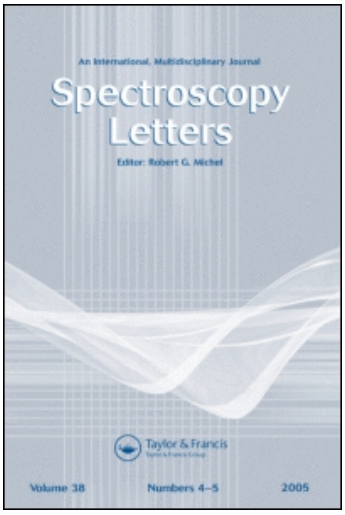

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Isocoumarines: Structural Study by NMR and by AM1 Semi-Empirical Method

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ISOCOUMARINES: STRUCTURAL STUDY BY NMR AND BY AM1 SEMI-EMPIRICAL METHOD

Keywords: ^{13}C and ^{17}O NMR Spectroscopies; AM1; Isocoumarines

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ABSTRACT

Study of a serie of isocoumarins by ^{13}C and ^{17}O NMR spectrometry and AM1 method is reported. These methods gave valuable informations on electronic effect and the structure of isocoumarins.

INTRODUCTION

Isocoumarins are compounds which have biologic effects (1). They have been extracted from plants like "*Artemisia cappilaris*"(2) or from some insects like beetles (*Apsena pubescens*) or ants (*Lasius niger*)(3). Recently

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L. BHOLIN and al. indicated inhibition effect, in vitro, of isocoumarins in prostaglandins synthesis (4). Isocoumarins are used also as synthesis intermediates. Thus, 3-alkyl and 3-aryl-iscoumarins are importants intermediates for preparation of many compounds like arylaliphatic diketones (5) and / or isobenzopyrylium salts (6), which can be used to obtain isoquinoleines.

Although isocoumarins have ben widely studied, more aspects of their structures are unknown. In this paper, the results of a structural study by ^{13}C, ^{17}O NMR and AM1 methods of these compounds are reported.No similar study is known up to now. AM1 method is a new one for compounds heat of formation (ΔH) and atomic charges densities (q) calculations in a molecule; therefore AM1 method can allow the chemical shift assignment in NMR spectra (7).

EXPERIMENTAL

All isocoumarins are obtained from 1,3-isochromandiones substituted in 4 position (8), by heating them in sulfuric acid (9).

Compound 1 have been prepared by acylation of homophtalic anhydride with acids anhydrides or acids chlorides (10). All isocoumarins are obtained in solid state. They are identified by IR and ^{1}H NMR spectroscopy, melting points and elementary analysis. ^{17}O and ^{13}C NMR spectra were recorded on BRUKER AMX 400 spectrometer in CD_3Cl or CD_3CN solutions at 54.24 and 100.61 MHz respectively. Typical experimental conditions for ^{17}O and ^{13}C NMR experiments were: Sweep width 45000 and 25000 Hz; pulse delay 20μs and 3μs; acquisition time 0.09 and 0.3 s data.

Table I gave ^{1}H NMR data and table II gave ^{13}C and ^{17}O NMR and AM1 calculation data.

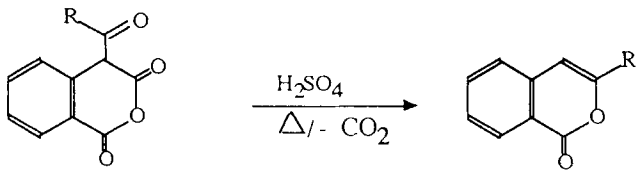
DISCUSSION

^{1}H NMR study of isocoumarins

^{1}H NMR spectra of isocoumarins present the following signals:

One singlet assigned to the proton H4 resonance between 6 and 7,2 ppm. The chemical shift of this proton depends on nature of R.

One doublet at 8,2-8,3 ppm assigned to the proton H8 (J= 8-8,2Hz) which δ is unaffected by the nature of R.



1 2

R= CH_3: 2a; R=C_2H_5: 2b; R=C_6H_5: 2c;
R=p$CH_3C_6H_4$: 2d R=p$CH_3OC_6H_4$: 2e; R=pClC_6H_4: 2f ;
R=pO_2N-C_6H_4 : 2g.

SCHEME 1

These two signals are characteristic of isocoumarins like compounds describe in this paper (10).

One multiplet at 7,3 ppm assigned to protons H5, H6 and H7 and to protons of R in the case of an arylic substitution.

In the case of an aliphatic substituant, the singlet at 6-7,2 ppm is observed at 6,1-6,3 ppm while in arylic substituant it is observed at 6,8-7,2 ppm, in a deshielded field.

This deshielding field is comparable to the withdrawing effect of a phenyl group. So, when R is aliphatic (R= CH_3 or C_2H_5) the δ value of these protons are respectively at 2,3 and 2,5 ppm like in the case of toluene and ethylbenzene.

^{13}C NMR study of isocoumarins

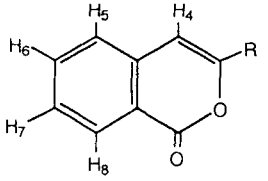
The chemical shifts assignment was made on the basis of the results obtained by R. N. AYYANGAR and al.(11) and H. DUDDECK and al. (12).

In isocoumarin system the substituant has a small effect on carbon chemical shifts. The carbone C_1 is the most deshielded carbon and C_4 is the most shielded one. The chemical shift of C_4 is about 100 ppm. The δ value of this carbon is 105,54 when R = p$NO_2C_6H_4$,but is between 101 and 102 ppm in the other case where R is arylic. The δ value of C_1 is 161-163 ppm.

Among the other carbons of the system, C_3 and C_{10} seemed to be perturbed by the nature of R. All these results are in good agreement with those found for AM1 calculations, which indicates the C_4 as the more negative charged carbon (q = -0,22ev) and the C_1 the more positive charged one

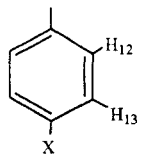
TABLE I

^1H NMR chemical shift (δ in ppm) of isocoumarin ring



Compd	H^4			H^8			H^5, H^6 H^7		
2a	6,3	s	1H	8,25	d	1H (J= 8Hz)	7,3	m	3H
2b	6,1	s	1H	8,25	d	1H (J= 8Hz)	7,3	m	3H
2c	6,9	s	1H	8,30	d	1H (J= 7,9Hz)	7,5	m	3H
2d	7,1	s	1H	8,30	d	1H (J= 8,1Hz)	7,5	m	3H
2e	6,8	s	1H	8,25	d	1H (J= 8,0Hz)	7,7	m	3H
2f	6,9	s	1H	8,25	d	1H (J= 8,2Hz)	7,5	m	3H
2g	7,2	s	1H	8,20	d	1H (J= 8,2Hz)	7,5	m	3H

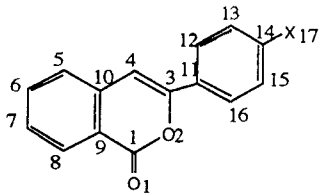
R =



Compd	R	H_{12}	H_{13}	X
2a	CH_3	2,3 s 3H	-	-
2b	C_2H_5	2,5 q 2H(J=8Hz)	1,2 t 3H(J=8Hz)	-
2c	C_6H_5	7,3 m 5H	-	-
2d	$pCH_3C_6H_4$	7,7 d 2H(J=10Hz)	7,2 d 2H(J=10Hz)	2,4 s 3H
2e	$pCH_3OC_6H_4$	7,9 d 2H(J=10Hz)	7,1 d 2H(J=10Hz)	3,9 s 3H
2f	$pClC_6H_4$	7,8 d 2H(J=8Hz)	7,3 d 2H(J=8Hz)	-
2g	$pNO_2C_6H_4$	8,1 d 2H(J=8Hz)	7,5 d 2H(J=8Hz)	-

TABLE II

Atomic charges densities and ^{13}C, ^{17}O NMR chemical shifts



a) δ in ppm from TMS for ^{13}C and for external water for ^{17}O
b) charge density obtained by AM1

	2a		2b	2c		2d		2e		2f		2g	
	δ	*q*	δ	δ	*q*	δ	*q*	δ	*q*	δ	*q*	δ	*q*
O_1	-	*-0,2966*	321,46	322;05	*-0,2963*	321,85	*-0,2952*	332,18	*-0,2957*	-	*-0,2921*	-	*-0,2862*
O_2	-	*-0,1962*	230,89	217,19	*-0,1924*	219,58	*-0,1826*	222,51	*-0,1838*	-	*-0,1842*	-	*-0,1843*
C_1	162,66	*+0,3472*	162,82	162,19	*+0,3436*	162,42	*+0,3435*	162,90	*+0,2957*	162,14	*+0,344*	162,31	*+0,3441*
C_3	154,35	*+0,3472*	159,40	153,56	*+0,1183*	153,93	*+0,1221*	155,00	*+0,1242*	152,62	*+0,1132*	156,54	*+0,0960*
C_4	103,34	*-0,2402*	101,85	101,76	*-0,2235*	101,12	*-0,2245*	101,32	*-0,2250*	102,18	*-0,2186*	105,54	*-0,2058*
C_5	127,33	*-0,1414*	127,41	128,10	*-0,1392*	127,95	*-0,1393*	127,03	*-0,1396*	128,50	*-0,1379*	129,52	*-0,1346*
C_6	129,20	*-0,0872*	129,31	129,55	*-0,0882*	129,68	*-0,0883*	128,80	*-0,0884*	130,52	*-0,0880*	129,72	*-0,0875*
C_7	124,75	*-0,1514*	125,01	125,97	*-0,1506*	125,90	*-0,1512*	126,61	*-0,1510*	126,13	*-0,1489*	127,20	*-0,1448*
C_8	134,54	*-0,0562*	134,58	129,92	*-0,0574*	129,26	*-0,0571*	129,92	*-0,0573*	129,81	*-0,0574*	129,13	*-0,0571*
C_9	119,73	*-0,1569*	120,07	120,50	*-0,1547*	120,48	*-0,1552*	120,07	*-0,1550*	120,63	*-0,1534*	121,76	*-0,1498*
C_{10}	137,50	*+0,0328*	137,58	131,92	*+0,0272*	137,78	*+0,0270*	136,00	*+0,0273*	135,08	*+0,0248*	135,03	*+0,0186*
C_{11}	19,40	*-0,1841*	26,57	137,47	*-0,0591*	140,32	*-0,0660*	139,00	*-0,0976*	137,35	*-0,0570*	137,59	*-0,0241*
C_{12}-C_{16}	-	-	11,12	128,78	*-0,0944*	129,60	*-0,0905*	127,62	*-0,0636*	129,20	*-0,0865*	123,83	*-0,0923*
C_{13}-C_{15}	-	-	-	125,20	*-0,1342*	125,23	*-0,1350*	115,33	*-0,2108*	126,57	*-0,1297*	126,75	*-0,0912*
C_{14}	-	-	-	134,81	*-0,1128*	134,86	*-0,1350*	162,00	*+0,0971*	136,10	*-0,0469*	148,44	*-0,0864*
C_{17}	-	-	-	-	-	21,44	-	56,15	-	-	-	-	-

(q = +0,34 ev) .The δ value of C_3 and C_{10} are 152-159 ppm and 131-138 ppm respectively. The AM1 calculation values of these carbon 's charges are respectively q = +0,11-0,12 ev for C_3 and q = +0,018-O,O33 ev for C_{10}.

In the AM1 data, the carbon C_4, C_5, C_7 and C_9 are negatively charged and they are more shielded than the others. These results are in good agreement with the NMR experimental data.

The positive charge of the C_3 carbon explain the electronic withdrawing effect of isocoumarins for subtituants which are in this position. Thus when R = CH_3, the carbon of this methyl group appear at 19,4 ppm while the carbons of an ethyl group appear at 26,57 for methylene and 11,12 ppm for methyl. For exemple in toluene the carbon of methyl group appear at 21,3 ppm while in ethylbenzene the carbons of ethyl group appear at 29,7 and 15,8 ppm (13)

^{17}O NMR study of isocoumarins

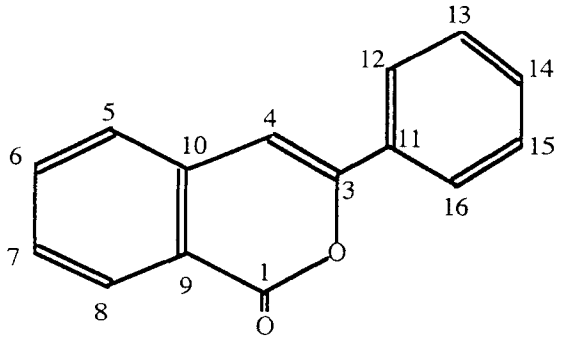
We reported the first ^{17}O NMR data for isocoumarins. The chemical shift of the two oxygens of these compounds are respectively 320-333ppm for carbonyl oxygen O^1 and 217-222,5ppm for lactonic one O^2 (Cf Table II).

The chemical shift of carbonyl oxygen (O^1) is similary to that observed for the benzenic esters and lactones . The chemical shift of lactonic oxygene (O^2) of isocoumarins is however more deshielded than that of their homologs of esters and lactones which δ values are about 120 and 170 ppm respectively (14).

AM1 study of geometrie of isocoumarins

This study is the first for isocoumarins. We do not found any correlation beetwen chemical shift and charge densities of oxygen in isocoumarins. This is probabily du to the geometry of these compounds which defavorise conjugaison of phenyl group in 3 position and isocoumarin ring.

We select 3-Phenylisocoumarin 2c as reference compound for this study



2c

The compound contain two plane systems: isocoumarin ring and phenyl ring. Although there is no proton on 2 position of isocoumarin ring, it is possible to suspect the existence of interaction like those of biphenyl. The protons H_4 and H_{12} (or H_{16}) could exerce on themseves Van der Waal type of interaction and put out the plane structure of the molecule.

AM1 calculation method is a successfull method in determining the more stable conformation of this kind of structure. The diedral angle chosen for the heat of formation calculation was $\theta = C_4\text{-}C_3\text{-}C_{11}\text{-}C_{12}$. It is found that the more stable conformation is that where $\theta = 30°$ (ΔH = -5,599Kcal/mole).

Conclusion:

THe AM1 semiempirical method is usefull for assignment of chemical shifts in NMR spectrometry and in geometrical and electronic effets study in organic polar compounds.

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