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NMR SPECTRA AND CONFORMATION OF 1,2-DIPHENYLPROPANE AND 2,3-DIPHENYLPROPANOIC ACID

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Abstract—The NMR spectral characteristics of 1,2-diphenylpropane, 2,3-diphenylpropionic acid and its methyl ester have been measured with the view to investigating the conformational equilibria arising from the rotation about the phenyl-bearing C atoms. The analysis of these data has demonstrated the predominance of the conformer with anti-periplanar phenyls in all the cases studied. The values of the gauche nonbonded interaction energies ($-\Delta E$ kcal/mole) are found to be for Ph/Ph 0·8, for Ph/COOH 0·6 and for Ph/$COOCH_3$ 0·4.

The conformational equilibria in substituted ethanes have been the subject of a great number of experimental and theoretical investigations.[1] For liquid-phase studies NMR spectroscopy is a particularly suitable technique. Direct NMR measurements of the conformational distribution have been achieved only for highly substituted ethanes,[1-3] but reliable information has been obtained also by studying the temperature[4,5] or solvent[6] dependence of the vicinal coupling constants in the fast-exchange spectra. In a vast number of studies the conformational preferences have been estimated on the basis of the Karplus rule. With the possible exception of some cases when one of the conformers strongly predominates, such results are necessarily of a qualitative character due to the well-known influence of perturbating factors.[7] A more quantitative approach is possible for 1,2-disubstituted and 1,1,2-trisubstituted ethanes in cases where the two vicinal coupling constants could be measured from the non-degenerate spectra.[5,8,9]

Most of the quantitative studies carried out so far have been devoted to systems containing at least two vicinal halogen substituents on the ethane fragment.

The work reported in this paper is concerned with the conformational analysis of compounds containing vicinal phenyl groups: 1,2-diphenylpropane, 2,3-diphenylpropionic acid and its methyl ester.

METHODS AND RESULTS

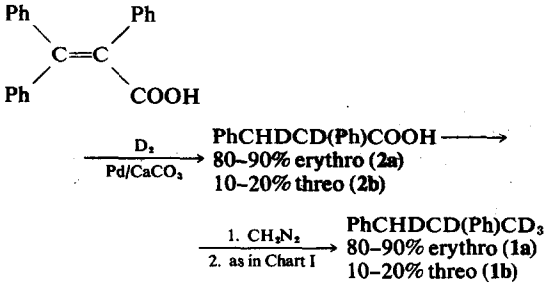
1,2-Diphenylpropane-3-d_3 (**1**) was synthesized as shown in Chart 1. 2,3-Diphenylpropionic acid (**2**) and its methyl ester (**3**) were prepared by standard methods. Compound **1** (soln in $CDCl_3$) measured at 100 MHz under deuterium decoupling gave a typical ABC spectrum which was analysed by the exact method.[10,11] The lowest-field chemical shift was assigned to H-2 on the basis of H-D coupling effects in the undecoupled spectra. The assignment of the chemical shifts of the geminal protons was achieved by the use of

CHART 1

$$PhCH_2CH(Ph)CO_2CH_3 \xrightarrow{LAD} PhCH_2CH(Ph)CD_2OH \xrightarrow{TsCl} PhCH_2CH(Ph)CD_2OTs \xrightarrow{LAD} PhCH_2CH(Ph)CD_3$$

the stereoselectively deuterated analogues[12,13] (Chart 2).

CHART 2



In this way the chemical shift of the methine proton in **1a**, respectively **1b** corresponds to that of

the respective proton from the diastereotopic methylene group in **1**. The stereochemistry of the products **1a** and **1b** was determined assuming predominance of *cis*-addition.[14]

The relevant NMR parameters for **1**, **1a** and **1b** are listed in Table 1.

The NMR spectra of **2** and **3** have already been measured by Fraser[12] in CCl_4 at 24 and 60 MHz and analyzed by the exact method.[10] His paper also contains some qualitative discussion of the conformational preference. For comparison purposes we measured the spectra of **2** and **3** at 60–100 MHz in $CDCl_3$. The spectra were first analyzed in ABX approximation and the parameters were then refined using an itirative computer procedure. The interpretation was aided by the spectra of the deuterated analogues erythro- and threo-PhCHDCD(Ph)COOH (Chart 2). The spectral results are collected in Table 1.

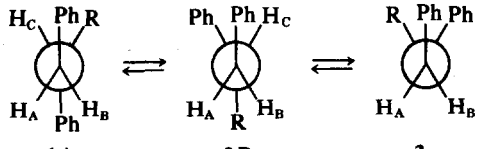
Table 1. NMR parameters for 1,2-diphenylpropane, 2,3-diphenylpropionic acid and its methyl ester[a]

Compound	Solvent	Conc. (w/v)	ν_A	ν_B	ν_C	J_{AB}	J_{AC}
$PhCH_2CH(Ph)CD_3$ (1)	$CDCl_3$	25%	289·0	271·1	293·0	−13·33	6·67
erythro-PhCHDCD(Ph)CD_3 (1a)	$CDCl_3$		288				
threo-PhCHDCD(Ph)CD_3 (1b)	$CDCl_3$			275			
$PhCH_2CH(Ph)COOH$ (2)	$CDCl_3$	10%	302·4	339·3	384·1	−13·69	7·06
	CCl_4[b]	25%				−13·75	7·29
erythro-PhCHDCD(Ph)COOH (2a)	$CDCl_3$		304				
threo-PhCHDCD(Ph)COOH (2b)	$CDCl_3$			338			
$PhCH_2CH(Ph)COOCH_3$ (3)	$CDCl_3$	10%	305	343	387	−13·4	6·5
	CCl_4[b]	14%				−13·56	6·50

[a] All parameters are in Hz; chemical shifts relative to internal TMS at 1 MHz.
[b] From Ref 12.

DISCUSSION

The three staggered conformations of compounds **1–3** are presented below.



1A **2B** **3**

R = CD_3(1), COOH(2), $COOCH_3$(3)

In the dideuterated analogues deuterium atoms are substituted for H_B and H_C in the *erythro*- and for H_A and H_C in the *threo*-form.

The observed vicinal coupling constants J_{AC} and J_{BC} are, of course, weighted averages of the corresponding constants in the individual conformers:

$$J_{AC} = N_I J^I_{AC} + N_{II} J^{II}_{AC} + N_{III} J^{III}_{AC} \quad (1)$$

$$J_{BC} = N_I J^I_{BC} + N_{II} J^{II}_{BC} + N_{III} J^{III}_{BC} \quad (2)$$

$$N_I + N_{II} + N_{III} = 1. \quad (3)$$

Here $N_{I,II,III}$ are the mole fractions of the respective conformers. Conformer III should be disfavoured on sterical grounds, although there are indications[15] that its amount might not be negligible, as thought earlier.[8]

Since Ph and R are similar in electronegativity[16] one may assume equality of the *anti*-, respectively *gauche* couplings:

$$J^I_{BC} > J^{II}_{AC}; \quad J^I_{AC} = J^{II}_{BC}; \quad J^{III}_{AC} = J^{III}_{BC}.$$

Thus

$$J_{BC} > J_{AC} = (N_I > N_{II})(J^I_{BC} - J^I_{AC}). \quad (4)$$

Taking into account that $J^I_{BC} > J^I_{AC}$ (Karplus rule) and $J_{BC} > J_{AC}$ (Table 1) it is concluded that $N_I > N_{II}$, i.e. conformer I is the favoured one for all compounds **1–3**.

In order to make a semiquantitative estimation of the conformer populations from Eqs. (1)–(3) one must assume certain values for the *anti* and *gauche* couplings. Taking the reasonable values $J^I_{BC} = J^{II}_{AC} = 12$ Hz and $J^I_{AC} = J^{II}_{BC} = J^{III}_{AC} = J^{III}_{BC} = 4$ Hz,[5,17–20] the data presented in Table 2 were obtained. The estimated error for uncertainties in the coupling constants of ±1 Hz is ±0·06 for the mole fractions N and ±0·1 kcal/mole for ΔE.

It is a well established fact at present that both steric and polar interactions are contributing to the internal energy of rotamers.[21] When appropriate, H-bonding might also be of various degrees of importance.[22] The application of an additive *gauche*-interaction scheme for calculating conformational energy differences seems unreliable, at least for compounds in which strong polar interactions are present (e.g., systems containing vicinal halogen substituents.[1,23] However, such an approach might be useful for semiquantitative predictions in cases where the steric interactions are dominating. In particular, it seems interesting

Table 2. Conformational distribution and energy differences (ΔE kcal/mole) for compounds (1)–(3)

Compound	Conformer mole fraction N I	II	III	Energy difference E_{II-I}[a] kcal/mole
$PhCH_2CH(Ph)CD_3$ (1)	0·54	0·33	0·13	0·3
$PhCH_2CH(Ph)COOH$ (2)	0·53	0·38	0·09	0·2
$PhCH_2CH(Ph)COOCH_3$ (3)	0·60	0·31	0·09	0·4

[a] $E_{II-I} = RT \ln (N_{II}/N_I)$.

to compare the CH_3/CH_3, Ph/CH_3 and Ph/Ph *gauche*-interactions energies in acyclic compounds.

Assuming the Ph/CH_3 interaction to be 0·5 kcal/mole (the *gauche-anti* conformational difference in $PhCH_2CH_2CH$[14]) and $CH_3/H = Ph/H = H/H = 0$, from the additivity of conformational effects:[8]

$$\Delta E_{II-I}^{(1)} = Ph/Ph - Ph/CH_3 \qquad (5)$$

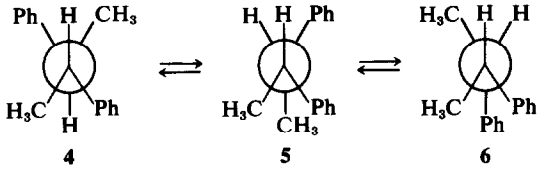
we obtain Ph/Ph = 0·8 kcal/mole. This value is the same as that accepted for the CH_3/CH_3 *gauche*-interaction energy.[21,24]

The value for Ph/Ph obtained by us is in agreement with the results from studies of the conformational distribution in 1,2-diphenylethane by IR,[25] as well as in 1,2-diarylethanes by IR,[26] dipole moments[27] and NMR.[18] In all cases mentioned the mole fraction of the *anti* conformer amounted to 0·65 – 0·70 ($-\Delta E_{anti/gauche} = 0·8 - 0·9$ kcal/mole).

In a similar manner (Eq. 5), by use of the ΔE_{II-I} values for compounds 2 and 3 and the Ph/Ph value of 0·8 kcal/mole one calculates the interaction energies Ph/COOH = 0·6 kcal/mole and $Ph/COOCH_3$ = 0·4 kcal/mole.*

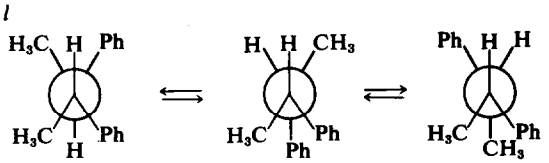
The utility of the additivity scheme for approximate prediction of the conformational distribution in systems lacking strong polar interactions might be illustrated on the 2,3-diphenylbutanes. Employing the values $CH_3/CH_3 = Ph/Ph = 0·8$ kcal/mole, $Ph/CH_3 = 0·5$ kcal/mole and $CH_3/H = Ph/H = H/H = 0$, it is calculated that for the *meso*-compound the rotamer with methine protons in *anti* position(IV) is favoured by 1·1 kcal/mole over each of the rotamers V and VI. For the *d,l*-form the difference is only 0·2 kcal/mole. Thus the calculated populations are IV:V:VI = 0·76:0·12:0·12 and VII:VIII:IX = 0·42:0·29:0·29. The result is in agreement with NMR-studies[17,28]: *meso* $J = 10$ Hz and *d,l* $J = 7$ Hz (CS_2, CCl_4, $CDCl_3$).

meso



4 5 6

d, l



7 8 9

*In the above consideration the entropy term due to the substituent anisotropy has been neglected.

EXPERIMENTAL

The NMR spectra were measured on JEOL model JNM-C-60S and JNM-4H-100 spectrometers at normal probe temperature (*ca.* 25°).

2,3-*Diphenylpropionic*-2,3-d_2 *acid* was prepared by reducing *cis*-α-phenylcinnamic acid[29] (2·00 g in 30 ml dimethoxyethane) with deuterium over a 10% pd/$CaCO_3$ catalyst (0·5 g). Recrystallization from petrol afforded the desired product (1·2 g, m.p. 88–90°).

Methyl 2,3-*diphenylpropionate*-2,3-d_2 (m.p. 30–33°) was obtained by treating the parent acid with diazomethane.

1,2-*Diphenylpropane*-1,2,3,3,3-d_5 (**1a** and **1b**). Methyl 2,3-diphenylpropionate-2,3-d_2 (1·00 g) dissolved in dry ether (20 ml) was treated with LAD (0·52 g) at ambient temp for 2 hr decomposition being effected with D_2O (3 ml). Filtration of the mixture and evaporation of the solvent afforded a crude product (1·10 g) which was directly tosylated with tosyl chloride (1·10 g) in dry pyridine (12 ml). The usual workup procedure yielded the desired tosylate (1·0 g, m.p. 78·5–79°). (Found: C, 71·01; H, 5·21. $C_{22}H_{18}D_4O_3S$ requires: C, 71·32; H, 4·90%).

$PhCHDCD(Ph)CD_2OTs$ (1·00 g) was reduced with LAD (0·34 g) by refluxing for 15 hr in dry THF (15 ml). Decomposition was accomplished with D_2O (2·5 ml). Filtering off the inorganic material, removing through a Widmer column the solvent and passing the residue over alumina (neutral, 11 g) using light-petroleum as eluant gave, after distilling off the solvent (Widmer column), 1,2-diphenylpropane-1,2,3,3,3-d_5 (b.p. 102°/2 mm Hg, 0·45 g).

No NMR signal was observed at the position of the $-CH_3$ group while a signal for only one proton in benzylic position was recorded.

1,2-Diphenylpropane-3-d_3 (**1**), 2,3-diphenylpropionic acid (**2**) and its methyl ester (**3**) were prepared in an analogous to the preparation of the labeled compounds manner.

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