Transmission of Substituent Effect in Ethyl 2-Aroyl - and Ethyl 2-Arylcarbamoyl-4, 5-dimethyl-1, 2, 3, 6-tetrahydropyridazine-1-carboxylates : An Infrared and Theoretical Study

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Abstract. Nineteen ethyl 2-aroyl- (**1a** - **1h**) and ethyl 2-arylcarbamoyl-4, 5-dimethyl-1, 2, 3, 6-tetrahydropyridazine-1-carboxylates (**2a** - **2k**) were synthesized and their FTIR spectra in CCl_4 and $CHCl_3$ were measured in the regions of C=O, C=C and N-H stretching vibrations. The wave numbers of the C=O and N-H stretching vibrations as well as the integrated intensities of the N-H stretching absorption bands exhibit significant linear correlations with Hammett σ substituent constants. In the series **2** the substituent effects are transmitted to the esteric C=O group comparably or even more readily as to the nearest carbamoyl C=O groups. The analysis of the effects of the substituents, solvents and temperature as well as the results of PM3 calculations show that such an efficient transmission is possible when the molecules exist in a conformation possessing a quasiplanar arrangement of the (O)C-N-N-C(O)-N(H)-C_6H_4X system of five σ-bonds.

Introduction

Reaction of azo compounds with 1, 3-butadiene leads in a [4 + 2] cycloadition to tetrahydropyridazines (1). A lot of such syntheses are described in the literature but there are only a few using unsymmetrically substituted azo compounds (2 - 4). In an one - pot - reaction ethyl 2-aroyl or ethyl 2-arylcarbamoylhydrazino-1-carboxylates (5 - 7) are oxidized with lead (IV) acetate yielding non - isolated azo compounds which smoothly react with 2, 3-dimethyl-1, 3-butadiene giving ethyl 2-aroyl- (**1a** - **1h**) and ethyl 2-arylcarbamoyl-4, 5-dimethyl-1, 2, 3, 6-tetrahydropyridazine-1-carboxylates (**2a** - **2k**) used in this study (see Scheme 1).

Compounds **1** and **2** represent interesting systems containing conformationally and tautomerically flexible fragments attached to both nitrogen atoms of the tetrahydropyridazine ring, which itself could be conformationally flexible (8, 9). Neither the structural nor IR the spectral properties of such an extraordinary structural grouping have been reported so far.

The aim of the present work was therefore to study the FTIR spectra of compounds **1** and **2** in CCl_4 and $CHCl_3$ in the regions of C=O, C=C and N-H stretching vibrations and to compare the results with those of PM3 structural calculations.

Results and Discussion

The FTIR data of compounds **1** and **2** measured at room temperature in CCl_4 and $CHCl_3$ are listed in Tables 1 and 2.

Table 1. Wave Numbers of Stretching Vibrations (in cm^{-1}) for Series of Compounds **1**[a]

Compound	Solvent	$\nu(C=O)^1$	$\nu(C=O)^2$	$\nu(C=C)$
1a	CCl_4	1663.6 (54.7)	1723.7 (41.3)	1691.6 (3.1)
	$CHCl_3$	1648.9	1716.0	1690.1
1b	CCl_4	1663.3 (33.4)	1726.5 (31.6)	1691.7 (5.9)
	$CHCl_3$	1651.6	1716.2	1689.9
1c	CCl_4	1667.0 (31.0)	1727.1 (32.7)	1692.1 (4.4)
	$CHCl_3$	1653.9	1717.4	1689.9
1d	CCl_4	1668.0 (25.5)	1728.5 (30.4)	1692.2 (7.8)
	$CHCl_3$	1655.2	1718.3	1690.9
1e	CCl_4	1671.4 (32.5)	1729.6 (37.3)	1693.8 (5.3)
	$CHCl_3$	1658.0	1719.8	1690.9
1f	CCl_4	1667.6 (25.0)	1728.9 (33.2)	1692.6 (8.6)
	$CHCl_3$	1654.8	1719.5	1689.4
1g	CCl_4	1673.1 (31.9)	1731.7 (34.6)	1693.9 (6.4)
	$CHCl_3$	1662.2	1722.1	1692.2
1h	CCl_4	1672.3 (22.6)	1731.7 (31.2)	1693.3 (9.3)
	$CHCl_3$	1660.8	1722.6	1691.4

[a]Integrated intensities ($l\ mol^{-1}\ cm^{-2}$) are given in parentheses.

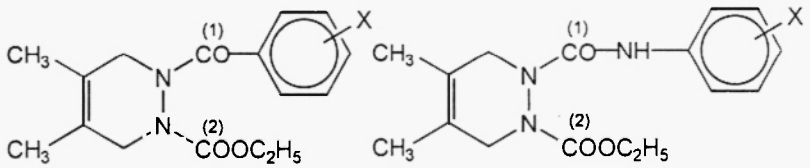
The assignment of the absorption bands to $\nu(C=O)^1$, $\nu(C=O)^2$ and $\nu(C=C)$ (see Scheme 1) in series **1** is rather trivial. However, it should also be noted that the integrated intensities of the C=C stretching absorption bands were much lower and the solvent effect ($CCl_4/CHCl_3$) was rather small compared to those of both C=O stretching absorption bands. In the series **2** the assignment of the $\nu(C=O)^2$ again was easy, however, to assign the bands $\nu(C=O)^1$ and $\nu(C=C)$ correctly we had to employ the analogy with the previously published IR spectral data for a series of N, N-dimethyl-N-arylureas as model compounds (10), the $CCl_4/CHCl_3$ solvent effect as well as the comparison integrated intensity values. The wave numbers of the N-H stretching vibration for series **2** were similar to of aforementioned N, N-dimethyl-N-arylureas (11). Table 2 shows also the effects of the temperature on the wave numbers of the characteristic stretching vibrations of parent compound **2e** measured in $CHCl_3$. It is evident that the N-H stretching vibration exhibit in both wave numbers and integrated intensities only a small temperature effect. In the case of the C=O stretching vibration of the ester group ($\nu(C=O)^2$) the temperature effect is somewhat higher, which is most probably connected with the conformational flexibility of the ethoxycarbonyl moiety. The observations mentioned above indicate that the occurrence of an intramolecular hydrogen bond between the N-H group and any electron - donating part of the molecule is improbable. The ^{13}C NMR spectra reveal (12) that compounds **2** do not undergo carbamoyl - iminohydroxy tautomeric changes and the rough structure of the molecules can be depicted as in Scheme 1.

The transmission of the substituent effects in both series **1** and **2** was assessed by using linear correlations with Hammett σ substituent constants (13). The results of the correlation analysis are given in Table 3. It is evident that for both series **1** and **2** (in CCl_4 and $CHCl_3$) significant wave number - σ correlations were obtained. The data for 2-substituted derivatives always exhibit more or less significant deviations from the straight lines and therefore were omitted from the correlations. The experimental $\nu(C=O)$ and $\nu(N-H)$ values for 2-CH_3 derivative **2b** are by 2 - 4 cm^{-1} and 8 - 11 cm^{-1} higher than expected from the correlations, which indicates that the 2 - substituted benzene ring is more twisted out of the coplanarity of the structure involved in an efficient transmission of substitutent effects. On the other hand for the 2 - chloro derivative **2k** quite an opposite shift is observed in the $\nu(N-H)$ wave numbers with regard

Table 2. Wave Numbers of Stretching Vibrations (in cm^{-1}) for Serries Compounds **2**[a]

Comp.	Solvent	ν(C=O)[1]	ν(C=O)[2]	ν(C=C)	ν(N-H)
2a	CCl_4	1700.6 (30.2)	1732.5 (31.6)	1687.2 (16.4)	3426.4 (5.3)
	$CHCl_3$	1674.1	1724.8	1692.3	3420.2
2b	CCl_4	1701.9 (36.0)	1733.3 (30.1)	1688.3 (13.4)	3437.1 (5.2)
	$CHCl_3$	1676.7	1725.3	1694.5	3429.7
2c	CCl_4	1700.7 (28.0)	1732.5 (33.2)	1687.4 (17.7)	3426.1 (5.3)
	$CHCl_3$	1674.2	1724.9	1692.2	3420.2
2d	CCl_4	1701.2 (29.1)	1733.0 (27.6)	1686.4 (16.8)	3424.8 (5.4)
	$CHCl_3$	1675.9	1724.8	1694.2	3418.9
2e	CCl_4	1701.3 (30.4)	1733.0 (26.2)	1686.3 (18.6)	3424.8 (5.4)
	$CHCl_3$	1676.9[b]	1725.0[c]	1694.4[d]	3418.6[e]
2f	CCl_4	1702.2 (36.2)	1735.3 (23.1)	1686.8 (25.6)	3422.9 (5.9)
	$CHCl_3$	1677.3	1727.3	1694.1	3417.3
2g	CCl_4	1702.0 (39.0)	1735.6 (27.0)	1687.5 (7.2)	3422.6 (5.8)
	$CHCl_3$	1677.0	1727.2	1693.8	3416.7
2h	CCl_4	1703.7 (33.4)	1737.5 (30.6)	1687.9 (8.8)	3420.1 (5.9)
	$CHCl_3$	1677.8	1728.7	1695.6	3414.5
2i	CCl_4	1698.4 (22.5)	1730.8 (30.8)	1685.1 (26.7)	3427.7 (5.0)
	$CHCl_3$	1673.4	1724.3	1692.9	3422.0
2j	CCl_4	1707.4 (25.8)	1740.4 (27.7)	1690.2 (13.9)	3413.5 (6.9)
	$CHCl_3$	1681.1	1732.5	1699.4	3407.6
2k	CCl_4	1703.0 (36.3)	1736.1 (33.8)	1687.0 (11.6)	3400.3 (5.9)
	$CHCl_3$	1678.6	1729.0	1695.9	3397.8

[a]Integrated intensities (l mol^{-1} cm^{-2}) are given in parentheses.[b]1670.8 at -50 °C, 1678.3 at 68 °C. [c]1714.8 at -50 °C, 1727.3 at 68 °C. [d] 1690.0 at -50 °C, 1695.3 at 68 °C. [e] 3473.8 at -44 °C, 3420.0 at 68 °C.



1a - 1h **2a - 2k**

X : **1a** - 4-OCH_3, **1b** - 4-CH_3, **1c** - H, **1d** - 4-F, **1e** - 2-F, **1f** - 4-Cl, **1g** - 3-NO_2, **1h** - 4-NO_2
2a - 4-CH_3, **2b** - 2-CH_3, **2c** - 4-C_2H_5, **2d** - 3-CH_3, **2e** - H, **2f** - 4-Cl, **2g** - 4-Br, **2h** - 3-Cl, **2i** - 4-OCH_3, **2j** - 4-NO_2, **2k** - 2-Cl

Scheme 1

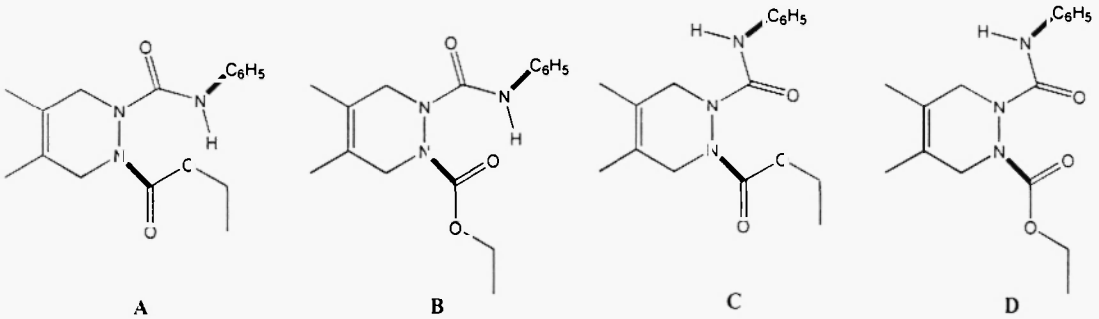
to the ν(N-H) vs. σ correlation straight line, i.e. the ν(N-H) values are by 16 - 17 cm^{-1} lower. This effect can be reasonably explained by intramolecular hydrogen bond between the N-H group and Cl atom. Similar examples of such a behaviour of 2-Cl derivatives were recently reported (14). Comparing the slopes ρ of the linear correlations ($y = \rho\sigma + q$) in Table 3 we can conclude that in the case of series **1** an usual transmission efficiency of substituent effects can be observed to the C=O[1] group, i.e. similar to that previously published for substituted N, N-dimethylbenzamides (15). However, when going to series **2** it can be asserted that the substitutent effects are transmitted to the esteric C=O group comparatively or even more efficiently as to the closer carbamoyl C=O group. This phenomenon suggests that compounds **2** must exist in a quasiplanar conformation of the bonds involved in the rut of the transmission of electronic effects to the more removed C=O group. It can also be stated that for the series **1** and **2** only the logarithm of the integrated intensities of the N-H stretching absorption bands (logA(N-H)) of series **2** in CCl_4 show quite a satisfactory correlation with σ substituent constants. Comparing the ρ constants for series **1** and **2** (see Table 3) the Jaffe's transmissive factor for NH group can be determined : $\pi'(NH) = \rho(C=O)^2 / \rho(C=O)^1$. The value of $\pi'(NH) = 0.91$ has been calculated for data in CCl_4 and $\pi'(NH) = 0.70$ for those in $CHCl_3$. The values determined above are in a good

Table 3. Correlation of Infrared Spectral Data with Hammett σ Substituent Constants for Series of Compound 1 and 2

Series	ν	Solvent	n	r	s	F	ρ	q
1	$\nu(C=O)^1$	CCl_4	7	0.967	0.93	72	7.88±0.92	1666.8
1	$\nu(C=O)^2$	CCl_4	7	0.989	0.39	224	5.76±0.38	1727.5
1	$\nu(C=O)^1$	$CHCl_3$	7	0.972	1.29	87	11.21+1.20	1653.2
1	$\nu(C=O)^2$	$CHCl_3$	7	0.995	0.29	500	6.45±0.29	1717.6
2	$\nu(C=O)^1$	CCl_4	9	0.966	0.69	97	7.20+0.73	1701.2
2	$\nu(C=O)^2$	CCl_4	9	0.993	0.37	510	8.89±0.39	1733.5
2	$\nu(C=O)^1$	$CHCl_3$	9	0.982	0.54	189	7.85±0.57	1725.7
2	$\nu(C=O)^2$	$CHCl_3$	9	0.966	0.65	98	6.83±0.69	1675.7
2	ν(N-H)	CCl_4	9	0.983	0.84	200	-12.63±0.89	3424.6
2	ν(N-H)	$CHCl_3$	9	0.978	0.96	152	-12.45+1.01	3418.7
2	$\log A(N-H)^b$	CCl_4	9	0.919	0.02	38	0.115±0.019	0.737

agreement with those published earlier (15) and show a significant solvent effect (CCl_4 / $CHCl_3$) due to the intermolecular hydrogen bond between the lone electron pair at the nitrogen atom of the NH group and the hydrogen atom of the $CHCl_3$ molecules.

To study the preferential conformation of compounds 2 and explain the efficient transmission of substituent effect from the substituted benzene ring to the esteric carbonyl group PM3 values were calculated with standard parametrization (16). The geometry was completely optimised. Considering the mutual orientation of the C=O bonds and the N-H bond four optimised conformations A - D can be obtained for the parent molecule 2e (see Scheme 2).



The dihedral angle γ is indicated by terminal bonds marked by thick lines.

Scheme 2

The optimised geometry showed that the tetrahydropyridazine ring has a semi - chair conformation which is in an agreement with earlier reported results (8, 9). The theoretical PM3 data (bond orders and charge densities) for conformation A of compounds 2 are listed in Table 4. The statistical treatment of linear correlations (y = px - q) between the IR characteristics and PM3 data of conformation A for compounds 2 is given in Table 5. The remaining PM3 data for conformations B - D and also the correlations of IR spectral characteristics with these data are missing in this paper, because the latter correlations are statistically unsignificant. Consequently, the preference of the conformations B - D is rather improbable. On the other hand. all IR spectral characteristics for conformation A exhibit very convincing statistical results in correlations with PM3 data (see Table 5). This indicates that the conformation A is the preferential one. In all correlations only the data for both 3- and 4- substituted compounds were employed. for the similar reason as in the ν(C=O) vs. σ and ν(N-H) vs. σ dependences. A question could be arisen why the conformation A is the most advantageous one. The selected PM3 geometrical and thermodynamical parameters of four considered conformations A - D of compound 2e obtained from optimised geometry were also calculated.The ΔH_f values indicate

Table 4. PM3 Atomic Charge Densities and Bond Orders for $C=O^1$, $C=O^2$ and N-H of Conformation **A** for Series **2**

Compound	$-q(O)^1$	$p(C=O)^1$	$-q(O)^2$	$p(C=O)^2$	q(H)	p(N-H)
2a	0.379	1.7634	0.387	1.7749	0.079	0.9582
2b	0.373	1.7728	0.384	1.7783	0.084	0.9553
2c	0.378	1.7641	0.387	1.7749	0.079	0.9582
2d	0.377	1.7652	0.386	1.7752	0.080	0.9580
2e	0.378	1.7639	0.386	1.7751	0.080	0.9581
2f	0.377	1.7649	0.385	1.7764	0.081	0.9580
2g	0.377	1.7641	0.384	1.7768	0.081	0.9575
2h	0.377	1.7648	0.385	1.7767	0.082	0.9577
2i	0.380	1.7618	0.387	1.7748	0.078	0.9585
2j	0.372	1.7675	0.379	1.7817	0.087	0.9556
2k	0.378	1.7639	0.385	1.7758	0.088	0.9522

Table 5. Correlation of Infrared Spectral Data with Theoretical Parameters of Conformation **A** for Series of **2**

ν	x	Solvent	r	s	F	ρ	q
$\nu(C=O)^1$	$q(O)^1$	CCl_4	0.964	0.71	93	1136.81±117.86	2130.90
$\nu(C=O)^1$	$p(C=O)^1$	$CHCl_3$	0.868	1.26	21	1348.14±291.41	-702.26
$\nu(C=O)^1$	$q(O)^1$	$CHCl_3$	0.911	1.05	34	1018.79±174.62	2060.83
$\nu(C=O)^2$	$p(C=O)^2$	CCl_4	0.920	1.25	39	1252.15+200.90	-489.66
$\nu(C=O)^2$	$q(O)^2$	CCl_4	0.925	1.22	42	1194.75±185.30	2194.49
$\nu(C=O)^2$	$p(C=O)^2$	$CHCl_3$	0.967	0.72	102	1175.06±116.28	-360.63
$\nu(C=O)^2$	$q(O)^2$	$CHCl_3$	0.970	0.70	112	1118.62±105.91	2157.28
ν(N-H)	p(N-H)	CCl_4	0.952	1.41	68	4865.16±590.57	-1236.44
ν(N-H)	q(H)	CCl_4	0.984	0.81	220	-1741.98±117.45	3563.69
ν(N-H)	p(N-H)	$CHCl_3$	0.960	1.27	83	4861.90±533.48	-1239.20
ν(N-H)	q(H)	$CHCl_3$	0.987	0.74	259	-1729.91±107.84	3556.84

that there are no significant differences between the stabilities of conformers **A** - **D** (5 kJ mol^{-1}). The interatomic distances (0.378 - 0.602 nm) between the oxygen atom of the esteric C=O group and the hydrogen atom of the N-H group show that no intramolecular hydrogen bond can be formed in conformations **A** - **D**, which is consistent with results of IR spectral temperature experiments discussed above. Finally, the dihedral angle γ between the planes of the (O)C-N and N(H)-C_6H_5 bonds was selected as a measure of coplanarity in the system of five σ-bonds : (O)C-N-N-C(O)-N(H)-C_6H_5. The value of γ calculated for **A** was 28°, for **B** 36°, for **C** 47° and for **D** 80°, reveals that the conformation **A** has the most planar arrangement of σ-bonds in the aforementioned system, which is in accordance with the efficient transmission of substituent effects to the esteric group assessed by IR spectral data.

Experimental

Compounds of series **1** and **2** were synthesised by using the following general procedure: A solution of lead (IV) acetate (25 mmol) in CH_2Cl_2 (50 cm^3) was added to a stirred and cooled (ice - water) suspension of corresponding ethyl 2-aroyl- or ethyl 2-arylcarbamoylhydrazine-1-carboxylate (25 mmol) in CH_2Cl_2 (100 - 200 cm^3) and 2, 3-dimethyl-1, 3-butadiene (25 mmol). After 2h, stirring is continued at room temperature until the yellow or orange - red colour disappeared (4 - 24 h). The solid formed is collected by filtration and the solvent washed with water, 0.1 N NaOH and 0.1 N HNO_3. After drying with Na_2SO_4 the solvent is removed and the residue crystallized from ethanol, ethanol-water or ethanol/n-hexane. The melting points (°C) / yields (%)of newly prepared compounds are : **1a** - 101-104/68, **1b** - 121-124/78, **1c** - 64-66/36, **1d** - 104-106.5/56, **1e** - 101-104/41, **1f** - 124-127/31, **1g** - 88-91.5/24, **1h** - 105-108.5/45, **2a** -

145-147/50, **2b** - 107-109/77, **2c** - 129-131.5/57, **2d** - 103-105/82, **2e** - 146-148.5/89, **2f** - 169-171/61, **2g** - 170-175/57, **2h** - 144-151/56, **2i** - 133-135/72, **2j** - 191-194/52, **2k** 55-65/76. The compositions of the compounds were in satisfactory agreement with the results of elemental analysis (C, H, N, Cl, Br). The rough structures of substances were confirmed using ^{1}H NMR, ^{13}C NMR and MS spectra (12).

The FTIR spectra were measured on a Bruker IFS25 spectrometer at room temperature using NaCl cells of 0.5 and 3.2 mm thickness. The concentrations of solutions varied in the range of 1 - 5 mg cm^{-3} in both solvents CCl_4 and $CHCl_3$ (Uvasol, Merck). Peak positions were determined with an accuracy of ± 0.1 cm^{-1} after deconvolution and separation of absorption bands in the region of C=O and C=C vibrations. The band positions were fitted using Lorenz-Gaussian sum functions. The integrals of the separated curves were taken as a measure for the concentration. The spectra of parent compound **2e** were measured at different temperatures using a standard low temperature equipment and 1.0 mm thick cells.

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