^{13}C-NMR SPECTRA OF AZACHALCONES

Tibor LIPTAJ[a], Vladimír MLYNÁRIK[b], Milan REMKO[c], Ján ĎURINDA[c]
and Jozef HEGER[c]

[a] *Central NMR Laboratory,*
Slovak Institute of Technology, 880 37 Bratislava,
[b] *Czechoslovak Institute of Metrology, 834 22 Bratislava and*
[c] *Pharmaceutical Faculty, Comenius University, 880 34 Bratislava*

Received May 19th, 1980

^{13}C-NMR spectral parameters were obtained for chalcone and fourteen its aza- and diazaanalogues. Relative conformation of the carbonyl group with respect to the double bond was studied using changes in $^3J(C_{(1')}—H_\alpha)$ and PCILO method. PCILO calculations together with experimental results show that with 2'-, 3'-, and 4'-azachalcones the *s-cis* isomer is the most stable form. Whereas the molecule of 2'-azachalcone is planar or nearly planar, in 3'- and 4'-azachalcones the carbonyl group and the olefinic bond planes make angle of 45°.

Physico-chemical properties of azachalcones were studied intensively using various experimental methods[1-4]. ^{1}H-NMR spectra of these compounds were also studied[1,5,6]. It was found that similarly to chalcone itself, the more stable forms of azachalcones are their *trans*-isomers. The effect of aromatic solvents on chemical shifts, well known as ASIS (Aromatic Solvent-Induced Shift[7]), was studied in the series of substituted azachalcones[1].

In this work, the ^{13}C-NMR spectra of chalcone and fourteen aza and diaza-chalcones were studied. Further, the stereochemistry of these compounds was investigated. In the case of 2'-, 3'- and 4'-azachalcones, the results of NMR studies are compared with theoretical PCILO calculations.

EXPERIMENTAL

All studied compounds were synthetized according to the procedures already described[8-10]. 0·1M solutions in $CDCl_3$ were used. ^{13}C-NMR spectra were measured on a Jeol FX-100 spectrometer equipped with the PG-200 programable pulse generator enabling selective spin excitations[11]. ^{13}C-NMR chemical shifts were determined from the 6 kHz spectra with accuracy ±0·1 ppm. Tetramethylsilane served as an internal standard. Proton-coupled spectra were recorded using the gated decoupling preserving NOE in order to improve the S/N ratio. Spectral width of 2·5 kHz and 16 K data table were used, providing the digital resolution of 0·3 Hz. Where an extensive signal overlap prevented the analysis of some subspectra, the method of selective excitation was employed (Fig. 1). The spectral parameters of H_α and H_β protons, necessary for analysis of the C_α-subspectra, were obtained from the ^{1}H-NMR spectra of 0·5M solutions in $CDCl_3$.

PCILO calculations[12] of carbonyl group rotation in 2′-, 3′- and 4′-azachalcones were performed on a Siemens 4004/100 computer using the QCPE (Quantum Chemistry Program Exchange) program No 220 (ref.[12]). For the theoretical calculations the experimental geometry[13] was used.

RESULTS AND DISCUSSION

Table I summarizes the ^{13}C chemical shifts of studied compounds. The signal assignment is based on the comparison of spectra and selective decoupling experiments. Change in the nitrogen atom position or its absence in the aromatic ring attached to the olefinic carbon atom has a marked effect on the chemical shifts of C_α and C_β, whereas the changes of the carbonyl carbon chemical shifts are negligible. On the contrary, any change in the nitrogen atom localization in the aromatic ring attached to the carbonyl has no substantial effect on the chemical shifts of these carbon atoms. This fact indicates a loss of conjugation between the olefinic bond and the aromatic ring attached to the carbonyl atom. The position of nitrogen also affects proton–carbon coupling constants observed on the olefinic carbon atoms. More suitable for the study of this effect is the signal of C_α carbon atom because its signal is less complicated by long-range couplings. Since the chemical shift difference between H_α and H_β is small, the spectrum of C_α carbon atom is not of the first order. The second-order effects are clearly manifested in the spectrum of 2,2′-diazachalcone only (Fig. 1). Other compounds display deceptively simple spectra, *i.e.* doublet of doublets but with unequal line spacings that cannot be taken as the coupling constants. The magnitudes of these constants were obtained using an iterative analysis program LAOCN3

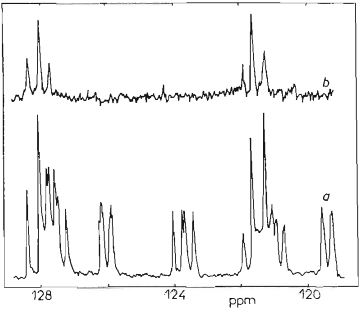


FIG. 1

Detail of the ^{13}C-NMR Spectrum of 2,2′-Diazachalcone

^{a} Proton-coupled spectrum. ^{b} C_α-proton-coupled subspectrum obtained by selective excitation of C_α-spins. Pulse sequence: train of fifty 0·5 μs (2°) exciting pulses spaced 5·66 ms. Exciting frequency was placed —176·6 Hz from the C_α-resonance.

(ref.[14]). From the results given in Table II it follows that the absolute value of the coupling constant $^2J(C_\alpha—H_\beta)$ decreases with the increasing distance of the nitrogen atom from the double bond. The largest value of the one-bond coupling constant $^1J(C_\alpha—H_\alpha)$ is observed with compounds containing nitrogen atom in the position 2 and 2′, respectively. Its magnitude is somewhat lower in compounds having nitrogen atom at the position 3 and 3′ or 4 and 4′, respectively.

The subspectra of pyridine ring carbons can be analyzed using the first-order approach. We found that a change in the nitrogen atom localization or its absence in the aromatic ring next to the olefinic carbon atom has a negligible effect upon the magnitude of $^{13}C—^1H$ coupling constants in the aromatic ring attached to the carbonyl group and *vice versa*.

Among various spin-spin couplings, the mos tinteresting is the coupling of H_α-proton to carbon C(1′) since it is a potential source of information on the conformation around the $C_\alpha—C{=}O$ bond. Besides the NMR method, we studied this conformation also by PCILO calculations. Fig. 2 gives the dependence of the potential energy of 2′-, 3′- and 4′-azachalcones on the rotation angle θ of the carbonyl group. As it is well known, the PCILO method uses as zeroth-order approximation a completely localized description of the molecule. In the compounds studied there is some ambiguity by choosing the appropriate zeroth- order wave function with respect to the existence of several classical resonance structures. Practical criteria for overcoming these inconveniences have been suggested[15,16]. We used that of Diner and coworkers[15] in the case of azachalcones, taking as a starting wave function that one having the best energy. According to our PCILO calculations, the *s-cis* isomers of 2′-, 3′- and 4′-azachalcones are more stable. Although the *s-cis* isomer of 2′-aza-

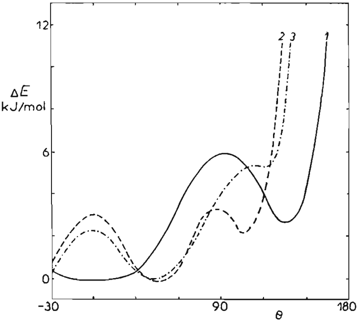
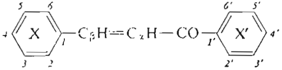


FIG. 2

PCILO Potential Energy Curves for the Carbonyl Group Rotation
1 2′-Azachalcone, *2* 3′-azachalcone, *3* 4′-azachalcone.

TABLE I

Chemical Shifts of Studied Azachalcones (in δ scale)



X, X′	$C_{(1)}$	$C_{(2)}$	$C_{(3)}$	$C_{(4)}$	$C_{(5)}$	$C_{(6)}$	C_{α}	C_{β}	CO	$C_{(1')}$	$C_{(2')}$	$C_{(3')}$	$C_{(4')}$	$C_{(5')}$	$C_{(6')}$
H,H	134·8	128·9[a]	128·5[a]	130·4	128·5[a]	128·9[a]	122·0	144·6	190·2	138·1	128·4	128·4	132·7	128·4	128·4
H,2′N	135·1	128·8	128·8	130·5	128·8	128·8	120·8	144·6	189·3	154·1	—	148·8	126·8	136·9	122·8
H,3′N	134·4	129·0[a]	128·5[a]	130·9	128·5[a]	129·0[a]	121·3	145·9	189·0	133·4	149·7	—	153·1	123·6	135·8
H,4′N	134·2	129·0	128·6	131·1	128·6	129·0	121·1	146·7	189·7	144·3	121·4	150·7	—	150·7	121·4
2N,H	153·0	—	150·1	124·3	136·8	125·2	125·4	142·7	190·2	137·8	128·6	128·6	133·0	128·6	128·6
2N,2′N	153·5[a]	—	150·1	124·3	136·6[b]	124·6	124·8	143·0	189·7	153·8[a]	—	148·9	127·0	136·9[b]	122·7
2N,3′N	152·6	—	150·1	124·6	136·9	125·6	124·6	143·7	188·9	132·9	149·9	—	153·3	123·5	135·8
2N,4′N	152·5	—	150·3	124·9	137·0	125·8	124·5	144·5	189·8	143·9	121·5	150·9	—	150·9	121·5
3N,H	130·6	150·0	—	151·0	123·7	134·5	123·7	140·7	189·5	137·7	128·6[a]	128·5[a]	133·1	128·5[a]	128·6[a]
3N,2′N	130·8	150·4	—	151·0	123·7	134·6	122·8[a]	140·6	188·8	153·7	—	148·9	127·1	137·0	122·9[a]
3N,3′N	130·3	150·2[a]	—	151·5	123·8[b]	134·6	123·1	142·0	188·5	133·1	149·8[a]	—	153·5	123·7[b]	135·9
3N,4′N	130·1	150·2	—	151·6	123·9	134·7	122·9	142·9	189·2	143·8	121·4	150·9	—	150·9	121·4
4N,H	141·8	122·0	150·5	—	150·5	122·0	125·9	141·2	189·4	137·3	128·7[a]	128·5[a]	133·2	128·5[a]	128·7[a]
4N,2′N	142·2	122·2	150·4	—	150·4	122·2	125·1	141·1	188·9	153·5	—	148·9	127·2	137·1	122·9
4N,3′N	141·6	122·0	150·8	—	150·8	122·0	125·3	142·6	188·5	132·8	149·8	—	153·7	123·8	135·9

[a,b] Assignment can be reversed.

chalcone is planar, the energy changes accompanying deviations from planarity are small for angles $\theta \leqq 30°$. With 3'- and 4'-azachalcone, the more stable forms are non-planar *s-cis* isomers having dihedral angle $\theta = 45°$.

From our NMR study it follows that the coupling constant of H_α to $C_{(1')}$ in 3'- and 4'-azachalcone is very small and is not observed in the spectra. This coupling is observed in the spectrum of 2'-azachalcone. However, owing to the complicated $C_{(1')}$-subspectral pattern caused by additional small long-range couplings, we made only a rough estimate of $^3J(C_{(1')}—H_\alpha)$ about 1 Hz. All vicinal $^{13}C—^1H$ coupling constants generaly show a characteristic Karplus-type dependence on the dihedral angle θ. Therefore we attempted to use the extracted $^3J(C_{(1')}—H_\alpha)$ values for the determination of conformation of studied molecules with respect to the $C_\alpha—C{=}O$ bond. To obtain some estimates of the magnitude of H—C—CO—C (sp^2) couplings in the *s-cis* and *s-trans* conformations, we measured the spectra of model compounds (*p*-quinone, enol form of 2,4-pentanedione and 4-phenyl-3-buten-2-one). Analysis of the high-resolution proton-coupled ^{13}C-NMR spectrum of *p*-quinone provided the value of 4·5 Hz for $^3J(C_{(2)}—H_{(6)})$, corresponding to the *s-trans* conformation. The enol form of 2,4-pentanedione served as a model for *s-cis* conformation; the coupling constant between the methyl group carbon and methine hydrogen atom amounted 1·7 Hz. The same value was also found for the corresponding coupling in 4-phenyl-3-buten-2-one.

Assuming validity of a Karplus-type model for the $^1H—^{13}C$ vicinal couplings in studied azachalcones, the following conclusions can be made: *a*) The value of $^3J(C_{(1')}—H_\alpha) = 1$ Hz H found in 2'-azachalcone indicates that this compound exist in nearly planar *s-cis* form. *b*) Since the value of $^3J(C_{(1')}—H_\alpha)$ is practically zero in 3'- and 4'-azachalcones, their *s-cis* isomers are non-planar. These conclusions are supported also by PCILO calculations for the above mentioned compounds.

TABLE II

$^2J(C_\alpha—H_\beta)$ and $^1J(C_\alpha—H_\beta)$ Coupling Constants (Hz)

Chalcone	$^2J(C_\alpha—H_\beta)$	$^1J(C_\alpha—H_\alpha)$
2'-aza	—2·9	161·6
3'-aza	—2·6	157·3
4'-aza	—2·4	157·8
2,2'-diaza	—3·8	165·4
3·2'-diaza	—3·3	162·0
4,2'-diaza	—3·2	162·7

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Translated by P. Sedmera.