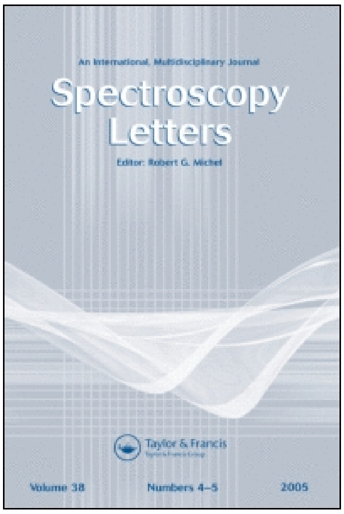

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NMR and AM1 Study of the Tautomeric Equilibrium of Isochroman-1,2-diones

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NMR AND AM1 STUDY OF THE TAUTOMERIC EQUILIBRIUM OF ISOCHROMAN-1,3-DIONES

Keywords: ^{1}H; ^{13}C and ^{17}O NMR; AM1; Isochroman-1,3-diones

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ABSTRACT

Reaction of homophtalic anhydrid with aliphatic or aryl anhydrids (or acid chlorides) and an appropriate base gives 4-acyl and 4-aroylisochroman-1,3-diones. The structure of these isochroman-1,3-diones was determined by ^{1}H, ^{13}C and ^{17}O NMR spectrometry. In solution, among the three possible tautomers , only the enolic one with exocyclic double bond was observed. These results are in good agreements with AM1 calculations ones.

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INTRODUCTION:

4-acyl and 4-aroylisochroman-1,3-diones are important intermediates for the synthesis of isocoumarins, 2-carboxybenzyl alkyl ketones, 3-alkyl-1-isoquinolones (1), etc. Nevertheless, only two methods of preparation were described by R. N. USGAONKAR *et al.* (2) and by J. SCHNEKENBURGER (3) and two structural studies of these compounds have been published (4)(5).

As observed by J. SCHNEKENBURGER, these compounds present a tautomeric equilibrium. The three possible tautomeric forms are reported in Scheme 1

In crystalline state, these compounds seemed to be in **I** tautomeric structure while in solution, an equilibrium between the two others forms **II** and **III** has been found(4). From electronic and infrared analysis,, USGAONKAR (5), suspected that the isochromandiones were in the tautomeric forms **I** and **II**.

To our knowledge, however, no NMR studies of the structures of these compounds have so far been reported. The aim of this work was to identify the stereoisomers present in solution. We report in this paper, the first study of 4-acyl and 4-aroylisochroman-1,3-diones by ^{1}H, ^{13}C and ^{17}O NMR spectrometry. For a better understanding of the parameters which play a role on the stability of these tautomers, AM1 semi-empirical calculations were performed

EXPERIMENTAL

Materials

Compounds studied in this work are described in Scheme 2

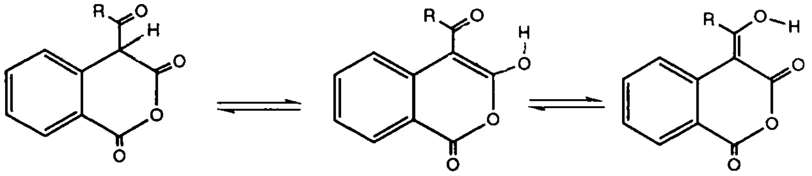
Aliphatic acid anhydrids react with homophtalic anhydrid **1** in diethyl ether and pyridin at room temperature for 2 hours to give the corresponding 4-acylisochroman-1,3-diones in good yield (2). 4-aroylisochroman-1,3-diones are obtained in good yield (3)(6) by reaction of aromatic acid anhydrids or aromatic acid chlorides with homophtalic anhydrid at reflux in diethyl ether or tetrahydrofuran for 2 hours. In both case, two molar equivalents of base (triethylamin) are required.

Isochromandiones **2** are colourless when R is aliphatic and yellow in other cases. They were obtained in solid state and identified by IR and ^{1}H NMR spectrometries, melting points and elementary analysis. IR data , melting points and elementary analysis data for isochroman-1,3-diones **2** are reported in Table 1.

IR spectra were recorded both in KBr pellet and in solution in $CHCl_3$ on a Mattson 1000 FTIR spectrometer. The following features were evidenced: all spectra present a strong band for C = O vibration in 1700-1770 cm^{-1} region and a weaker band at 1640-1650 cm^{-1} for C = C. As previously observed (4,5), in both cases, no bands were observed for the O-H vibration in the 3600- 3200 cm^{-1} region (Cf. Table 1).

NMR measurements

The ^{1}H NMR spectra were recorded in $CDCl_3$ solution on BRUKER AC-80 spectrometer. The ^{1}H chemical shift parameters are reported in Table 2. The ^{13}C NMR



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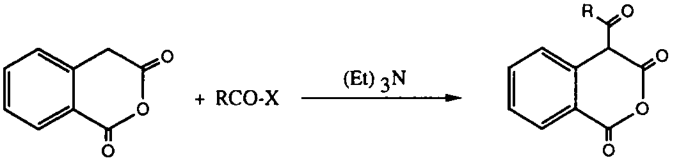


1 2

X = Cl or OCOR

2a: $R= CH_3$; **2b**: $R= C_2H_5$; **2c**: $R= C_6H_5$;
2d: $R= pCH_3C_6H_4$; **2e**: $R=p(CH_3)_3CC_6H_4$; **2f** : $R= pCH_3OC_6H_4$;
2g: $R=pNO_2C_6H_4$; **2h**: $R=pClC_6H_4$; **2i** : $R=pFC_6H_4$.

Scheme 2

spectra were recorded both on BRUKER AMX-400 and BRUKER AC-80 spectrometers and the ^{17}O NMR spectra on a BRUKER AMX-400 spectrometer. In this latter studies, saturated sample solutions in $CDCl_3$ were used. Assigment of ^{13}C and ^{1}H chemical shifts follows from the concerted use of homonuclear (COSY) (6) and both direct (HMQC) (7) and long range (HMBC) heteronuclear correlation experiments (8). Typical spectra setting for ^{17}O and ^{13}C NMR experiments were as follow: Sweep width 45000 and 25000 Hz; pulse delay P90 20 μs and 4.5 μs; acquisition time 0,09 and 0,3 s. ^{13}C and ^{17}O NMR data are reported inTable 3.

RESULTS AND DISCUSSION

NMR analysis

In the ^{1}H NMR spectra of isochromandiones, the most striking features were as follows:

TABLE 1 Melting points, elementary analysis and characteristic ν_{CO} wave numbers of isochroman-1,3-diones **2**

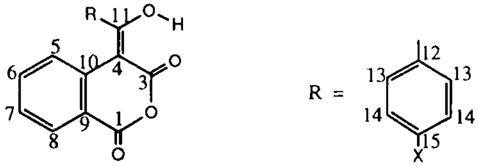
	Yield %	m.p. °C (lit)	IR cm^{-1} ν C=O	elementary calculated %	analysis found %
2a	98	162-163 (162)	1740	C: 64,70 H: 3,92	C: 64,75 H: 3,89
2b	90	116-118 -	1730	C: 66,055 H: 4,587	C : 66,11 H : 4,61
2c	94	130-132 (132,5)	1760	C: 72,18 H: 3,76	C: 72,21 H: 3,86
2d	70	114-115 -	1762	-	-
2e	60	137-139 -	1766	C: 74,53 H: 5,59	C :74,25 H :5,65
2f	85	194-195 (192-193)	1762	C: 68,92 H: 4,05	C: 68,89 H: 4,20
2g	90	190-192 -	1762	C:61,73 H: 2,89 N: 4,50	C: 60,65 H: 3,04 N: 4,53
2h	87	159-160 -	1761	C: 63,89 H: 2,99	C: 63,80 H: 3,10
2i	85	151-153 -	1766	C: 67,605 H: 3,169	C: 67,62 H: 3,18

The aliphatic groups (R) appear between 1,3 and 3,3 ppm as singlet for methyl groups, triplet and quadruplet for ethyl, while the other protons appear between 6,8 and 8,3 ppm as two or three multiplets. Among these latter resonances, the signal which appears at 6,8-6,9 ppm was attributed to an hydroxylic proton. Effectively, by treatment of the sample with D_2O, this signal disappears. This result suggests an enolic form like **II** or **III** for isochromandiones.

In ^{13}C NMR spectra, the most shielded carbons are C_4 , C_5 and C_9. The chemical shift of C_4 is about 94 ± 4 ppm, the carbon C_9 resonates between 114 and 120 ppm and C_5 resonated between 120 and 130 ppm. The more deshielded carbons are C_{11} (170-192 ppm), C_3 (163-169 ppm) and C_1 (159,5-163 ppm)

The chemical shifts of the three carbons C_3, C_4 and C_{11} are in very good agreement with those of the carbons of the enolic form of compounds like the β–keto-ester (7) described in the Scheme 3.

TABLE 2 : ^1H NMR data of isochroman-1,3-diones **2**. δ in ppm from TMS.



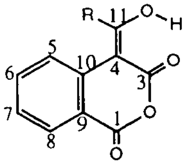
	H_8 and/or H_{13}	H_4	other Ar-H	H aliphat.
2a	8,2 d 1H	6,8 m 1H	7,1-7,8 m 3H	2,7 s 3H
2b	8,2 d 1H	6,9 m 1H	7,3-7,8 m 3H	2,9 q 2H 1,6 t 3H
2c	8,2 m 2H	6,8 m 1H	7,2-7,7 m 7H	-
2d	8-8,2 m 2H	6,9 m 1H	7,2-7,8 m 6H	2,5 s 3H
2e	8,0 m 2H	6,9 m 1H	7,2-7,5 m 6H	1,3 s 9H
2f	8,0 m 2H	6,8 m 1H	6,9-7,5 m 6H	3,3 s 3H
2g	8,2-8,8 m 2H	6,9 m 1H	7,5-8,2 m 6H	-
2h	8,0 m 2H	6,8 m 1H	7,3-7,5 m 6H	-
2i	8,1 m 2H	6,8 m 1H	7,2-7,7 m 6H	-

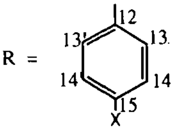
The chemical shifts of C_4 (90-97 ppm) evidence a sp^2 hybridization state, as the chemical shifts of C_{11} between 170 and 192 ppm are indicative of its enolic structure (7). Subsequent DEPT experiments confirm the lack of methine aliphatic resonance. These results suggest the structure III for isochroman-1,3-diones **2**:

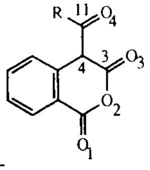
Isochromandiones have three possible kinds of oxygens: two anhydrid carbonyl oxygens (C=O), one anhydrid oxygen (-O-) and one enolic oxygen (-O-H).

By comparison with the chemical shift data of other aromatic anhydrid oxygens (8), the O_1 and O_2 chemical shifts are easily assigned ($298 \leq \delta O_1 \leq 305$ ppm and $356 \leq \delta O_3 \leq 361$ ppm). These values are substantially different from those reported for

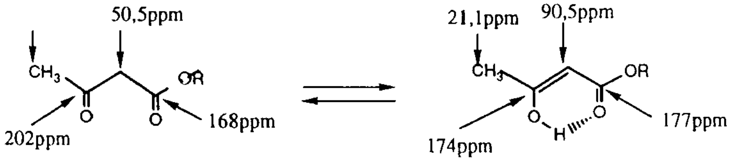
TABLE 3 : ^{13}C and ^{17}O NMR data of isochroman-1,3-diones **2** . δ en ppm from TMS and Water respectively



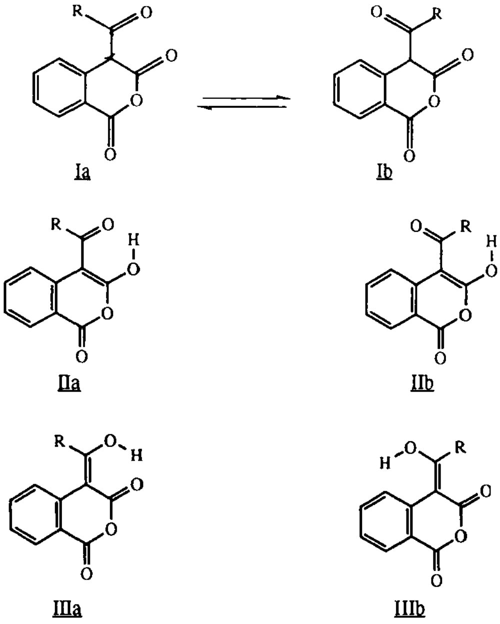




	2a	**2b**	**2c**	**2d**	**2e**	**2f**	**2g**	**2h**	**2i**
C_1	159,71	159,80	159,84	159,95	159,99	160,94	162,87	161,98	159,76
C_3	168,51	168,68	168,85	168,76	168,2	163,77	163,57	162,81	168,74
C_4	97,28	96,67	96,47	95,98	96,06	90,20	92,41	96,26	96,47
C_5	124,34	124,35	125,82	125,82	125,82	120,81	122,97	125,38	126,83
C_6	135,21	135,20	134,02	133,94	133,95	133,42	129,09	134,64	134,14
C_7	126,46	126,46	126,64	126,44	126,44	123,34	123,81	125,63	125,74
C_8	131,30	131,22	130,61	130,40	130,42	128,39	128,31	129,47	130,72
C_9	119,23	119,30	119,57	119,55	119,36	114,52	116,37	118,53	119,66
C_{10}	135,04	134,84	134,77	134,98	135,00	131,42	140,21	137,52	134,58
C_{11}	182,84	187,00	179,72	170,93	179,88	192,03	184,56	178,58	178,13
C_{12}	24,35	29,49	134,43	143,35	131,28	135,78	146,98	137,08	166,42
C_{13}	-	10,29	129,32	129,89	128,75	129,96	134,46	129,98	131,58
C_{14}	-	-	128,83	128,92	126,15	112,81	123,17	128,46	116,78
C_{15}	-	-	132,39	131,32	156,47	142,62	150,16	134,75	163,89
$C_{14'}$	-	-	128,83	128,92	126,15	112,81	123,17	128,46	116,57
$C_{13'}$	-	-	129,32	129,89	128,75	129,96	134,46	129,98	131,49
X	-	-	-	21,742	35,222 31,152	56,00	-	-	-
O_1	-	298,94	304,48	304,81	-	-	-	-	-
O_2	-	258,98	260,41	260,52	-	-	-	-	-
O_3	-	356,74	360,10	357,15	-	-	-	-	-
O_4	-	166,99	161,92	162,59	-	-	-	-	-



Scheme 3



Scheme 4

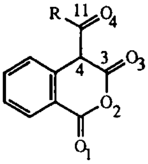
homophtalic anhydrid (372 ppm for O_1 and 397 ppm for O_3). These results show a 70 ppm shielding difference for O_1 and a 40 ppm shielding difference for O_3. The chemical shift of anhydrid oxygen (-O-) is about 259 ± 1,5 ppm for isochroman-1,3-diones and 273 ppm for homophtalic anhydrid.

The signal observed in the 164 ± 3 ppm area is assigned to the enolic oxygen. It is the more shielded one. However, it is known that an enolic system with chelated hydroxy group shifted strongly the hydroxy oxygen resonance (8, 9). These results are in good agreement with the proton and carbon 13 NMR results and are indicative that the isochroman-1,3-diones are in enolic tautomeric form **III**.

AM1 study of isochroman-1,3-diones

AM1 calculation is a successfull method in determining the more stable isomer of polar compounds (10, 11). To obtain a further proof of the stable structure of isochroman-1,3-diones, we have calculated the Heat of Formation (ΔH) of the different conformations of each tautomers of compounds 2a and 2c by the AM1 semi empirical method. The possible structures are represented in scheme 4.

TABLE 4 Heat of formation values versus ϕ for **2a** (R = CH_3) and **2c** (R= C_6H_5)



compound	isomers	ϕ (degree)	ΔH (Kcal/mol)
2a	Ia	0	-113,750
"	Ib	180	- 58,147
"	IIa	0	-115,610
"	IIb	180	no conv.
"	**IIIa**	**0**	**-121,240**
"	IIIb	180	-119,210
2c	**IIIa**	**0**	**-84,337**
"	IIIb	180	-77,105

For each structure, the diedral angle ϕ = O_4-C_{11}-C_4-C_3 was varied from 0° to 180°. The results obtained are reported in Table 4. They confirm that the enolic structures **III** of isochroman-1,3-diones are the more stable.

CONCLUSION

The ^{1}H, ^{13}C and ^{17}O NMR and the AM1 calculation results show that the enolic structures III of isochromandiones with an exocyclic double bond are the more stable.

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REFERENCES

1) a) J. Schnekenburger , *Arch. Pharm. 298Bd.* **1965**, 715.

b) R. B. Tirodkar and R. N. Usgaonkar, *J. Indian Chem. Soc.* **1969**, *46* , 935.

2) D. R. Nadkarni and R. N. Usgaonkar, *Indian J. Chem. 1978 ,16B* , 320

3) J. Schnekenburger, *Arch. Pharm. 298Bd* **1965**, 4.

4) J; Schnekenburger, *Arch. Pharm. 298Bd* **1965** ,411-

5) a) see 1b

b) R. B. Tirodkar and R. N. Usgaonkar, *J. Indian Chem. Soc.* **1971**, *48*, 192.

6) a) W. P. Aue; E Bartholdi; R. R. Ernst *J. Chem. Phys* **1976,** *64,* 2229.

b) K. Nagayama; A. Kumar; K. Wüthrich; R. R. Ernst *J. Mag. Res.* **1980,***40*, 321.

7) A. Bax; S. Subramanian *J. Mag. Res.* **1986,***67,* 565.

8) A. Bax; M.F. Summers *J. Am. Chem. Soc.* **1986,** *108 ,2093.*

9) A. Saba , *Thèse d'état ès Sciences Physiques* ,Ouagadougou **1996.**

10) E. Breitmaier and W. Voelter; in *CARBON 13 NMR SPECTROSCOPY* Third Ed, **1991**, p. 229.,EditsVCH; (Weinheim , Germany))

11) a) D. W. Boykhin, in *^{17}O NMR SPECTROSCOPY IN ORGANIC CHEMISTRY* Ph. D. CRC Press. **1991** p197 (Boston- New-York)

b) P. C. Vasquez; D. W. Boykhin and A. L. Baumstark, *Mag. Res. Chem.* **1986**, *24*, 409 (.

12) V. V. Lapachev; I. Y. Mainagachev; S. A. Stekhova; M. M. Fedotov; V. P. Krivopalov and V.P.Mamaev, *J.Chem.Soc.Chem.Comm.* **1985,** 494-495

13) a) M. J. S. Dewar; E. G. Zoebish; E. F. Healy; J. P. P. Stewart, *J. Am Chem. Soc.* ***1985***, *107,* 3902.

b) M. J. S. Dewar and K. M. Dieter; *J. Am. Chem. Soc.* **1986,** *108*, 8075.

14) A. Saba; S. F. Sib and J. P. Aycard, *Spectroscopy Letters* **1995,** *28,* 1053

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