the present studies we also observed the n-δ* transitions in our compounds as hypsochromic (blue) shifted, as the solvent changed from methanol to water due to an increase in polarity. This feature suggests that the band is due to a transition of non bonding electron from lone pair of a nitrogen atom in the pyrimidine bases (Youseef, 1989).

The π-π* transitions undergo a bathochromic shift with increasing polarity. This can be described to the momentary polarization of the solvent by transition dipole of the solute. It is evident that there is a marked bathochromic shift in the π-π* transition of our 2-amino-4,6-diphenyl-1,3-dihydropyrimidines with increasing polarity of the solvent. Three absorption bands appear in the electronic spectra of 2-methylthiopyrimidine at 287 nm, 251 nm, and 251 nm. This is quite clear that the first two appear in the blue shifts region. An other similar compound, 2-mercaptopurine, exhibited an absorption peak at 330 nm of a longer wavelengths, a region in which the C = S group shows absorption maxima, and hence it is confirmed that the electronic transitions are hypsochromic (blue) shift when a powerful electron donor group is present in the heterocyclic nucleus (Table 1).

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