Tetrahedron. Vol. 27, pp. 4643 to 4651. Pergamon Press 1971. Printed in Great Britain

CIRCULAR DICHROISM OF (*S*)-2-METHYL BUTYROPHENONES

O. KORVER
Unilever Research, Vlaardingen, The Netherlands

(*Received in the UK* 19 *May* 1971; *Accepted for publication* 26 *May* 1971)

Abstract—Circular dichroism spectra of (*S*)-2-methyl butyrophenone and six substituted derivatives, viz. 4'-CH_3, 4'-F, 4'-Cl, 4'-Br, 4'-CH_3O and 2'-Cl, 4'-CH_3O are reported.

From the CD band of the $n \rightarrow \pi^*$ transition it is concluded that two conformations of the non-planar benzoylchromophore predominate. The conformational equilibrium is both temperature- and solvent-dependent. CD bands of the $'L_a$ and $'L_b$ transitions can be observed in only a few cases.

INTRODUCTION

CD INVESTIGATIONS on open-chain aromatic compounds are scarce. The conformational mobility of these compounds and the still inadequate knowledge[1] of the chiroptical properties of the aromatic chromophore often prohibit interpretation of the CD spectra. Measurements of the CD spectra at low temperature (−185°), where conformational mobility is restricted will probably give more information on these properties.

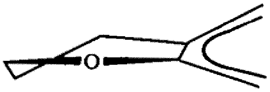
Following the study on the influence of substituents on the CD spectra of mandelic acids[2] (non-conjugated aromatic chromophore) it seemed of interest to investigate a similar influence on the spectra of compounds containing the substituted benzoyl chromophore. Because of their easy availability[3] we chose *para*-substituted (*S*)-2-methyl butyrophenones.

To understand the electronic transitions that are possible in these molecules, we shall briefly discuss the electronic spectra of acetophenones.

The benzoyl chromophore gives rise to three bands in the accessible ultraviolet:[4] (1) a weak $n \rightarrow \pi^*$ band ($\varepsilon \sim 5$–100) at about 320 nm; (2) a moderately intense band ($\varepsilon \sim 1000$–2000) between 270 and 290 nm, corresponding to the forbidden $'L_b$ transition in benzene; (3) a high-intensity band at about 240 nm, corresponding to the benzene $'L_a$ transition.

From the study of substitution effects on the UV spectra of acetophenone and comparison with benzaldehyde spectra Suzuki[5] inferred that an appreciable steric interaction exists between the Me group and the *ortho*-hydrogens of the Ph group, which precludes planarity of the benzoyl chromophore. This is, *a fortiori*, the case in the 2-methyl butyrophenones.

The CD spectra of several compounds containing the benzoyl chromophore such as tetralins have been studied by Snatzke.[6] In these compounds the conformational mobility was restricted because the carbonyl group was part of a ring system. Snatzke concludes that a non-planar conformation of the benzoyl chromophore as indicated in Formula I gives rise to a positive Cotton effect for the $n \rightarrow \pi^*$ transition.



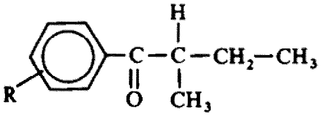
I

RESULTS

UV spectra. Comparison of the UV spectrum of compd **1** (Table 1) with that of acetophenone reveals that for compd **1** the intensity of the $'L_a$ band is lower. Such a lowering is generally ascribed to an increase in steric interactions, resulting in a decrease of the planarity of the chromophoric system.[7] The wavelength differences between the spectra of the butyrophenones are due to substitution effects.

CD spectra (Tables 2–4 and Figs 1–7). It is clear that both a solvent and a temperature effect on the CD spectra is present. It seems appropriate to discuss the optical purity of the (S)-butyrophenones here. The (+)(S)2-methyl butyric acid, obtained from (−)(S)2-methyl butanol-1, which was used as a starting material had $[\alpha]_D^{25} = +18{\cdot}9°$ (EtOH), whereas optically pure (+)(S)2-methyl butyric acid has $[\alpha]_D^{25} = +19{\cdot}8°$.[8] The optical purity of the starting material could not therefore be higher than 95%. Racemization apparently occurs during the Friedel–Crafts reaction between (+)(S)-2-methyl butyroyl chloride and the appropriately substituted benzene, the degree of racemization depending on the way the reaction is carried out. Thus Desai *et al.*[3] find $[\alpha]_D^{25} = +5{\cdot}10°$ for **1** while our value is $+28{\cdot}5°$. Our other values are also appreciably higher than those reported by Desai *et al.*[3] Another value for the specific rotation of (S)-**1** has been reported by Seebach *et al.*:[9] $[\alpha]_D^{25} = +44°$ ($c = 5$, ether). Assuming that this value represents optical purity, we obtain an optical purity of 65% for **1**. There is no reason to assume that the optical purity of the other

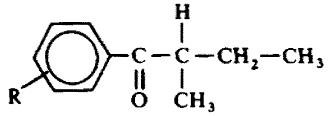
Table 1. UV data of 2-methyl butyrophenones in hexane



Compound No.	R	$'L_a$		$'L_b$		n → π*	
		λ	ε	λ	ε	λ	ε
1	4'-H	239	11,960	280	shoulder	328	56
2	4'-CH_3	248	13,300	290	shoulder	327	64
3	4'-F	241	11,820	280	shoulder	325	57
4	4'-Cl	250	17,590	280–300	shoulder	330	63
5	4'-Br	254	18,420	280–300	shoulder	322	87
6	4'-CH_3O	265	18,030	280–300	shoulder	315	116
7	2'-Cl—4'-CH_3O	257	9,710	280	shoulder	310	280
	acetophenone[a]	239	13,130	279	890	320	41

[a] From Ref. 7

TABLE 2. CD SPECTRA OF 2-METHYL BUTYROPHENONES IN ETHANOL



Compound No.	*R*	$n \rightarrow \pi^*$		Compound No.	*R*	$n \rightarrow \pi^*$	
		λ	$\Delta\varepsilon$			λ	$\Delta\varepsilon$
1	4'-H	348	−0·013[a]	**4**	4'-Cl	325	−0·020
		332	−0·016				
		300	+0·014	**5**	4'-Br	370	−0·019
						350	−0·034
2	4'-CH_3	355	−0·005[b]			325	−0·053
		344	−0·021				
		331	−0·034	**6**	4'-CH_3O	320	−0·082
		324	−0·031				
				7	2'-Cl—4'-CH_3O	325	−0·217[d]
3	4'-F	360	−0·005[c]				
		352	−0·017				
		330	−0·025				
		319	−0·023				

[a] $'L_b$: $\lambda = 280$; $\Delta\varepsilon = -0{\cdot}101$

[b] $'L_a$: $\lambda = 250$; $\Delta\varepsilon = +1{\cdot}267$

[c] $'L_a$: $\lambda = 245$; $\Delta\varepsilon = +0{\cdot}773$

[d] $'L_a$: $\lambda = 262$; $\Delta\varepsilon = +0{\cdot}737$

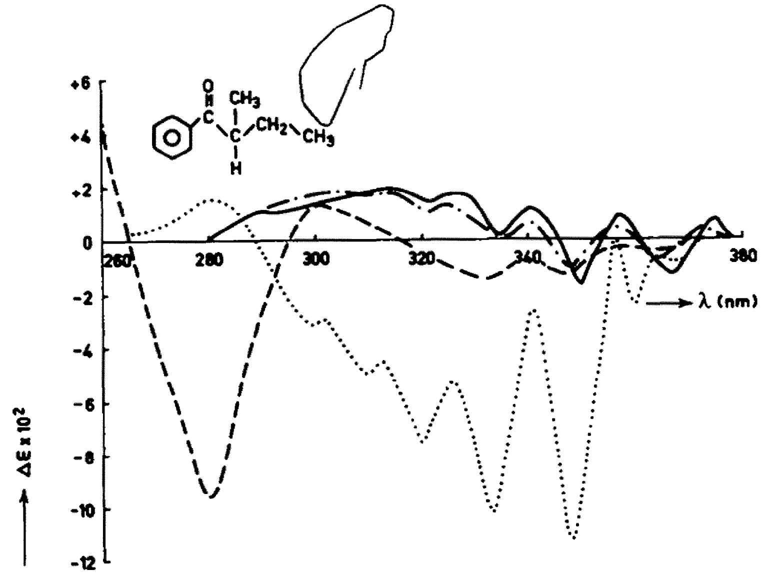
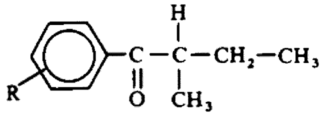


FIG 1. CD spectrum of 2-methyl butyrophenone in hexane (—), ethanol (— — —), EPA at −185°C (· · · · ·) and EPA at 25°C (— · — · — ·)

TABLE 3. CD SPECTRA OF 2-METHYL BUTYROPHENONES IN HEXANE



Compound No.	R	$n \to \pi^*$		Compound No.	R	$n \to \pi^*$	
		λ	Δε			λ	Δε
1	4'-H	374·5	+0·008[a]	3		338	+0·006
		368	−0·015	(contd.)		332	−0·007
		357·5	+0·006			312	+0·013
		351	−0·017				
		342	+0·011	4	4'-Cl	370	−0·015[d]
		327·5	+0·016			352	−0·026
		315	+0·020			336	−0·016
						325	−0·007
2	4'-CH_3	372	+0·005[b]				
		366	−0·017	5	4'-Br	371	−0·018
		353	+0·004			354	−0·027
		349	−0·020			338	−0·019
		334	−0·012			325	−0·009
		326	+0·006				
		313	+0·011	6	4'-CH_3O	371	−0·018
						354	−0·027
3	4'-F	370	+0·008[c]			338	−0·019
		363	−0·016			325	−0·009
		354	+0·005				
		347	−0·020	7	2'-Cl—4'-CH_3O	325	−0·153[e]

[a] $'L_a$: $\lambda = 240$; $\Delta\varepsilon = +1{\cdot}200$

[b] $'L_a$: $\lambda = 245$; $\Delta\varepsilon = +0{\cdot}493$

[c] $'L_a$: $\lambda = 243$; $\Delta\varepsilon = +0{\cdot}802$

[d] $'L_a$: $\lambda = 250$; $\Delta\varepsilon = +0{\cdot}540$

[e] $'L_a$: $\lambda = 260$; $\Delta\varepsilon = +0{\cdot}624$

products is much higher. All Δε values in the tables should therefore be viewed with caution*

DISCUSSION

1 in hexane clearly shows positive and negative CD in the region of the n → π* transition. Apparently two overlapping bands of opposite sign are present. The maximum negative and the maximum positive intensity are found at about 30 nm apart (350 and 320 nm respectively). This suggests that we have to do with the sum curve of a positive and negative band of about equal magnitude, separated by a small distance.[10] The presence of two CD bands can be explained by assuming two conformations. If we consider (S)-1 in Newman projection along the C_1—C_2 bond and assume that the Ph group is more bulky than the carbonyl oxygen, the following two conformations may occur: Planarity of the benzoyl chromophore is impossible for steric reasons.

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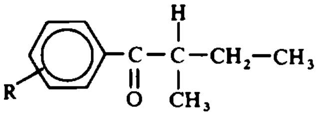
* A recent paper by Mamlok, Marquet and Lacombe (Tetrahedron Letters (1971) 1039) gives a method for the determination of optical purity of ketones by an NMR method. Chemical shift differences between the antipodes were smaller for our compounds (2–5 Hz at 220 Mc) than in the cases reported. Therefore only a rough estimate of optical purity can be made; it is in the range 65–75% for all compounds.

TABLE 4. CD SPECTRA OF 2-METHYL BUTYROPHENONES IN EPA [ETHANOL : ISOPENTANE : DIETHYLETHER (2 : 5 : 5, v/v)] AT −185°



Compound No.	*R*	$n \to \pi^*$		Compound No.	*R*	$n \to \pi^*$	
		λ	$\Delta\varepsilon$			λ	$\Delta\varepsilon$
1	4′-H	364	−0·134[a]	4	4′-Cl	333	−0·056
		348	−0·230	(contd.)		322	−0·039
		333	−0·208			311	−0·025
		320	−0·156				
		309	−0·109	5	4′-Br	368	−0·047
						360	+0·030
2	4′-CH_3	362	−0·107[b]			351	−0·111
		354	+0·020			343·5	+0·036
		345	−0·176			335	−0·092
		339	+0·009			329·5	+0·011
		331	−0·141			322	−0·056
		318	−0·085			310	−0·030
		308	−0·047			300	−0·013
3	4′-F	361	−0·096[c]	6	4′-CH_3O	356	−0·084[d]
		353	+0·003			349	+0·052
		344	−0·176			340	−0·098
		330	−0·169			333	+0·089
		318	−0·122			327	−0·016
		307	−0·073			319	+0·078
						307	+0·077
4	4′-Cl	368	−0·032				
		359	+0·005	7	2′-Cl—4′-CH_3O	322	−0·319[e]
		350	−0·059				

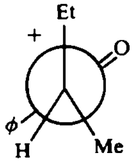
[a] $'L_b$: $\lambda = 278$; $\Delta\varepsilon = +0{\cdot}159$
$'L_a$: $\lambda = 249$; $\Delta\varepsilon = -0{\cdot}732$

[b] $'L_a$: $\lambda = 250$; $\Delta\varepsilon = -0{\cdot}942$

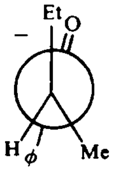
[c] $'L_a$: $\lambda = 245$; $\Delta\varepsilon = -0{\cdot}515$

[d] $'L_a$: $\lambda = 265$; $\Delta\varepsilon = -0{\cdot}390$

[e] $'L_a$: $\lambda = 260$; $\Delta\varepsilon = +0{\cdot}540$



IIa



IIb

The Ph group may be between the Et group and the hydrogen atom (IIa) or between the Me group and the hydrogen atom (IIb). Conformations IIa and IIb will differ only slightly in energy, IIb probably being the more stable. Therefore at low temperature IIb should predominate. From the CD data it is clear that for (*S*)-1 the negative band becomes much stronger at low temperature. Consequently conformation IIb should give rise to a negative CD band. This would imply that in IIb the chirality of the benzoyl chromophore (i.e. the twist around the Ph—C single bond) would be opposite

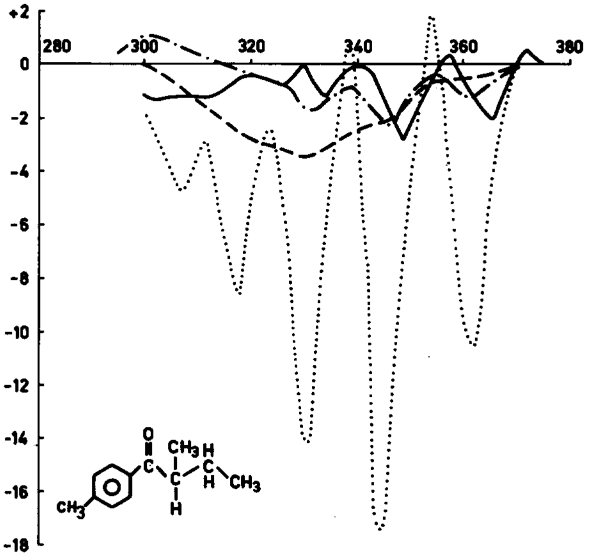


FIG 2. CD spectrum of 2-4′-dimethyl butyrophenone in hexane (—), ethanol (— —), EPA at −185°C (· · · ·) and EPA at 25°C (— · — · — ·)

to the situation depicted in I. In IIa the situation of I would prevail.[6] From model building it may be concluded that the assumptions made are not unreasonable.

Similar CD spectra are found for **2** and **3**. In **4** and **5** and, *a fortiori*, in **6** the positive band can be observed much clearer at low temperature than at room temperature. The UV spectra (Table 1) show that in these compounds the $n \to \pi^*$ transition and the $'L_b$ transition are at closer distance than in **1**, **2** and **3**. This is especially so in **6**. Therefore it is conceivable that in the CD spectrum of **4**, **5** and **6** the $n \to \pi^*$ and the $'L_b$ band

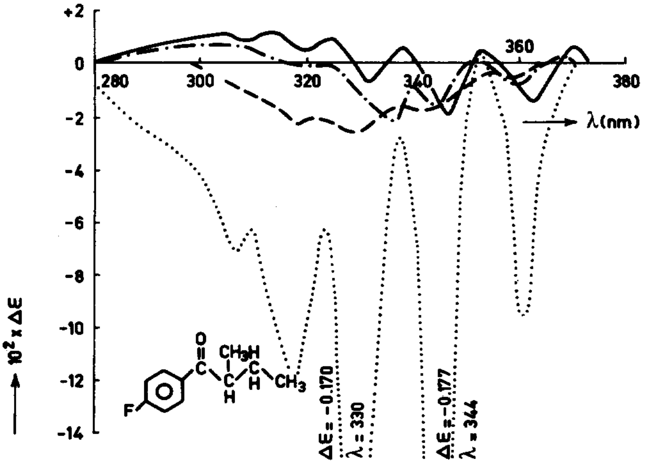


FIG 3. CD spectrum of 2-methyl-4′-fluorobutyrophenone in hexane (—), ethanol (— — —), EPA at −185°C (· · · ·) and EPA at 25°C (— · — · — ·)

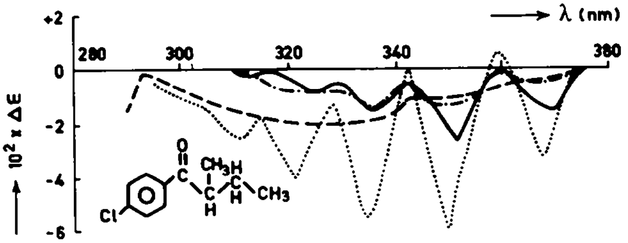


FIG 4. CD spectrum of 2-methyl-4'-chlorobutyrophenone in hexane (—), ethanol (— — —), EPA at 185°C (· · · ·) and EPA at 25°C (— · — · — ·)

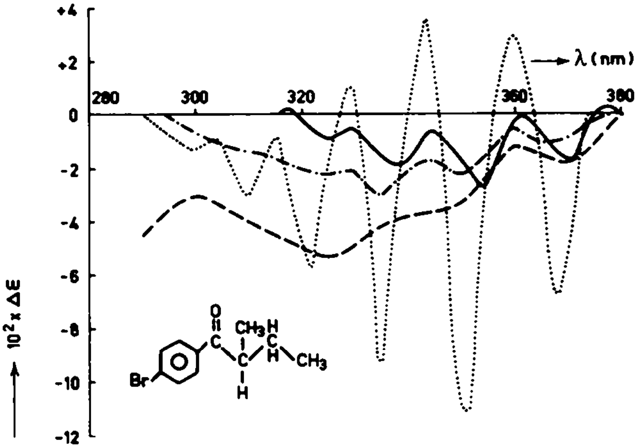


FIG 5. CD spectrum of 2-methyl-4'-bromobutyrophenone in hexane (—), ethanol (— — —), EPA at − 185°C (· · · ·) and EPA at 25°C (— · — · — ·)

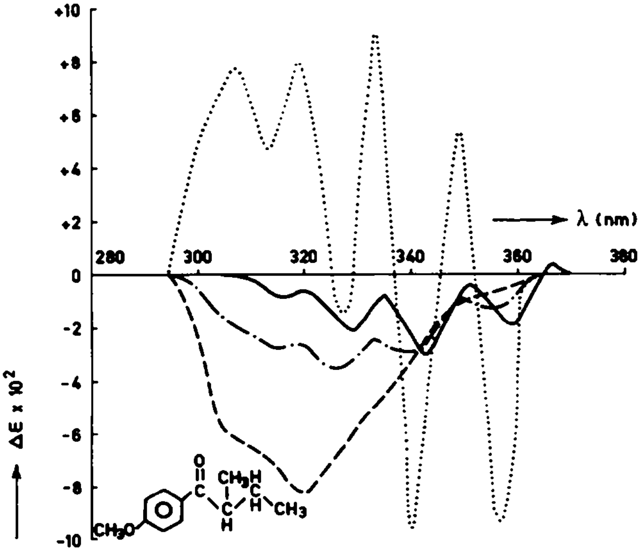


FIG 6. CD spectrum of 2-methyl-4'-methoxybutyrophenone in hexane (—), ethanol (— — —), EPA at − 185°C (· · · ·) and EPA at 25°C (— · — · — ·)

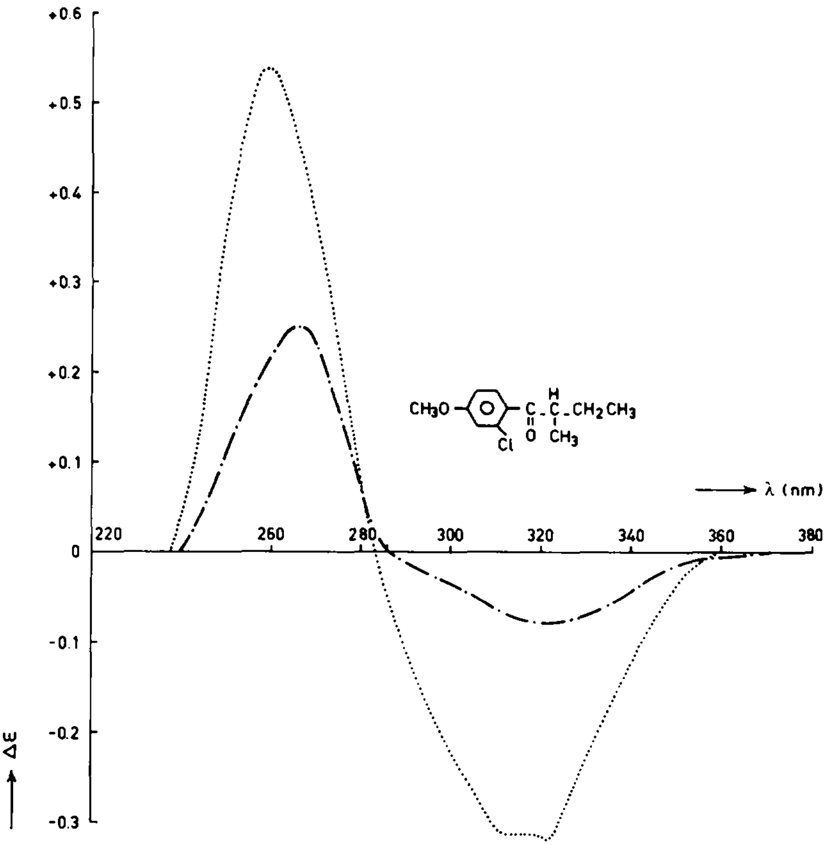


FIG 7. CD spectrum of 2-methyl-2'-chloro-4'methoxybutyrophenone EPA at −185°C(·····) and EPA at 25°C(—·—·—·—)

are overlapping. In agreement with this suggestion is the fact that in the only compound where the $'L_b$ band is clearly observable (**1**), it is indeed positive at −185° and negative at room temperature in EtOH.

The negative $\Delta\varepsilon$-values[*] of the CD-spectrum of **7** largely exceed those of the other compounds. Probably the conformational equilibrium is shifted more to formula IIb because of the larger size of the *ortho*-substituted Ph group.

We conclude that two conformations (IIa and IIb) predominate in 2-methyl butyrophenones at room temperature and that the conformational equilibrium is shifted from IIa to IIb by lowering the temperature or changing the solvent from apolar to polar.

The $'L_a$ and $'L_b$ CD bands cannot be observed in many cases, probably because the intensities and therefore the $\Delta\varepsilon/\varepsilon$ ratio are very small as a result of cancelling of positive and negative bands.

[*] Because of the unknown optical purity it might be argued that it is not warranted to draw conclusions from the intensity of the CD bands. It is hardly likely, however, that during synthesis a large difference in degree of racemization occurs for **6** and **7**. If a difference does exist, the latter compound is expected to be least optically pure, because the reaction conditions were more severe.

EXPERIMENTAL

The (S)-2-methyl butyrophenones were prepared as described by Desai *et al.*[3] The optical purity of the products was discussed under Results section. Specific rotations and b.ps are as follows:

Compound	b.p. (°/mm Hg)	$[\alpha]_D^{25}$ (EtOH)
1	62/0·25	+28·5
2	80/0·5	+25·1
3	85/0·4	+20·3
4	95/0·4	+9·4
5	105/0·8	+12·9
6	105/0·4	+15·4
7	120/0·45	+1·3

CD measurements were made on a Jouan Dichrograph 185^{II}, provided with a low-temperature accessory. The UV spectra were measured on a Cary 14 spectrophotometer. The low-temperature $\Delta\varepsilon$ values were corrected for shrinkage of the solvent[11])

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