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# **Conformational Analysis of Indan-1-ols**

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The conformations of some new indan-1-ols have been assigned from their mode of synthesis and from their n.m.r. spectra. Those with a substituent  $RCH_2$  on C-1 show an unexpected correlation between the chemical shifts of the methylene protons and the configuration of the 2,3-substituents.

In the course of studying the conformation of the fivemembered ring in a series of substituted indanes, we have prepared some model derivatives in which the stereochemistry was partially known from chemical evidence. Some 3-phenylindan-1-ones (II) were made by stereospecific reduction of the corresponding inden-1ones (I), or by internal Friedel-Crafts cyclisation of 3,3-diphenylpropionic acid (IV).

A series of 3-phenylindan-1-ols (III) was finally obtained by the appropriate Grignard reactions. The 100 MHz proton magnetic spectra were recorded for both series (II) and (III).

### EXPERIMENTAL

Indenones (I).-2,3-Diphenylinden-1-one was obtained from Ralph Emmanuel Ltd. 2-Methyl-3-phenylinden-1one was prepared by the cyclisation of ethyl 3,3-diphenyl-2methyl-3-hydroxypropionate.1



Indanones (II).-The indenones were hydrogenated with 'White spot' hydrogen (British Oxygen Co.) in the presence of Adams catalyst (PtO2), using the method of Zimmermann,<sup>2</sup> i.e. neutral benzene for cis-reduction and 1% sodium hydroxide in ethanol-ethyl acetate (2:1)

TABLE 1

Analytical data for indan-1-ols (III)

		2-H3-H	Mn	Found	<b>i (%</b> )	Req	d. (%)
R	R'	config.	(°Č)	c	н	C	н
н	Me	•	Oil a	85.6	7.7	85.6	7.6
	Ph		87	87.8	6.7	88.0	6.6
Me	н	trans	90	85.4	7.6	85.6	7.6
	$\mathbf{Me}$	trans <sup>b</sup>	100	84·9	7.9	85.0	<b>8</b> ∙0
	$\mathbf{Ph}$	cis	100	86.4	7.1 }	07.0	7.0
		trans	126	86.9	7.1∫	01.9	1.0
Ph	н	cis	130	87.9	6•5 ો	00 0	6.7
		trans	125	<b>88</b> ·1	6-8 ∫	99.0	0.1
	Me	cis	74	$88 \cdot 2$	7։1 ∖	07.0	7.0
		trans	169	87.8	7.0 ∫	01.9	1.0
	$\mathbf{Ph}$	cis •	153	88.9	6.4 ∖	00.0	G. A
		trans	163	<b>90·0</b>	6.5 ∫	89.2	0.4
	o-Tolyl	cis	138	<b>89·4</b>	6.8	89.3	6.7
		1 2000 1					

<sup>a</sup>  $n_D^{25} = 1.5628$ . <sup>b</sup> cis-Isomers could not be isolated. <sup>e</sup> First prepared by E. Bergmann and W. Schreiber, Annalen, 1933, 500, 118, but configuration unknown.

for trans-reduction. 3-Phenylindan-1-one was obtained by cyclising 3,3-diphenylpropionic acid (IV), using the method of Koelsch.<sup>3</sup> The acid was supplied by Ralph Emmanuel Ltd.

All the indanones have been prepared previously,2-4 and since their analyses were satisfactory, only their

<sup>1</sup> E. Bergmann and H. Weiss, Annalen, 1930, 480, 64.

<sup>2</sup> H. E. Zimmerman, J. Amer. Chem. Soc., 1956, **78**, 1168.
<sup>3</sup> C. F. Koelsch, J. Amer. Chem. Soc., 1934, **56**, 1337.
<sup>4</sup> C. F. Koelsch, H. Hochmann, and C. D. Le Claire, J. Amer.

Chem. Soc., 1943, 65, 59; C. F. Koelsch, J. Org. Chem., 1961, **26**, 2590.

<sup>5</sup> A. I. Vogel, 'Elementary Practical Organic Chemistry,' Part 1, Longmans, London, 1957.

m.p.s are quoted here (Table 2). These agree with, or indicate greater purity than, the earlier values.

Indanols (III).—The Grignard reactions were conducted by the standard method.<sup>5</sup> The products (30—70% yield) were oils, most of which crystallised on trituration with light petroleum (b.p. 60-80°) (from which they were recrystallised). cis-2,3-Diphenyl-1-ethylindan-1-ol was crystallised by allowing the oil to stand for several days with aqueous ethanol.

Analytical data for the indanols are summarised in Table 1.

Spectra and Analyses.-All spectra were recorded on a Varian HA-100 D at the Physico-Chemical Measurement Unit, Harwell, using (unless otherwise stated) 8% solutions in deuteriochloroform at ambient temperature, with tetramethylsilane as internal reference. Two of the spectra involved the analysis of ABC<sub>3</sub> patterns (see Table 3) at the Atlas Computer Laboratory, Didcot, Berks. All elemental analyses were performed by the Alfred Bernhardt Microanalytical Laboratory (West Germany).

### **RESULTS AND DISCUSSION**

Table 2 summarises the n.m.r. parameters for the indan-1-ones (II), and confirms the assignments given

TABLE	2
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Chemical shifts  $\delta$  (p.p.m.) and coupling constants J (Hz) for indan-1-ones (II) in CDCl<sub>3</sub> at ambient temperature

	:	2-H3-H					M.p.		
	R	config.	$J_{23}$	2-H	3-H	R	(°Ĉ)		
(i)	$\mathbf{Ph}$	cis	8.1	4·39 (d)	5·02 (d)		138		
(ii)		trans	<b>4</b> ·8	3·72 (d)	4·48 (d)		101		
(iii)	CH3	cis	8.0	3∙33 (qi)	4·70 (d)	0·82 (d)	60		
(iv)	-	trans	<b>4</b> ·9	2.60 (dq)	3.85 (d)	1·33 (d)	62		
(v)	н		<b>4</b> and 8	3·19 (dd)	4∙55 (q)	2.67 (dd)	76		
d = Doublet, dd = double doublet, q = quartet, dq =									
dou	ble qua	artet, qi	= quinte	et.	· •	1 /	•		

in column 2, which are based on the stereospecific

reduction of (I). The coupling constants  $J_{23}$  are similar to those for other indanones.<sup>6</sup> Values of 8 Hz are consistent with the small dihedral angle between cisprotons in the planar (or near planar) five-membered ring, and those of 4-5 Hz correspond to the larger angle ( $\sim 120^{\circ}$ ) between *trans*-protons. (We wish to point out that the assignments given by Bertoli and Plesch<sup>7</sup> to the coupling constants in 3-methylindan-1one appear to have been interchanged.)

The chemical shifts of 2-H and 3-H are also consistent with their configurations, and may be ascribed to their different degrees of shielding by the 2- and 3-substituents.8 In the trans-2,3-isomers, the 2-proton is shielded by the cis-phenyl group at C-3 and the 3-proton is shielded by the *cis*-substituent R at C-2. In the cis-isomers, these protons are not shielded by the 2- and 3-substituents and hence appear at lower field strengths.

<sup>8</sup> J. MacMillan, I. L. Martin, and D. J. Morris, Tetrahedron, 1969, 25, 905.

<sup>&</sup>lt;sup>6</sup> E. Marechal, J. J. Basselier, and P. Sigwalt, Bull. Soc. chim. France, 1964, 1740; E. Lustig and E. P. Ragelis, J. Org. Chem., 1967, 32, 1398; G. Agahigian, H. Plant, G. D. Vickers, and J.

van der Veen, Analyt. Chem., 1967, 39, 1583. <sup>7</sup> V. Bertoli and P. H. Plesch, Spectrochim. Acta, 1969, 25A, 447.

The n.m.r. data for the indan-1-ols (III) are shown in Table 3. The 2-H-3-H configurations are based on those of the indanone precursors (Table 2), and show a definite correlation with the coupling constants  $J_{23}$ and the chemical shifts of  $H_A$  and  $H_B$ . In the 2,3-cisconfigurations,  $J_{23} = 7-7.5$  Hz and the methylene protons A and B are isochronous (except when R' = o-tolyl), while in the *trans*-configurations,  $J_{23} =$ 9-11 Hz and the A and B protons are nonisochronous is attached to the chiral centre C-1, is the sum of two effects:  $^{12}$   $\Delta v_{AB} = UCP + intrinsic non-equivalence, where UCP = contribution due to unequal conformer populations, which varies with temperature, and the second term is an irreducible component due to the low symmetry of the system, and is temperature independent. Table 4 shows that <math>\Delta v_{AB}$  for *trans*-1-benzyl-2,3-diphenylindan-1-ol decreases from 0.17 p.p.m. at  $-50^{\circ}$  to 0.10 p.p.m. at  $+100^{\circ}$ . This indicates that the UCP

		2-H-3-H	-				<b>D</b> /-	011	H₄		$H_{\mathbf{B}}$	$J_{AB}$
R	R'	config.	$J_{2.3}$	2-H	3-H	R ª	R' a	OH	<u> </u>	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	······································	
H٥	H۰	cis <b>tra</b> ns	7 10	2·49(dd) } 2·10(dd) ∫	3·97(dd)	See 2-H	1·40(s)	3.31		See R'		
	Me	cis t <b>ra</b> ns	7·5 9·0	2·78(dd)) 2·10(dd)∫	4·18(dd)	,,	0 <b>·97</b> (t)	$2 \cdot 00$		1·83 ª		
	Ph	cis trans	7·2 9·5	2.84(dd) 2.06(dd)	<b>3·85(</b> dd)	,,		2.14		2.14		
Мe	н	trans	10.2	2.25(da)	3.59(d)	1.08(d)	1.32(s)	2.00		See $R'$		
	Me	trans	10.2	2·32(dq)	3•68(d)	1·09(d)	0•94(t)	1.86	1.56 •		1.80•	-13.8
	Ph	cis	7.5	2·75(qi)	<b>4∙29</b> (d)	0∙50(d)	• •	1.84		3.25(s)		
		trans	10.8	2.43(da)	3·70(d)	1·19(d)		2.03	$2.64^{f}$	( )	3.101	-13·0
Ph	H	cis	7.5	3.71(d)	4.75(d)	· · /	1·61(s)	$2 \cdot 24$		See R'		
		trans	10.8	3.66(d)	4·53(d)		1·11(s)	$2 \cdot 15$		,,		
	Ме	cis	7.5	3.83(d)	4·79(d)		1·02(t)	1.94		1.93 d		
		trans	11.0	3.79(d)	4.60(d)		0·80(t)	2.05	1.25 •		1.46.	-13.5
	Ph	cis	7.5	3.87(d)	4.61(d)		( )	2.13		3.21(s)		
		trans	11.0	3-88(d)	4.66(d)			$2 \cdot 26$	2.491	~ /	2.60	-13.0
	o-Tolvl	cis	7.2	3.94(d)	4.88(d)			$2 \cdot 16$	3.231		3.341	-13.8

TABLE 3

s = Singlet, t = triplet. Other multiplets as in Table 2.

• Aliphatic region only. <sup>b</sup> cis-trans assignments based on shielding effect of vicinal cis-phenyl group.<sup>8</sup> • Yu. S. Tsybin, A. V. Kessenikh, and R. N. Volkov, *Zhur. org. Khim.*, 1969, 5, 806. <sup>d</sup> Quartet with 2nd order splitting ( $A_2B_3$  system). • A and B part of ABC<sub>3</sub> spectrum (computer fitted). <sup>f</sup> AB quartet.

(except when R or R' = H). A detailed study of Dreiding models shows that the following explanation is the most consistent with these facts.



The 2,3-trans-disubstituted compounds are assigned structure (IIIa). A model shows that this has a dihedral angle of ca. 150° between the 2,3-protons, which are both pseudo-axial. According to the method of Pachler et al.,<sup>9</sup> which allows for the effect of substituent electronegativities on the Karplus equation, this angle should give a coupling constant of ca. 10 Hz, which agrees very well with the observed range. (The required electronegativities were assumed to be  $C_6H_5 = 2\cdot8,^{10}$  H =  $2\cdot1$ , and  $CH_3 = 2\cdot6.^{11}$ ) The alternative diequatorial conformation can be excluded because it would have a dihedral angle of ca. 90° and a coupling constant close to zero.

The difference in chemical shifts,  $\Delta v_{AB}$ , between the methylene protons in the  $CH_2R'$  group  $(R' \neq H)$ , which

K. G. R. Pachler, J. P. Tollenaere, and P. L. Wessels, *Tetrahedron*, 1969, 25, 5255.
J. R. Cavanaugh and B. P. Dailey, *J. Chem. Phys.*, 1961,

<sup>10</sup> J. R. Cavanaugh and B. P. Dailey, *J. Chem. Phys.*, 1961, **34**, 1102.

term contributes to the observed non-equivalence in this compound and that the rotamer populations become more equal with increasing temperature. The Dreiding model of (IIIa) confirms that the rotameric conformations of the  $CH_2R'$  group differ considerably

TABLE 4

Effect of temperature on n.m.r. spectra of 1-benzyl-2.3-diphenylindan-1-ols

		Temp	_	(p.p.m.)	
Isomer	Solvent	(°C)	HA		HB
cis	CDCl <sub>3</sub>	-50		3.21(s)	
	-	ambient		3.21(s)	
trans	CDCl <sub>a</sub>	-50	2.35		2.62
	Ū	ambient	$2 \cdot 49$		2.60
	C <sub>6</sub> D <sub>5</sub> NO <sub>9</sub>		2.54		2.66
		+100	2.57		2.67
		+150		Decomp.	

in energy, due to interaction with the group R on C-2 (except when R = H). By analogy with other systems,  $\Delta v_{AB}$  would be expected to approach a constant limiting value at a high enough temperature,<sup>12</sup> but in this case further heating above 100° caused dehydration to the indene.

The *cis*-isomers are assigned structures (IIIb) or (IIIc):

<sup>11</sup> R. Nyholm, J. Roy. Soc. Arts, December 1970, CXIX, p. 28. <sup>12</sup> L. M. Jackman and S. Sternhell, 'Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry,' Pergamon Press, Oxford, 1969, 2nd edn., ch. 5-2.



A model shows that both conformers have 2,3-proton dihedral angles of  $ca. 30^{\circ}$ . The corresponding theoretical coupling constant, with appropriate corrections for the 2.3-substituents,<sup>9</sup> is ca. 8 Hz. This agrees closely enough with the observed values to make the assignment unambiguous. If there is interconversion between (IIIb) and (IIIc), it must be very rapid on the n.m.r. time scale, because only one species is detectable and the lines are quite sharp. The model also shows that the nonbonded interactions are negligible for all the rotamers of the CH<sub>2</sub>R' group in either conformer (IIIb) or (IIIc) (except when R' = o-tolyl), in contrast to the situation for the trans-configuration (IIIa). Hence we would expect the rotamer populations to be nearly equal, and the UCP term to approach zero. However the coincidental shifts of the methylene protons (Table 3) indicate that the intrinsic non-equivalence term is also undetectable at 100 MHz. Such a possibility has been discussed by Siddall and Stewart,13 and examples have

\* A referee has suggested that the non-equivalence could also be due to the magnetic anisotropy of the tolyl ring, but the same effect would be expected when R' is phenyl itself.

<sup>13</sup> T. H. Siddall and W. E. Stewart, in 'Progress in Nuclear Magnetic Resonance Spectroscopy,' Pergamon Press, Oxford, 1969, vol. 5, p. 33.

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been reported for other indane derivatives  $^{14}$  and for some amino-acids  $^{15}$  and pyrazines.  $^{16}$ 

Our interpretation is supported by the absence of any temperature effect (Table 4) for cis-1-benzyl-2,3-diphenylindan-1-ol. Alternative explanations for this temperature-independence are (1) that the molecule exists virtually entirely in a single rotameric conformation throughout the temperature range or (2) that coincidentally the chemical shift difference between the methylene protons is undetectable for individual populated conformers. However, the models indicate that (1) is unlikely, and (2) requires an extraordinary series of coincidences for the variety of substituents R and R'. A model of (IIIb) and (IIIc) predicts that if R' = o-tolyl, and this is spinning rapidly about the C-R' bond, then the o-methyl group will interact with the 2-proton (and other parts of the molecule). This would give rise to unequal populations, which may contribute to the observed non-equivalence (Table 3).\* This method for inducing non-equivalence in cyclic systems was first reported (for the similar case of 2-benzylindan-1-one) by Imbach et al.14

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  J. J. M. Rowe, J. Hinton, and K. L. Rowe, Chem. Rev.,
- 1970, 70, 1.
- <sup>16</sup> R. E. Lyle and J. J. Thomas, Tetrahedron Letters, 1969, No. 11, 897.