Reference Data

¹³C NMR Study of *ortho-*, *meta-* and *para-*Alkoxycarbonylalkyloxychalcones and Their α,β -Dibrome Derivatives

MARIA SZAJDA Faculty of Chemistry, Adam Mickiewicz University, Grunwaldzka 6, 60–780 Poznań, Poland

The ¹³C NMR spectra of eighteen new derivatives of chalcone have been recorded, calculated and fully assigned. The A_i empirical parameters of the styrylketone, *p*-alkoxycarbonylalkyloxystyrylketone and benzoylethylene group were calculated for the prediction of the chemical shifts of substituted benzenes and chalcones.

KEY WORDS Chalcone Alkoxycarbonylalkyloxy-chalcone $\alpha_i\beta$ -Dibromochalcone ¹³C NMR Chemical Shifts A_i empirical parameters

INTRODUCTION

Chalcone and its derivatives form an important group of organic compounds of interesting antimicrobial activity.¹⁻³ Hydroxychalcone and its phenyl-substituted derivatives are known as drugs for the treatment of ulcers and inflammation.⁴ They are also valuable intermediates for the production of neumatic liquid crystals⁵ and photosensitive polymers⁶ and in the biosynthesis of flavonoids.⁷

During our extensive programme on the investigation of physico-chemical and biological properties of chalcone derivatives, we have reported⁸ the synthesis and antimicrobial activity of new 2-, 3and 4-alkoxycarbonylalkyloxy-substituted



© 1989 by John Wiley & Sons, Ltd.

Table 1. Characterization of new compounds

		Formula and	Found	(%)	Require	ed (%)
Compound	М.р. (°С)	molecular mass	С	н	c	Ĥ
3	Oil	C ₁₉ H ₁₈ O ₄ 310 33	72.80 72.95	5.43 5.62	73.53	5.85
4	Oil	$C_{20}H_{20}O_4$ 326.36	73.38	6.01 5.94	74.14	6.22
7	72–73	C ₁₉ H ₁₈ O ₄ 310.33	73.65 73.57	6.18 6.26	73.53	5.85
8	Oil	C ₂₀ H ₂₀ O₄ 326.36	74.36 74.47	5.93 5.98	74.14	6.22
11	55	C ₁₉ H ₁₈ O₄ 310.33	73.28 73.39	5.72 5.58	73.53	5.85
12	71	C ₂₀ H ₂₀ O₄ 326.36	74.01 73.93	6.32 6.24	74.14	6.22

chalcones and their α,β -dibromo derivatives. In this paper we report the ¹³C NMR spectra of these compounds (Scheme 1).

EXPERIMENTAL

Compounds

The syntheses of 1, 2, 5, 6, 9, 10 and 13–18 have been described previously.⁸ Compounds 3, 4, 7, 8, 11 and 12 were obtained by condensation of 2-, 3- or 4-hydroxychalcone with methyl or ethyl β -bromopropionate according to Ref. 8. Their physical data are given in Table 1.

The structures of the compounds obtained were confirmed by elemental and spectral analysis (IR, ¹H NMR, MS).

Spectra

The spectra of 1-12 and 15-18 were recorded at 19.6 °C on a Varian XL-200 spectrometer



Scheme 1

operating at 50.32 MHz with full proton decoupling. A pulse width of 3.6 μ s (90°) was used with a 0.97-s acquisition time. The spectral width was 10000 Hz with 32K data points, giving a digital resolution of 0.6 Hz per point. The number of transients varied from 400 to 5000 per spectrum. The spectra of 13 and 14 were recorded in the range 20-22 °C on a JEOL FX-100 spectrometer at 25.1 MHz with a PW of 9 µs (90°) and a 1.2 s acquisition time. The spectral window was 4000 Hz with 8K data points, giving a digital resolution of 0.98 Hz per point. CDCL₃ was used as the solvent and lock. Carbon chemical shifts were determined with reference to the centre signal of CDCl₃ (77.0 ppm).

RESULTS AND DISCUSSION

The chemical shifts for all the compounds investigated are shown in Table 2–4.

The assignments were made on the basis of the signal multiplicities and spectral characteristics of model compounds and by comparing measured and calculated chemical shifts.

A few reports on the ¹³C NMR investigation of some chalcone derivatives have previously been published,9,10 and unsubstituted (E)-chalcone was used as a model. However, the assignment of the chemical shifts of the unsubstituted calcone in Ref. 9 varied from our results (see Table 5). In the ¹³C NMR spectrum of (E)-chalcone we observed four signals in the region 128-129 ppm and determined their intensity, on the basis of their integrations, as double the intensity of the signals at 130.42 and 132.67 ppm. As the value of 132.63 ppm was previously⁹ assigned to C-4', we suggest that the signal at 130.42 ppm is that of C-4 and that the four signals at 128.32, 128.36, 128.48 and 128.82 ppm are

Reference Data

Table 2.	Measured c	hemical shi	fts (ppm) o	f 1–12 in C	DCI3										
Carbon	-	7	m	4	Average value	م ا	9	7	œ	Average value	ŋ	10	F	12	Average value
с <u>-</u> 1	124.23	124.24	124.63	124.63	124.43	136.27	136.21	136.28	136.48	136.31	128.44	128.40	128.26	128.15	128.31
C-2	156.83	156.89	156.66	156.70	156.77	116.41	116.47	116.76	117.19	116.71	130.06	130.08	130.12	130.05	130.08
C-3	111.88	111.95	112.70	112.80	112.33	157.94	157.98	157.74	158.15	157.95	114.86	114.88	115.18	115.21	115.03
C-4	130.82	130.66	129.83	129.80	130.28	114.27	114.22	114.80	115.02	114.58	159.45	159.58	159.35	159.41	159.45
C-5	121.73	121.68	121.68	121.63	121.68	129.92	129.86	129.93	129.98	129.92	114.86	114.88	115.18	115.21	115.03
C-6	131.31	131.29	131.47	131.45	131.38	121.92	121.90	121.80	122.56	122.05	130.06	130.08	130.12	130.05	130.08
C-¤	123.81	123.77	123.38	123.36	123.58	122.42	122.37	121.36	121.91	122.02	120.14	120.12	120.04	120.00	120.08
C-B	140.08	140.09	140.27	140.35	140.20	144.06	144.09	144.19	144.17	144.13	144.06	144.10	144.16	144.18	144.13
C=0	190.84	190.89	191.03	191.09	191.46	190.14	190.10	190.16	189.86	190.06	190.22	190.22	190.25	190.23	190.23
с-1,	138.23	138.21	138.42	138.45	138.33	137.83	137.84	137.88	138.16	137.92	138.18	138.22	138.20	138.22	138.21
C-2' or	128.37	128.37	128.50	128.55	128.45	128.46	128.43	128.46	128.57	128.48	128.24	128.24	128.26	128.26	128.25
C-3,	128.50	128.50	128.65	128.55	128.55	128.33	128.30	128.31	128.46	128.35	128.42	128.40	128.42	128.39	128.41
C-4,	132.48	132.48	132.57	132.53	132.50	132.70	132.68	132.71	132.74	132.71	132.51	132.47	132.47	132.44	132.47
C-5' or	128.50	128.50	128.65	128.55	128.45	128.33	128.30	128.31	128.40	128.35	128.42	128.40	128.42	128.39	128.41
C-6′	128.37	128.37	128.50	128.55	128.55	128.46	128.43	128.46	128.57	128.48	128.24	128.24	128.26	128.26	128.25

Table 3.	Measured	chemical s	hifts (ppm)	of 13–18 i	n CDCl ₃	
Carbon	13ª	14ª	15	16	17	18
C-1	127.16	127.00	139.86	139.84	131.41	131.30
C-2	155.98	155.98	115.23	115.24	129.72	129.68
C-3	112.64	112.59	157.88	158.04	114.84	114.84
C-4	130.74	130.68	114.96	115.13	158.20	158.26
C-5	122.02	121.85	129.96	129.93	114.84	114.84
C-6	130.95	130.90	121.83	121.74	129.72	129.68
C-α	47.30	47.35	49.25	49.47	49.74	49.76
C-β	45.75	45.57	46.65	46.76	46.97	46.98
C=0	191.85	191.80	191.03	190.99	191.14	191.15
C-1′	134.80	134.69	134.33	134.42	134.32	134.29
C-2′	128.84	128.78	128.96	128.95	128.81	128.78
C-3′	129.17	129.17	128.85	128.84	128.93	128.90
C-4′	133.88	133.88	134.17	134.04	134.11	134.08
C-5′	129.17	129.17	128.85	128.84	128.93	128.90
C-6′	128.84	128.78	128.96	128.95	128.81	128.78
* Data re	corded on a	a Jeol FX-9	0 MHz spec	trometer.		

Table 4. C	hemical shi	fts (ppm) o	f 1–18	_							
0_0	2 CHCO	-0ČH_	C	0ČH ₂ Ċ0OČH ₂ ĆH ₃							
3 4	1	5	-	3 4 1 6 7							
O-CH(C	H ₃)—CO—	-OCH ₃	C	-CH(C	H ₃)CO-	ОСН	2CH3				
•	0,	U		Carbon	0,						
Compound	1	2	3	4	5	6	7				
1	168.60	65.33			52.14	_					
2	168.10	65.45	—	—		61.27	13.97				
3	172.10		73.04	18.55	52.37	_					
4	171.63	—	73.16	18.51		61.38	14.05				
5	168.91	65.04		—	52.09	_	_				
6	168.44	65.17			—	61.26	13.99				
7	172.21		72.38	18.36	52.24	—	—				
8	171.65	<u> </u>	72.76	18.42		61.17	14.14				
9	168.70	64.91			52.17	—	_				
10	168.24	65.07	—	—		61.33	13. 9 9				
11	171.99	—	72.28	18.35	52.30		_				
12	171.55	_	72.35	18.27		61.26	13.98				
13	168.61	65.72			52.28	—					
14	168.07	65.78				61.39	14.20				
15	168.99	65.39			52.30	-	—				
16	168.45	65.56				61.33	14.14				
17	168.95	65.20			52.27		—				
18	168.46	65.32				61.37	14.06				

Table 5.	¹³ C chemi	cal shifts (j	opm) of cha	licone in Cl					
				C-1	C-2	C-3	C-4	C-5	C-6
Source ^a	C-a	С- <i>В</i>	CO	C-1′	C-2′	C-3'	C-4′	C-5′	C-6′
Α	121.91	144.48	190.09	134.91	128.73	128.73	128.41	128.73	128.73
				138.13	130.35	130.35	132.63	130.35	130.35
В	121.89	144.46	190.35	134.71	128.82 or	128.32	130.42	128.32 or	128.82
				138.04	128.48 or	128.36	132.67	128.36 or	128.48

Table 6. Empirical narameters for the calculation of	chemical	shifts of	substituted	benzenes
--	----------	-----------	-------------	----------

	Α,		
C-1	ortho	meta	para
+9.9	0.0	0.0	+4.17
+9.71	-0.05	+0.05	+4.0
+29.1	-13.45	+1.25	-6.29
+6.21	0.0	0.0	+1.92
	C-1 +9.9 +9.71 +29.1 +6.21	$\begin{array}{ccc} A, \\ \hline C-1 & ortho \\ +9.9 & 0.0 \\ +9.71 & -0.05 \\ +29.1 & -13.45 \\ +6.21 & 0.0 \end{array}$	$\begin{array}{cccc} A_{i} & meta \\ +9.9 & 0.0 & 0.0 \\ +9.71 & -0.05 & +0.05 \\ +29.1 & -13.45 & +1.25 \\ +6.21 & 0.0 & 0.0 \end{array}$

due to C-2, 6, C-3, 5, C-2', 6' and C-3', 5'. The differences in these chemical shifts are very small and so it is difficult to assign them unambiguously. It is for this reason that common averaged values for C-2, C-3, C-5 and C-6 have been used in further calculations. (E)-Chalcone was used as a model after assignment in this manner.

The carbon assignment in the carbonyllinked aromatic system was based on the fact that the substituent effect on all carbons of the unsubstituted ring is very small compared with the unsubstituted chalcone. Differences in the 13 C chemical shifts of vinyl and carbonyl carbons between substituted and unsubstituted chalcone are also very small.

Phenyl carbons in the ethylene-linked aromatic system were identified by comparison of the data obtained and calculated according to the additivity scheme. The alkoxycarbonylalkyloxy group contributions to the chemical shifts of the aryl fragment were taken from Ref. 11.

The ¹³C chemical shifts of (E)-2-, -3- and -4-alkoxycarbonylalkyloxychalcones assigned in such manner are presented in Tables 2 and 4. Conversion of alkoxycarbonylalkyloxychalcones to their α , β -dibromo derivatives causes the largest changes in chemical shifts for C- α and C- β because of the changes in hybridization of these carbons. The value at lower field is assigned to C- α , which is connected to the strong electron-withdrawing carbonyl group. The signal at higher field is that of C- β .

The chemical shifts of all ring carbons in the α,β -dibromo-substituted derivatives (Tables 3 and 4) were compared with those of corresponding alkoxycarbonylalkyloxychalcones. Slight differences were observed in the chemical shift values in the case of C-1, C-1' and C-4. The assignment of C-4 was unambiguous as it is a tertiary carbon. Differentiation of C-1 from C-1' was based on the fact that the signals of C-1' have almost the same chemical shift values in the 2-, 3and 4-substituted derivatives of these compounds.

The A_i empirical parameters of the styrylketones, benzoylethylene and p-alkoxycarbonylalkyloxystyrylketone groups for the prediction of the chemical shifts of substituted benzenes and chalcones are given in Table 6. They were calculated from the benzene-chalcone and benzene-p-alkoxycarbonylalkyloxychalcone pairs. The A_i parameter of the benzoylethylene group (Table 6) was used for the calculations of the chemical shifts in the ethylene-linked benzene ring in 1-12. In 1-4 good agreement was found for C-2 (0.2-0.8 ppm), C-5 (0.5-0.6 ppm) and C-6 (1.6-1.7 ppm). Carbon atoms ortho to the alkoxycarbonylalkyloxy group have much greater differences (2.3-3.4 ppm). In 5-8 the largest differences were also obtained for carbon atoms ortho to the alkoxycarbonylalkyloxy group (1.4-2.7 ppm) and for carbons bearing this group (1.1-1.5 ppm). Good agreement was found for C-1, C-5 and C-6 (0.3-0.7 ppm). The best results were achieved for 9-12, where chemical shift values of all ethylene-linked aromatic carbons differ by less than 1 ppm.

Comparison of the number and positions of the signals of the carbon atoms in the regions 120–125, 130–135 and 135–140 ppm of 1–12 allows the differentiation of 2-, 3- and 4-alkoxycarbonylalkyloxy-substituted chalcones: 1–4, 121.68 ppm (C-5), 123.58 ppm (C- α), 124.43 ppm (C-1), 130.28 ppm (C-4), 131.38 ppm (C-6), 132.5 ppm (C-4), 138.33 ppm (C-1); **5–8**, 122.02 ppm (C- α), 122.05 ppm (C-6), 132.71 ppm (C-4), 136.31 ppm (C-1), 137.92 (C-1); **9–12**, 120.08 ppm (C- α), 130.08 ppm (C-2), 132.47 ppm (C-4'), 138.21 ppm (C-1').

Acknowledgements

I thank Dr Jamshed N. Lam for his help in recording the 200 MHz spectra. This work was supported by the Ministry of National Education within project RP.II.13.

References

- S. C. Kushwaha, S. S. Misra and J. B. Lal, *Proc. Natl. Acad. Sci., India, Sect.* A 40, 301 (1970).
- M. Gabor, J. Sallai, T. Szell and Gy. Sipos, Acta Microbiol. Acad. Sci. Hung. 14, 45 (1967).
- R. Laliberte, D. Campbell and F. Bruderlein, *Can. J. Pharm. Sci.* 2, 37 (1967).
- A. E. Vanstone and G. K. Maile, Ger. Offen 2810253; Chem. Abstr. 90, 22628w (1979).
- K. Hanemann, H. Schubert, D. Demus and G. Pelzl, *E. Ger. Pat.* 115 283; *Chem. Abstr.* 87, 76418j (1977).
- M. Kato, M. Hasegawa and T. Tchijyo, US Pat. 3873500; Chem. Abstr. 83, 26065z (1975).
- M. Flammang, C. G. Wermuth and H. Delassue, *Chim. Ther.* 5, 431 (1970).
- 8. M. Szajda, Pharmazie in press.
- E. Solianova, S. Toma and S. Gronowitz, Org. Magn. Reson. 8, 439 (1976).
- 10. G. Musumarra and F. P. Ballistreri, Org. Magn. Reson. 14, 384 (1980).
- E. Wyrzykiewicz and U. Sylwestrzak, Abstracts of Third Regional Chemical Meeting, Poznań, 1983, p. 144.

Received 21 March 1988; accepted (revised) 3 October 1988