Tetrahedron. Vol 26, pp. 3917 to 3925 Pergamon Press 1970. Printed in Great Britain

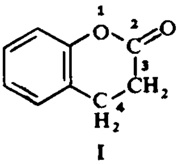
A STUDY OF DIASTEREO AND ROTATIONAL ISOMERISM IN BISDIHYDROCOUMARIN BY DIPOLE MOMENT AND INFRARED MEASUREMENTS

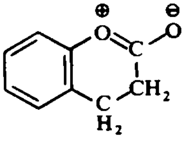
H. H. HUANG
Chemistry Department, University of Singapore, Singapore 10

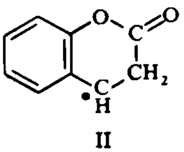
(*Received in Japan* 27 *April* 1970; *Received in the UK for publication* 6 *May* 1970)

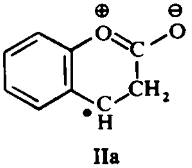
Abstract—Hydrogen-abstraction, by t-butoxy radicals, from dihydrocoumarin produces radicals which dimerize to give bisdihydrocoumarin in the normal and iso-forms. The higher melting isomer (the normal-form) is shown by dipole moment measurements to be the "meso", and the lower melting isomer (the iso-form) the "racemic" diastereoisomer. IR measurements support these assignments.

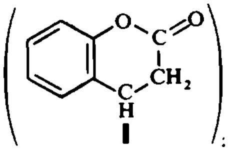
THE reaction of t-butoxy radicals[1] with dihydrocoumarin (I) may be expected to proceed by abstraction of a benzylic α-hydrogen to generate the radical II which being stabilized by resonance hybrids such as IIa, should then be capable of dimerizing to give bisdihydrocoumarin (III) in the normal and iso-forms.


I


Ia


II


IIa


III

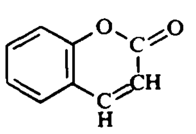
When dihydrocoumarin was heated with di-t-butyl peroxide as the source of t-butoxy radicals, a solid product was isolated which indeed proved to be the two diastereoisomeric forms of the expected dimer, the more soluble form having a m.p. of 263–265° and the less soluble, 288–289°. The higher melting isomer is designated the normal-form, and the lower melting the iso-form. Two isomeric forms of bisdihydrocoumarin (tetrahydrodicoumarinyl) have been produced by the polarographic reduction of coumarin[3, 4] but the elemental analyses of the compounds isolated were not quite satisfactory and there was doubt as to whether the two coumarin nuclei were joined at position 4. Comparison of the m.ps and solubilities of the two diastereoisomers reported in this work with those mentioned in the literature confirm that the compounds obtained by polarographic reduction were diastereoisomeric forms of tetrahydrodi-4-coumarinyl. Since these compounds have now been obtained in a state of higher purity, it should be possible in principle to assign the correct configurations to the two diastereoisomers from their electric dipole moments because relevant stereochemical principles[2] predict appreciable differences between these values. The results of a dipole moment study are now recorded together with supplementary IR evidence.

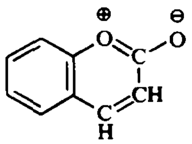
DISCUSSION

Dipole moments

Dihydrocoumarin. The moment of dihydrocoumarin itself merits some comment.

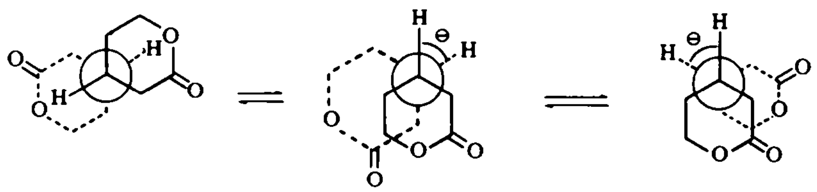
Its value (3·80D in benzene) is substantially lower than that of coumarin (IV; 4·48D) indicating that in the latter compound, the presence of the conjugated double bond in the cyclic side chain enhances the effects of resonance hybrids such as IVa in augmenting the moment of the molecule as a whole. Le Fèvre and Le Fèvre[7] have pointed out that the difference between the moment calculated from the primary moments of


IV


IVa

the $\mathrm{C}\overset{\mathrm{O}}{\diagup\ \diagdown}\mathrm{C}$ and C=O units by vector addition (which gives a resultant of about 2·9D roughly 17° anticlockwise to the C=O axis) and the observed moment (4·48D) can be largely attributed to intramolecular electrostatic induction by the polar groups. When this effect is taken into account, the calculated resultant moment becomes 4·05D inclined at 15° anticlockwise to the C=O axis. The balance of 0·43D required to make up the observed moment can be attributed to resonance between IV and excited states such as IVa. In dihydrocoumarin (I), the skeletal bond lengths and angles are almost identical with those of coumarin,[7] the only modification being introduced by replacing the side chain ethylenic C=C bond (1·32Å) by an aliphatic C—C bond (1·5Å). The cyclic side chain may also be assumed to be essentially coplanar with the benzene ring in both cases.[8] Calculations show that the electrostatic inductive contributions to the molecular moment estimated by the method described[7] are little changed by the slightly different molecular dimensions but since the observed moment of dihydrocoumarin is only 3·80D i.e. appreciably lower than that of coumarin (4·45D) and there is independent evidence that resonance forms such as Ia have some importance (e.g. from the mere fact that bisdihydrocoumarin can be prepared in appreciable quantity by free-radical dimerization) it follows therefore that the electrostatic contribution appears to have been overestimated. Hence the resultant moment of dihydrocoumarin must lie between the direction inclined anticlockwise at 17° to the C=O axis and this axis itself, with its negative end pointing away from the molecule. A knowledge of the direction of the resultant moment of this molecule is required if it is desired to make an estimate of the *gauche*=*trans* population distribution in the bisdihydrocoumarin which corresponds to the "meso" diastereoisomer.

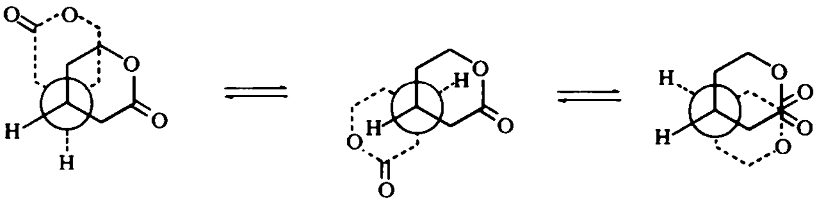
The bisdihydrocoumarins. The two isomers isolated can be identified as the two diastereosiomeric forms of bisdihydrocoumarin (III). They differ from simpler diastereoisomers of derivatives of ethane of the type $(R^1R^2R^3C)_2$ in that two of the bonds attached to a central ethane C atom form part of a cyclic system. In bisdihydrocoumarin, the principal moments reside in the planes of the 4,4- or 4′,4′-diaxally substituted ring segments. The stereochemical principles[2] which underlie the existence of meso and (±) racemic diastereoisomers are applicable here and the problem now is to assign the correct configurations to the isomers separated. Since rotational isomerism may be expected for these flexible stereoisomers, the following equilibria involving *trans* and *gauche* conformers should be found in solution for the "meso" type of compound.



V
trans

VI VII
gauche

For the "racemic" type of isomer the following equilibria should apply.



VIII IX X

(±)-form
(Only one enantiomer shown)

In the Newman projections for these molecules, the benzene ring has been omitted for clarity of presentation. It is clear that owing to the unusual bulk of the dihydrocoumarin moiety, the *trans* configuration (V) in the "meso" isomer will be much favoured. Since in this rotamer the principal dipoles are antiparallel, the overall dipole moment of this isomer should be relatively low. This is true even if the lactone ring were not coplanar with the benzene ring to which it is fused, for the symmetry and optical properties of the "meso" compound would otherwise be violated. (Both the normal and isobisdihydrocoumarins are optically inactive.) By contrast, the rotamers depicted in VIII to X invariably have the resultant moments of each moiety inclined mutually at an angle thus causing all the rotamers to be highly polar. The fact that IX may be recognized on steric grounds as the preferred rotamer in solution ensures that the effective dipole moment of the (±) diastereoisomer will be relatively high, i.e. appreciably higher than that of the "meso" isomer. Examination of the dipole moment data in Table 2 reveals that the higher melting and less soluble normal bisdihydrocoumarin compound has the lower moment: clearly it must be the "meso" isomer. The more soluble lower-melting iso compound with the much higher dipole moment must therefore be its (±) racemic diastereoisomer. The proportion of the *gauche* rotamer in the normal (meso) bisdihydrocoumarin can be estimated if the direction of the moment of the dihydrocoumarin segment and its interatomic distances and angles are known. It has been argued that the moment of dihydrocoumarin should lie between the C=O bond and a direction making an angle of 17° with it. Scale drawings show that with the following bond lengths, O(1)C(2) = C(5)C(6) = O(1)C(6) = 1·41Å; C(2)C(3) = C(3)C(4) = C(4)C(5) = 1·5Å, the angles at O(1) = 122°, C(2) = 122°, C(3) = 116°, C(5) = C(6) = 120° and at C(4) = 116° are consistent with the above specifications. For our calculations, it is especially necessary to know the angle at C(4) as this is directly related to the moment of the *gauche*-form of the "meso" isomer. Thus neglecting the small polarity of the C—H bond, the moment of any molecular configuration of this isomer is given by Eq (1)

$$\mu(\theta) = 2\mu_0 \sin \alpha \cos \frac{\theta}{2} \quad (1)$$

where μ_0 is the moment of the dihydrocoumarin moiety, α is the supplement of the angle subtended by C(4)—C′(4) and the direction of μ_0; and θ, the azimuthal angle, has a value of 180° for the *trans* configuration but is expected to be between 60–90° for the *gauche* configuration. With the geometrical dimensions specified, inspection of molecular models and trigonometrical considerations show α to be about 72°, if μ_0 lies along C=O and 73° if it makes an angle of 17° with C=O. Thus μ_g should have values between 5·11D and 6·29D if θ is allowed to take on the extreme values of 60° and 90°. Recalling that the mean-square dipole moment of the molecular mixture of N_t *trans*-rotamers with moment μ_t (effectively equal to zero) and N_g *gauche*-rotamers with moment μ_g is given by Eq (2)[9] the proportion of *gauche*-rotamers emerges as 19·9 and 13·1%

$$\overline{\mu}^2 = \frac{\mu_t^2 N_t + \mu_g^2 N_g}{N_t + N_g} \quad (2)$$

respectively, which may be regarded as the limits of the most probable range of values. This low result is consistent with general expectations for the "meso" isomer of bisdihydrocoumarin and therefore supports the assignment of configuration made.

IR data. A comparison of the IR spectrum of dihydrocoumarin with that of coumarin would be interesting as there appears to be no record of the spectrum of the former compound in the standard literature. The spectrum of the latter compound has been retaken as previous spectra[10, 11] did not extend below 600 cm^{-1}. The characteristic carbonyl absorption occurs in dihydrocoumarin at 1770 cm^{-1} which is practically the frequency at which the band appears in Δ^5-lactones.[12] Unlike the dihydro compound, coumarin exhibits two bands in the CO region at 1705 and 1730 cm^{-1} with the former much more intense than the latter. This splitting of the CO band, attributable to Fermi resonance with an overtone, is characteristic of 5- and 6-membered ring lactones containing a C=C bond conjugated with the CO group.[13, 14] The occurrence of the main band at 1705 cm^{-1} is reminiscent of the behaviour of Δ^3-lactones[12] (1710–1708 cm^{-1}). The band at *ca* 3520 cm^{-1} in dihydrocoumarin attributable to the first overtone of the CO stretching at 1770 cm^{-1} is however absent in coumarin. Other absorptions in dihydrocoumarin are consistent with its structure. For example, stretching vibrations of the C—H links appear at 3040 cm^{-1} (aromatic) and at 2850 and 2900 cm^{-1} (ν in CH_2). Characteristic CH_2 scissor vibrations are probably responsible for some of the absorptions in the region 1400–1500 cm^{-1} while ring C—O stretching modes would give rise to those within the range 1200–1290 cm^{-1}. There would also be considerable overlapping with phenyl ring stretching modes (1300–1600 cm^{-1}) though ring breathing (near 1000 cm^{-1}), β-ring in-plane (700–600 cm^{-1}) and γ-ring out-of-plane vibrations (700–300 cm^{-1}) would appear at lower frequencies. Thus the strong bands in the 700–300 cm^{-1} region in dihydrocoumarin attributable to ring deformation vibrations, are almost all reproduced in coumarin, peak for peak.

Bisdihydrocoumarin. Many of the absorptions found in dihydrocoumarin may also

TABLE 1. INCREMENTAL DIELECTRIC CONSTANTS, DENSITIES AND REFRACTIVE INDICES OF DIOXAN SOLUTIONS AT 25°

Dihydrocoumarin

$10^5 W_2$	569	1364	1615	1980	2735
$10^4 \Delta\varepsilon$	730	1727	2087	2503	2597
$10^5 \Delta d$	80	187	212	301	411
$10^4 \Delta n^2$	28	54	63	77	106

whence $\frac{\Sigma\Delta\varepsilon}{\Sigma W_2} = 12{\cdot}88$ $\frac{\Sigma\Delta d}{\Sigma W_2} = 0{\cdot}144$

$\frac{\Sigma\Delta n^2}{\Sigma W_2} = 0{\cdot}398$

Normal Bisdihydrocoumarin

$10^5 W_2$	233	335	413	469
$10^4 \Delta\varepsilon$	56	97	108	133
$10^5 \Delta d$	48	123	130	148
$10^4 \Delta n^2$	15	18	18	19

whence $\frac{\Sigma\Delta\varepsilon}{\Sigma W_2} = 2{\cdot}72$ $\frac{\Sigma\Delta d}{\Sigma W_2} = 0{\cdot}310$

$\frac{\Sigma\Delta n^2}{\Sigma W_2} = 0{\cdot}483$

Iso-Bisdihydrocoumarin

$10^5 W_2$	400	666	893	1048
$10^4 \Delta\varepsilon$	333	551	743	838
$10^5 \Delta d$	90	145	196	245
$10^4 \Delta n^2$	17	28	37	42

whence $\frac{\Sigma\Delta\varepsilon}{\Sigma W_2} = 8{\cdot}17$ $\frac{\Sigma\Delta d}{\Sigma W_2} = 0{\cdot}224$

$\frac{\Sigma\Delta n^2}{\Sigma W_2} = 0{\cdot}394$

In Benzene at 25°

Dihydrocoumarin

$10^5 W_2$	1388	1561	2010	2948
$10^4 \Delta\varepsilon$	1547	1741	2251	3324
$10^5 \Delta d$	315	339	440	695
$10^4 \Delta n^2$	21	27	33	48

whence $\frac{\Sigma\Delta\varepsilon}{\Sigma W_2} = 11{\cdot}12$ $\frac{\Sigma\Delta d}{\Sigma W_2} = 0{\cdot}226$

$\frac{\Sigma\Delta n^2}{\Sigma W_2} = 0{\cdot}163$

TABLE 2. POLARIZATIONS, REFRACTIONS AND DIPOLE MOMENTS AT INFINITE DILUTION FOR SOLUTIONS AT 25°

Solvent	Solute	$\alpha\varepsilon_1$	β	P_2 (cc)	R_D (cc)	R_D (calc) (cc)	μ (D)*
Dioxan	Dihydrocoumarin	12·98	0·140	348·0	42·0	40·13	3·86 ± 0·03
Benzene	Dihydrocoumarin	11·12	0·259	346·7	41·4	40·13	3·85 ± 0·03
Dioxan	Normal bisdihydrocoumarin	2·76	0·301	188·7	76·2	76·92	2·28 ± 0·20
Dioxan	Iso-bisdihydrocoumarin	8·17	0·217	457·9	77·6	76·92	4·28 ± 0·05

* μ is calculated assuming that $_DP \approx 1{\cdot}05\ R_D$ (calc)

TABLE 3. IR ABSORPTIONS (cm^{-1}) OF NORMAL BISDIHYDROCOUMARIN

Nujol mull	*Hexachlorobutadiene mull*	$CHCl_3$ *Soln*
x	2980 vw	x
x	2940 vw	x
x	2910 w	x
1810 w	1810 w	x
1760 vs	1760 vs	1770 vs
1619 s	1619 s	1619 m
1598 s	1598 m	1590 m
1490 s	1490 s	x
x	1460 s	x
1420 s	1420 s	x
1350 sh, m	1350 sh, m	x
1340 s	1340 s	1340 s
1298 sh, w	1298 sh, w	x
1265 s	1265 s	x
1238 s	1235 s	x
1210 s	1210 s	x
1195 s	1195 s	x
1179 vs	1179 vs	x
1145 vs	1145 vs	1140 vs
1110 s	1110 s	1110 s
1008 s	1008 s	1000 s
955 sh, s	x	x
950 s	x	960 s
—	—	945 w
910 s	910 s	910 s
880 w	880 w	x
875 w	875 w	x
842 s	x	x
775 vs	775 vs	x
755 m	755 m	x
739 w	739 w	x
709 m	709 m	x
618	618	x
568 m	568 m	570 m
525 s	525 s	520 m
491 s	491 s	489 m

TABLE 3 (*cont.*)
Iso-bisdihydrocoumarin

Nujol *mull*	*Hexachlorobutadiene* *mull*	$CHCl_3$ *Soln*
3060 m	3060 m	x
3030 m	3030 m	x
x	2910 s	x
1760 vs	1760 vs	1770 vs
1610 s	1610 s	1610 m
1590 s	1590 s	1590 m
1485 s	1485 s	1485 s
x	1455 s	1455 s
x	1435 s	x
1415 s	1415 s	x
1340 s	1340 s	1340 m
1330 s	1330 s	x
1310 w	1310 w	x
1290 m	1290 m	1290 w
1245 s	1245 s	x
1210 vs	1210 vs	x
1200 vs	1200 vs	x
1185 s	x	x
1165 br, vs	1165 br, vs	1160 br, vs
1150 s	1150 s	x
1110 s	1110 s	1110 m
1048 s	1048 s	x
1030 m	1030 m	x
1020 m	1020 m	x
1000 w	x	x
960 m	960 m	x
942 m	x	942 w
913 s	913 s	913 m
900 s	900 s	900 m
870 m	870 m	x
840 s	x	x
785 m	x	x
770 vs	770 vs	x
760 vs	760 vs	x
733 m	733 m	x
717 m	717 m	x
709 m	709 m	x
627 m	627 m	x
620 m	620 m	x
600 m	600 m	x
563 s	563 s	x
554 w	554 w	x
543 m	543 m	x
510 m	510 m	x
495 s	495 s	495 m
482 m	482 m	x
437 m	437 m	x

TABLE 3 (*cont.*)
Dihydrocoumarin (Liquid Film)

3510 br, m
3040 br, m
2900 m
2850 m
1770 vs
1610 s
1590 vs
1490 vs
1460 vs
1440 s
1420 s
1350 s
1320 m
1280 s
1245 vs
1225 vs
1190 s
1150 br, vs
1105 vs
1032 s
1025 s
988 s
940 m
915 s
900 s
785 s
760 vs
745 s
720 m
685 s
610 m
565 m
535 w
515 s
465 s
435 s

sh = shoulder; br = broad; x = masking by mull or solvent

be expected in the IR spectra of the dimers. The most conspicuous and unmistakable of these, namely the absorption of the CO function, now occurs at a slightly lower frequency in the solid-state spectra (1760 cm^{-1}) though at essentially the same frequency of 1770 cm^{-1} in $CHCl_3$. If normal ("meso") bisdihydrocoumarin were to exist entirely in the *trans* configuration in the solid state as is usually true of ethane derivatives,[15] it would be reasonable to expect the solid "racemic" diastereoisomer to exhibit more absorption bands than the "meso" for reasons of symmetry as they affect the selection rules. Thus the vibrations which are IR inactive in the *trans* configuration of the "meso" compound with essentially C_{2h} symmetry would be allowed in the racemic system which has virtually no center of symmetry. Comparison of the spectra of the two isomers (Table 3) reveal that this is indeed the case, especially in the fingerprint region although some of the lines observed in the "meso" compound would be shifted in the "racemic". A further point of interest is that the spectrum of "meso" bisdihydrocoumarin in $CHCl_3$ shows an extra line at 945 cm^{-1} which is absent in the solid state spectra. It is unfortunate that the lack of solubility of this compound in the common spectroscopic solvents prevents this line from being confirmed and possibly other extra lines from being revealed, but its presence may be taken as evidence for the suggestion that only the *trans* rotamer exists in the solid state. It may be concluded therefore that the experimental evidence discussed above provides strong support for the configurations assigned to the diastereoisomers.

EXPERIMENTAL

Preparation of bisdihydrocoumarin. Dihydrocoumarin (40 g) and t-butyl peroxide (30 g) were sealed under N_2 (the two liquids are only partially miscible) and heated for 48 hr at 130°. On cooling, *ca* 2 g of a solid product appeared. This was filtered off and the filtrate was distilled under reduced press giving small amounts of t-BuOH and acetone, *ca* 15 g of unchanged dihydrocoumarin, and a residue (*ca* 2 g) consisting mainly of a yellowish resinous material and a further minor crop of crystals. The combined crystalline material was dissolved in benzene and fractionally recrystallized to give (i) *ca* 0·7 g of needle-like crystals of the less soluble normal *bisdihydrocoumarin*, m.p. 288–289°. (Found: C, 73·2; H, 4·9; M, 287; $C_{18}H_{14}O_4$ requires: C, 73·44; H, 4·80%; M, 294·11) and (ii) 0·6 g of *isobisdihydrocoumarin* as fluffy light white crystals, m.p. 242–248°, raised to 263–265°. (Found: C, 73·6; H, 4·9%; M, 289). The yellowish resin is polymeric in nature being formed as a result of further attack of the remaining benzylic hydrogens in the dimer by the t-butoxy radical.

Polarization measurements. Dielectric constants of solns of dihydrocoumarin and its dimers in dioxan were determined with apparatus previously described,[5] densities and refractive indices being obtained by standard procedures.[6] The dipole moment of dihydrocoumarin itself is not on record and its value in benzene soln was also determined for comparison with the known moment of coumarin[7] in the same solvent. The dielectric results are collected in Tables 1 and 2, using notation explained in Ref 6. The IR spectra were recorded with the Perkin–Elmer 337 and are listed in Table 3.

Acknowledgement—Thanks are due to Mrs. H. K. Tong for microanalyses.

REFERENCES

[1] H. H. Huang and P. K. K. Lim, *J. Chem. Soc.* (C) 2432 (1967)
[2] E. L. Eliel, *Stereochemistry of Carbon Compounds*. McGraw-Hill, New York (1962)
[3] R. Patzak and L. Neugebauer, *Monatsh* **82**, 662 (1951)
[4] A. J. Harle and L. E. Lyons, *J. Chem. Soc.* 1577 (1950)
[5] H. H. Huang and E. P. A. Sullivan, *Austral. J. Chem.* **21**, 1721 (1968)
[6] R. J. W. Le Fèvre, [a] *Dipole Moments* (3rd Edition), Chap. 2, Methuen, London (1953); [b] *Adv. Phys. Org. Chem.* **3**, 1 (1965)
[7] C. G. Le Fèvre and R. J. W. Le Fèvre, *J. Chem. Soc.* 1088 (1937)
[8] G. A. Jeffrey and S. H. Lim. *Acta Cryst.* **22**, 725 (1967)
[9] S. Mizushima, *Structure of Molecules and Internal Rotation*. Academic Press, New York (1954)
[10] F. Bohlmann, *Chem. Ber.* **90**, 1519 (1957)
[11] V. Prey, B. Kerres and H. Berbalk, *Monatsh. Chem.* **91**, 774 (1960)
[12] F. Korte, K. H. Buchel and K. Gohring, *Angew. Chem.* **71**, 523 (1959)
[13] R. N. Jones, C. L. Angell, T. Ito and R. J. D. Smith, *Canad. J. Chem.* **37**, 2007 (1959)
[14] C. L. Angell, B. S. Gallagher, R. J. D. Smith and R. N. Jones, *The Infrared Spectra of Lactones*. National Research Council, Ottawa, Canada (1960)
[15] N. Sheppard, *Adv. Spectroscopy* **1**, 288 (1959)