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Saturated Heterocycles, 68[1]
Application of the *Seth-Paul-Van Duyse* Equation, IX[2]
The C = O Stretching Frequencies and Substituent Effects in 5,6-Polymethylenepyrimidin-4(3*H*)-one Derivatives

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The C = O stretching frequencies of 32 5,6-polymethylenepyrimidin-4(3H)-one (**1 a**–**1 w**) and *cis*-5,6-polymethylene-5,6-dihydropyrimidin-4(3*H*)-one (**2 a**–**2 h**) derivatives were measured in tetrachlormethane and in chloroform and correlated with the substituent constants X^+ (R) in the sense of the modified and extended *Seth-Paul-Van Duyse* equation. It was found that the C = O stretching frequency and the transmission of substituent effects through the heterocyclic ring are significantly influenced by the size of the fused hydrocarbon ring. Evidence was obtained that in molecules linked by intermolecular hydrogen bonds the substituent effects are transmitted to the C = O group predominantly via the C = N—C = C part of the pyrimidinone ring. In the free molecules the transmission of substituent effects takes place mainly through the NH group.

(Keywords: C = O Stretching frequencies; 5,6-Polymetylenepyrimidin-4(3 H)-ones; Seth-Paul-Van Duyse equation; Substituent effects)

Gesättigte Heterocyclen, 68. Mitt.: Anwendung der Seth-Paul-Van Duyse-Gleichung, IX. Die C = O-Streck-Frequenzen und Substituenteneffekte bei 5,6-Polymethylenpyrimidin-4(3H)-on Derivaten

Es wurden die C = O-Streck-Frequenzen von 32 5,6-Polymethylenpyrimidin-4(3*H*)-onen (**1 a**—**1 w**) und *cis*-5,6-polymethylen-5,6-dihydropyrimidin-4(3*H*)-onen (**2 a**—**2 h**) in CCl_4 und $CHCl_3$ gemessen und mit den Substituentenkonstanten X^+ (R) im Sinn der modifizierten und erweiterten *Seth-Paul-Van Duyse*-Gleichung korreliert. Es wurde festgestellt, daß die C = O-Streck-Frequenzen und die Übertragung von Substituenteneffekten durch den heterocyclischen Ring von der Größe des kondensierten Kohlenwasserstoffringes signifikant beeinflußt werden. Es konnte belegt werden, daß in Molekülen, die mit Wasserstoffbrücken verbunden sind, die Substituenteneffekte vorwiegend über den C=N—C=C-Teil des Pyrimidinonringes zur C=O-Gruppe übertragen werden. In den freien Molekülen erfolgt die Übertragung der Substituenteneffekte hauptsächlich über die NH-Gruppe.

Introduction

Our preceding papers[2—9] dealt with the application of the modified and extended *Seth-Paul-Van Duyse* equation (1)[3] correlating the C=O stretching frequencies of compounds R^1—CO—R^2 with substituent constants X^+ (R^1) and X^+ (R^2) of structural fragments R^1 and R^2:

$$\nu(\mathrm{C=O}) = \rho\,[X^+ (R^1) + X^+ (R^2)] + q \qquad (1)$$

where ρ and q stand for the slope and intercept of the linear correlation, respectively, having a similar physical meaning as in the case of well known *Hammett* equation.

Recently *Dinya* et al.[10] investigated the infrared spectra and transmission of substituent effects in E-3-arylideneflavones and pointed out the possibility of application of the substituent constants X^+ (R) of the modified and extended *Seth-Paul-Van Duyse* equation in correlation with the ν(C=O) values of compounds containing an endocyclic C=O group as part of the six-membered heterocyclic ring.

The purpose of the present communication was to apply the modified and extended *Seth-Paul-Van Duyse* equation (1) to further series of compounds containing an endocyclic C=O group and to investigate the transmission of substituent effects in these systems. Therefore, the C=O stretching frequencies of 5,6-polymethylenepyrimidin-4(3*H*)-ones (**1a**–**1w**) and *cis*-5,6-polymethylene-5,6-dihydropyrimidin-4(3*H*)-ones (**2a**–**2h**) were measured and correlated with the constants of X^+ (R) of the substituents R.

Experimental

The preparation, purification and properties of the compounds under investigation (**1a**–**1w** and **2a**–**2h**) were described earlier[11, 12].

The infrared spectra of CCl_4 and $CHCl_3$ solutions of the compounds were taken on a Zeiss 75 IR Specord grating spectrophotometer at room temperature, using NaCl cells 0.1, 1.0 and 10 mm in thickness. The concentrations of the measured solutions were chosen to give absorptions between 70% and 75%. Peak positions were determined by averaging the results of three measurements and are believed to be accurate to $\pm 0.5\,\mathrm{cm}^{-1}$. The instrument calibration was verified by using water vapor and indene standard spectra.

Results and Discussion

The C=O *Stretching Frequencies*

The C=O stretching frequencies of the pyrimidinones **1a**–**1w** and dihydropyrimidinones **2a**–**2h**, measured in $CHCl_3$ and dilute CCl_4 solutions, are listed in Table 1.

Table 1. *The* C=O *stretching frequencies (in cm*$^{-1}$*) and the substituent constants* X^+ *(R) for 5,6-polymethylenepyrimidin-4(3H)-one derivatives of type* **1** *and* **2**

Compound	R	CCl_4		$CHCl_3$	X^+ (*R*)
		$\nu(C=O)_b$	$\nu(C=O)_f$	$\nu(C=O)_b$	
1a	C_6H_5	1 658.5	1 694.0	1 656.5	1.070
1b	4-BrC_6H_4	1 659.0	1 693.5	1 657.5	1.113
1c	3,4-$(OCH_3)_2C_6H_3$	1 657.0	1 680.0	1 653.5	0.903
1d	3,4-$(OCH_3)_2C_6H_3CH_2$	1 661.5	1 687.5	1 661.5	1.662
1e	4-ClC_6H_4	1 659.0	1 688.5	1 657.0	1.103
1f	C_6H_5	1 646.0	1 681.5	1 643.0	1.070
1g	4-ClC_6H_4	1 646.5	1 683.5	1 645.0	1.103
1h	4-BrC_6H_4	1 646.5	1 683.5	1 643.0	1.113
1i	3,4-$(OCH_3)_2C_6H_3$	1 644.0	1 678.0	1 641.0	0.903
1j	4-$ClC_6H_4CH_2$	1 650.5	1 682.0	1 650.0	1.678
1k	3,4-$(OCH_3)_2C_6H_3CH_2$	1 650.0	1 679.5	1 650.0	1.662
1l	3-ClC_6H_4	1 646.5	1 682.5	1 645.0	1.172
1m	C_6H_5	1 640.0	1 672.0	1 637.5	1.070
1n	3,4-$(OCH_3)_2C_6H_3$	1 638.0	1 666.0	1 634.5	0.903
1o	3-ClC_6H_4	1 642.0	1 673.0	1 640.0	1.172
1p	$C_6H_5CH_2$	1 645.5	1 671.0	1 645.5	1.675
1q	$(C_6H_5)_2CH$	1 645.5	1 672.0	1 645.0	1.542
1r	C_6H_5	1 643.0	1 672.5	1 640.0	1.070
1s	4-ClC_6H_4	1 641.5	1 673.0	1 639.5	1.103
1t	4-$OCH_3C_6H_4$	1 641.0	1 670.0	1 637.0	0.891
1u	$(C_6H_5)_2CH$	1 646.5	1 675.0	1 646.0	1.542
1v	3-ClC_6H_4	1 641.5	—[a]	1 639.5	1.172
1w	$C_6H_5CH_2$	1 646.5	1 673.0	1 649.5	1.675
2a	3-ClC_6H_4	1 695.5	1 716.5	1 701.0	1.172
2b	3-$CH_3C_6H_4$	1 695.5	1 714.5	1 701.0	1.060
2c	3-$CF_3C_6H_4$	1 697.0	1 720.0	1 702.0	1.201
2d	3-FC_6H_4	—[b]	1 721.0	1 710.0[c]	1.160
2e	3-ClC_6H_4	1 698.0	1 724.0	1 703.0	1.172
2f	3-BrC_6H_4	1 698.5	1 724.5	1 703.0	1.172
2g	3-$CH_3C_6H_4$	1 698.0	1 720.5	1 703.0	1.060
2h	3-$CF_3C_6H_4$	1 698.5	1 726.0	1 703.5	1.201
2i	C_4H_3O[d]	1 699.5	1 726.0	1 704.5	1.307[e]

[a] The $\nu(C=O)_f$ absorption band was not observed.
[b] The $\nu(C=O)_b$ absorption band was not observed.
[c] The absorption band corresponds to $\nu(C=O)_f$.
[d] 2-Furyl.
[e] For the O,O-*cis* conformation of the 2-furyl group.

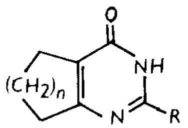
The infrared spectra of CCl_4 solutions of both series of compounds **1** and **2** exhibit two well resolved absorption bands in the C=O stretching region (1 730–1 640 cm^{-1}). The frequency separation between the two maxima is 23.0–37.0 cm^{-1} and 19.0–27.5 cm^{-1}, for series **1** and **2**, respectively. The intensity ratio of the two bands varies significantly as the concentration and polarity of the solution changes.

In harmony with expectations the pyrimidinones **1** and their dihydro derivatives **2** in CCl_4 and $CHCl_3$ solutions occur in equilibrium mixtures of free and intermolecularly hydrogen bonded molecules. Thus, the higher-frequency band, $\nu(C=O)_f$, can be assigned to the free C = O group and the lower-frequency one, $\nu(C=O)_b$, to the hydrogen-bonded C = O group in the structure of cyclic dimers **3**.

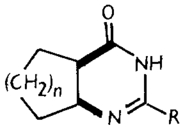
An evidence was obtained also by X-ray diffraction analysis[13], that 2-phenyl-*cis*-5,6-tetramethylene-5,6-dihydropyrimidin-4(3*H*)-one (**2**, $n = 2$, $R = C_6H_5$) exists in the structure **3**, containing intermolecular hydrogen bonds.

It is evident from Table 1 that the $\nu(C=O)$ values of both the free and the hydrogen bonded C = O groups of the polymethylenepyrimidinones **1** in the case of 2-phenyl derivatives (**1 a**, **1 f**, **1 m** and **1 r**) are influenced by the size of the fused hydrocarbon ring:

$$\nu(C=O)_{n=1} > \nu(C=O)_{n=2} > \nu(C=O)_{n=4} \gtrapprox \nu(C=O)_{n=3}$$



1a – 1e : n = 1
1f – 1l : n = 2
1m – 1q : n = 3
1r – 1u : n = 4
1v – 1w : n = 5



2a – 2c : n = 1
2d – 2i : n = 2

Such a decrease in C = O stretching frequency with increasing size of the fused ring can be assigned to changes in hybridization[14]. In the smaller fused hydrocarbon rings of compounds **1** the C—C bonds become enriched in p-component, diminishing the p-character of the C = C bond. Since the C = C bond occurs in both the hydrocarbon and the heterocyclic rings and is directly conjugated with the C = O group, the above change in hybridization results in a significant alteration of the C = O stretching frequency. The C = O stretching frequencies of the 5,6-hexa-($n = 4$), and 5,6-pentamethylenepyrimidinone derivatives ($n = 3$) are close to those of simple pyrimidin-4(3*H*)-ones without a fused hydrocarbon ring[15]. The same is also true for the $\nu(C=O)$ values of some 5,6-decamethylene derivatives (**1**, $n = 8$). In the tri- ($n = 1$) and tetramethylene derivatives ($n = 2$) (in CCl_4) the frequency $\nu(C=O)_f$ rises by 12.5 cm^{-1} and 9.5 cm^{-1}, respectively. It can be supposed that such a change is probably connected with a significant deformation of the valence angles in the heterocyclic part of compounds **1**. A similar phenomenon is observable for *cis*-5,6-polymethylene-2,3,5,6-tetrahydro-1,3-oxazin-4-ones[16, 17] by X-ray diffraction analysis.

On the other hand, in the *cis*-5,6-polymethylene-5,6-dihydropyrimidin-4(3*H*)-ones (**2**) the change in the size of the fused hydrocarbon ring causes a much smaller variation in the C=O stretching frequency. On passing from the tri- ($n = 1$) to the tetramethylene ($n = 2$) derivatives, the $\nu(C=O)_f$ values (in CCl_4) rise only by 6.0–7.5 cm^{-1}. The smaller effect of fused hydrocarbon ring on the C=O stretching frequency of the dihydropyrimidinones **2** is evidently caused by the lack of conjugation between the C=O group and the hydrocarbon ring.

Transmission of Substituent Effects

To evaluate the effects of substituents *R* on the C=O stretching frequencies in series **1** and **2**, we used the substituent constants X^+ (*R*) of the modified and extended *Seth-Paul-Van Duyse* equation[3]. The reason for this was that the investigated pyrimidinones **1** contained both aromatic and aliphatic substituents *R*, which cannot be described by a simple *Hammett* or *Brown*-type correlation between the $\nu(C=O)$ values and the substituent constants.

The X^+ (*R*) constants of substituents *R* for compounds **1** and **2** were taken from earlier communications[2, 3, 18] or calculated according to the equations published in paper[18] (given in Table 1).

The stretching frequencies of hydrogen bonded C=O group, $\nu(C=O)_b$, for the series of pyrimidinones **1** ($n = 1, 2, 3$ and 4) in both solvents CCl_4 and $CHCl_3$ correlate satisfactorily with the X^+ (*R*) values of substituents *R* according to equation (2):

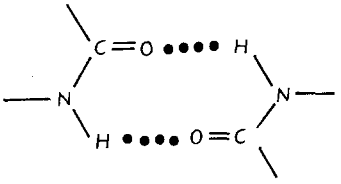
$$y = \rho X^+(R) + q \qquad (2)$$

The results of statistical treatment of these correlations are summarized in Table 2.

The slope ρ of the linear correlation $\nu(C=O)_b$ vs. X^+ (*R*) for both CCl_4 and $CHCl_3$ solutions increases in the same sequence as the experimental $\nu(C=O)$ values for 2-phenyl derivatives of compounds **1** decrease:

$$\rho n=1 < \rho n=2 < \rho n=4 < \rho n=3$$

This indicates that not only the C=O stretching frequency, but also the transmission of substituent effect through the pyrimidinone ring is influenced by the size of the fused hydrocarbon ring. On passing from smaller rings to larger ones, the transmission of substituent effects becomes more efficient, which is undoubtely connected with a change in the hybridization of the carbon atom orbitals in the small hydrocarbon



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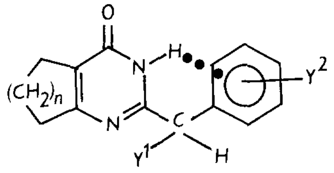

$Y^1 = H;\ C_6H_5$

$Y^2 = H;\ 4\text{-}Cl;\ 3,4\text{-}(OCH_3)_2$

4

rings, resulting in an increase of p-character of the C=C bond conjugated with the C=O group. Thus, it can be concluded from the above results that in pyrimidinones **1** linked by intermolecular hydrogen bond (**3**) the transmission of the substituent effects to the C=O group takes place predominantly via the C=N—C=C part of the molecule. Further evidence for this is the fact that the $\nu(C=O)_b$ values for the dihydropyrimidinones **2**, having no direct conjugation between the C=O group and the substituted part of the molecule, are influenced only slightly by the substituent effects (see data in Table 1).

In contrast, the stretching frequencies of the free C=O group, $\nu(C=O)_f$, in compounds **2** show a tendency to correlate with the constants $X^+ (R)$ of substituents R. However, because of the small number of available compounds, the results were evaluated statistically only for the tetramethylene derivatives ($n = 2$).

Similarly, in the case of compounds **1** the correlations $\nu(C=O)_f$ vs. $X^+ (R)$ were not evaluated statistically for all series, because the $\nu(C=O)$ values of compounds containing substituents of types $R = CH_2Ar$ and $R = CHAr_2$ deviate markedly from the straight lines. The cause of these deviations may be the existence of structure **4**, possessing an intramolecular hydrogen bond between the NH group and the π-electrons of the benzene ring.

Table 2. *Statistical treatment of linear correlations according to Equ. (2) for series of compounds* **1** *and* **2**

Series	n	Solvent	y	r^a	ρ	q	s^b	i^c
1	1	$CHCl_3$	$\nu(C=O)_b$	0.949	8.83	1646.9	0.98	5
1	2	$CHCl_3$	$\nu(C=O)_b$	0.980	11.30	1631.2	0.77	7
1	3	$CHCl_3$	$\nu(C=O)_b$	0.987	14.45	1622.1	0.89	5
1	4	$CHCl_3$	$\nu(C=O)_b$	0.995	13.73	1624.8	0.48	4
1	1	CCl_4	$\nu(C=O)_b$	0.973	5.48	1652.6	0.43	5
1	2	CCl_4	$\nu(C=O)_b$	0.988	7.51	1637.8	0.39	7
1	3	CCl_4	$\nu(C=O)_b$	0.979	10.03	1629.4	0.78	5
1	4	CCl_4	$\nu(C=O)_b$	0.952	8.55	1633.6	0.93	4
1	2	CCl_4	$\nu(C=O)_f$	0.902	20.27	1660.1	1.14	5
2	2	CCl_4	$\nu(C=O)_f$	0.807	24.43	1694.9	1.58	6

[a] Correlation coefficient.
[b] Standard deviation.
[c] Number of compounds used in correlation.

In spite of this, the tendencies of the correlations $\nu(C=O)_f$ vs. X^+ (R) for compounds **1** and **2**, for which anomalously high values of constant ρ can be expected (see Table 2), indicate that in the free molecules of the pyrimidinone and dihydropyrimidinone derivatives the substituent effects are transmitted mainly through the NH group.

In conclusion, it can be stated that the modified and extended *Seth-Paul-Van Duyse* equation is well applicable to the endocyclic C=O group in pyrimidinone derivatives and can be used advantageously for investigations of the transmission of substituent effects through six-membered heterocyclic systems.

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