THE MASS SPECTRA OF SUBSTITUTED 2-METHYLBENZOPHENONES

JAMES GRIMSHAW, CHARLES S. SELL and REGINALD J. HASLETT Department of Chemistry, Queen's University, Belfast BT9 5AG, Northern Ireland

(Received 6 July 1973; accepted 7 August 1973)

Abstract—The mass spectra of some methoxy and methyl derivatives of 2-methylbenzophenone have been examined. Loss of a substituent from 3'- and 4'- positions as well as the previously known loss from 2'-positions are important fragmentation processes. Thus, these fragmentations are of little use in locating substituents on benzophenones of unknown structure. Deuterium labelling shows the $[M - 1]^+$ ion from 3',4,4',5,5'-pentamethoxy-2-methyl benzophenone to be due largely to loss of hydrogen from 2'- and 6'-positions.

IN THE course of fragmentation studies on a large number of substituted benzophenone ions, Ballantine and Pillinger¹ found that for 2'-substituted derivatives of 2-hydroxy- and 2-methylbenzophenone an important fragment ion results from the expulsion of the 2'-substituent. The substituent may be OH, OMe, CO_2H , CO_2Me or Me and the corresponding fragment ion usually shows greater abundance than the [ArCO]⁺ or [Ar]⁺ ions formed by fragmentation α - to the ketone function. This latter process has been well studied and is usually the dominant process in the mass spectra of benzophenones.² 2-Hydroxy- and 2-methylbenzophenone ions also give an important [M - 1] fragment. In the case of 2-hydroxybenzophenone the [M - 1]⁺ fragment was demonstrated by deuterium labelling, not to be due to the loss of the hydroxyl hydrogen atom. Ballantine and Pillinger proposed the scheme illustrated below (Scheme 1) for a 2-methylbenzophenone derivative (I) to account for the expulsion of a 2'-substituent, R, which may be H or one of those mentioned previously,



and the corresponding scheme for a 2-hydroxybenzophenone where the intermediate (a) cyclises to expel the R group.

Methoxy derivatives of 2-methylbenzophenone

If this expulsion is specific for a 2'-substituent as suggested, then it may be useful for determining the orientation of substituents in a benzophenone of unknown structure. The specificity of the fragmentation process for the one particular group of substituents was tested using a number of methoxy substituted 2-methylbenzophenones. Some ethoxy derivatives were also examined. We found it convenient to examine derivatives of 2-methyl-4,5-methylenedioxybenzophenone (II) and 4,5dimethoxy-2-methylbenzophenone (III) since these are relatively easy to prepare.



The mass spectra of four derivatives of 2-methylbenzophenone with methoxy substituents in positions other than 2'- are illustrated in Fig. 1. Formation of a daughter ion by expulsion of a methoxyl group is not limited to compounds with this group in the 2'-position. From these and other results listed in Table 1 it appears that methoxy and ethoxy groups can be expelled from 2'-, 3'- and 4'-positions of the 2-methylbenzophenone ion to give a strong daughter ion but not from 4- and 5-positions.

				(1)	0								
		(11	l) (1	$R_1 = 0$	OMe,	(]	(I)		(11	I)e			
(11)		$R_2 = OMe$,		$R_2 = OEt$,		$R_2 = Me$,			$R_3 = H$,			(III)	
$\mathbf{R_1} = \mathbf{R_2} =$	$R_3 = H$	$\mathbf{R}_1 = \mathbf{R}$	3 = H	R ₃ =	Η	$R_1 = F$	₹ 3 = F	ŦŦ	$R_1 = R$	$_2 = ON$	Me 1	$R_1 = R_2 =$	$R_3 = OMe$
m e	%1	m/e	%1	m/e	%I	m/e	%1	r	m/e	%	I	m/e	%I
240	88	270	93	314	100	254	60)	316	9	8	346	100
239	100	269	100	313	73	253	51	l	315	5	7	345	27
223	12	255 ^b	15	299 ^b	26	240	20)	301 ^b	1.	5	331 ^b	21
181	12	253	20	285 ^d	18	239ъ	100)	286	2	2	316	20
163	31	240	19	283ª	39	163	23	;	285ª	10	0	315ª	84
105	17	239ª	87	270	20	119	19)	179	1	8	299	13
77	50	163	21	269°	92	91	37	7	165	2	2	195	10
		117	10	151	37	77	17	7				179	20
		92	17										
	3,3	',4,4'-Tet	rameth	oxybenz	cophei	none ^f	m e	302	271ª	165			
					-		%I	91	24	100			
3,3',4,4',5-Pentamethoxybenzo				nzopł	henone ^g	m e	332	317ъ	301ª	195	165		
				·	-		%I	100	14	8	17	37	

TABLE 1. RELATIVE INTENSITIES OF THE MAJOR IONS IN THE MASS SPECTRA OF SOME BENZOPHENONES

^a $[M - OMe]^+$, ^b $[M - Me]^+$, ^c [M - OEt], ^d [M - Et].

^e Ref. 3, ^f Ref. 4, ^g Ref. 5.



By contrast 3,3',4,4',5-pentamethoxy- and 3,3',4,4'-tetramethoxybenzophenone show only a small $[M - OMe]^+$ peak and predominantly cleavage to give the $[ArCO]^+$ type fragments at m/e 195 and/or, 165.

It seems likely that intermediates of the type b suggested by Ballantine and Pillinger¹ are involved in the expulsion of methoxy groups. The intermediate can be written as the enolic molecular ion. The fact that a methoxy group is preferentially expelled from the ring not involved in enolization suggests that cyclization reactions of the enol on this second ring are involved in the reaction sequence. Expulsion of the methoxy group from 3'- and 4'-positions may involve hydrogen migration as shown, but other reaction schemes can be drawn and at this stage the reaction cannot be defined completely. (Scheme 2.)



2,4'-Dimethyl-4,5-methylenedioxybenzophenone

2-Methylbenzophenone shows no significant $[M - Me]^+$ ion.¹ In contrast II $(R_1 = R_3 = H, R_2 = Me)$ has $[M - Me]^+$ as the base peak. Hence it appears that methyl radicals can also be expelled from the 4'- position, probably by a similar mechanism to that discussed for the methoxy derivatives.

3',4,4',5,5'-Pentamethoxy-2-methylbenzophenone-2',6'-d₂

This deuterium labelled benzophenone was prepared in order to check if the $[M - 1]^+$ fragment in the undeuterated benzophenone arises from hydrogen loss at 2'- and 6'- positions. The extent of deuterium labelling was obtained from mass spectra measured at 12 eV when the $[M - 1]^+$ peak is negligible. At 70 eV there is loss of deuterium from the molecular ion corresponding to loss of hydrogen from the undeuterated molecule (see Table 2). Furthermore, after correction for the d_1 content,



The mass spectra of substituted 2-methylbenzophenones

 m/e	(IV), R = H	(IV), R = D
		$95\% d_2, 5\% d_1$
350		3.2
349		22
348	3.2	100
347	23	10
346	100	14
345	24	0.0
344	0.0	

Table 2. Mass spectra of IV and its d_2 -derivative at 70 eV in the region of the molecular ion, normalized to $[M]^{+} = 100$

there is evidence for a small loss of hydrogen from the d_2 -molecular ion. Thus we conclude that loss of hydrogen from the molecular ion of 3',4,4',5,5'-pentamethoxy-2-methylbenzophenone occurs largely from 2'- and 6'- positions, but that another mechanism accounts for about 20% of the $[M - 1]^+$ ions.

EXPERIMENTAL

Mass spectra were obtained using an AEI MS-902 instrument and the direct insertion technique operating at 70 eV (unless otherwise specified).

Substituted benzophenones: (a) Using 3,4-methylenedioxytoluene. A solution of the relevant acid (25 mmol) in dichloromethane (50 ml) and phosphorus trichloride (8.3 mmol) was refluxed for 1 h, cooled and decanted from phosphorus acid. Anhydrous ferric chloride (25 mmol) and 2,3methylene dioxytoluene⁶ (25 mmol) were added and the mixture stirred at 0° C for several hours. The mixture was then decomposed with ice and hydrochloric acid, the organic layer washed with sodium hydrogen carbonate solution and water, dried ($MgSO_4$), evaporated and the product crystallized from methanol or distilled (10 to 50% yield). 2-Methyl-4,5-methylenedioxybenzophenone, m.p. 53 to 54°C (Found: C, 74.9; H, 4.9. C₁₅H₁₈O₃ requires C, 75.0; H, 5.0%); 2,4'-dimethyl-4,5-methylenedioxybenzophenone, m.p. 102 to 103°C (Found: C, 75.2; H, 5.7. C₁₆H₁₄O₃ requires C, 75.6; H, 5.6%); 3'-methoxy-2-methyl-4,5-methylenedioxybenzophenone, m.p. 82 to 83°C (Found: C, 70.9; H, 5.4. C16H14O4 requires C, 71.1; H, 5.2%; 4'-methoxy-2-methyl-4,5-methylenedioxybenzophenone, m.p. 111 to 112°C (Found: C, 71·1; H, 5·3%); 4'-ethoxy-3'-methoxy-2-methyl-4,5-methylenedioxybenzophenone, m.p. 91 to 92°C (Found: C, 69 0; H, 5 8. C₁₈H₁₈O₅ requires C, 68 8; H, 5 8%); 3'-ethoxy-4'-methoxy-2-methyl-4,5-methylenedioxybenzophenone, m.p. 133 to 134°C (Found: C, 68.8; H, 5.8%). (b) Other benzophenones were prepared by the Friedel-Crafts reaction with aluminium chloride. o-Toluoyl chloride and anisole gave 4'-methoxy-2-methylbenzophenone, b.p. 118 to 124°C/0.01 mm Hg (Found: C, 79.9; H, 5.9. C₁₅H₁₄O₂ requires C, 79.6; H, 6.2%), n.m.r. spectrum $(CHCl_3) \tau 2.24 (2H, d, J = 8.8 Hz), 3.11 (2H, d, J = 8.8 Hz), 2.76 (4H, m), 6.17 (3H, s, OMe), 7.71$ (3H, s, Me). The appropriate acid chloride and 3,4-dimethoxytoluene gave 4,5-dimethoxy-2-methylbenzophenone, b.p. 143 to 145°C/0.05 mm Hg (Found: C, 74.4; H, 6.3. C₁₆H₁₆O₃ requires C, 75.0; H, 6·3%); 3',4,4',5,5'-pentamethoxy-2-methylbenzophenone, m.p. 105 to 107°C (Found; C, 66·0; H, 6.3. C₁₉H₂₂O₆ requires C, 65.9; H, 6.4%). Other derivatives are described in the literature.

3,4,5-*Trimethoxybenzoic acid*-2,6-d₂. Acetic anhydride (7 g) and deuterium oxide (25 ml) were mixed when zinc dust (14 g) and 2,6-dibromo-3,4,5-trimethoxybenzoic acid (5 g) (both washed with deuterium oxide *in situ*) were added and the mixture refluxed for 6 days. The solution was then filtered, the residue washed with hot methanol, and the combined filtrates diluted with water and extracted with ethyl acetate. Evaporation of the solvent left 3,4,5-trimethoxybenzoic acid-2,6-d₂, crystallized from water, m.p. 167°C (Found ~ 95% d₂).

3',4,4',5,5'-Pentamethoxy-2-methylbenzophenone-2',6'-d₂. Much of the deuterium label was lost in a preparation by the usual Friedel Crafts reaction. Deuterated trimethoxybenzoic acid was reduced with lithium aluminium hydride to the benzyl alcohol which was oxidized by chromium trioxidepyridine in dichloromethane to the benzaldehyde. A Grignard reagent was prepared from 2-bromo-4,5-dimethoxytoluene (4.0 g) and magnesium (0.4 g) in tetrahydrofuran (20 ml). The deuterated benzaldehyde (1.4 g) was added and after 8 h the reaction mixture was poured into dilute sulphuric acid and the product isolated with ether. This ethereal solution was stirred overnight with chromium trioxide (3.0 g) in water (20 ml) and sulphuric acid (3 ml), washed with water, dried (MgSO₄) and the solvent removed. Chromatography of the residue over alumina and elution with ether-light petroleum (b.p. 30 to 40°C) (1:1) gave 4,4',5,5'-tetramethoxy-2,2'-dimethylbiphenyl, m.p. 119 to 120°C (Lit.⁷ m.p. 117°C). Elution with ether gave 3',4,4',5,5'-pentamethoxy-2-methylbenzophenone-2',6'-d₂, m.p. 105 to 107°C, crystallized from ether.

Acknowledgement—We thank the Ministry of Education, N. Ireland, for a maintenance award (to CSS).

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