Conformational Analysis of 3-Arylpropanoic Acids and Their Methyl Esters by ¹H Nuclear Magnetic Resonance Spectroscopy

By **Stefan L. Spassov*** and **Svetlana D. Simova**, Institute of Organic Chemistry, Bulgarian Academy of Sciences, 1113 Sofia, Bulgaria.

The *gauche–trans* conformational equilibria for a series of substituted ethanes of the type $ArCH_2CH_2CO_2R$ have been studied on the basis of their ¹H n.m.r. spectra. A correlation has been found between the population of the favoured *trans*-form and the inductive effect of the substituent in the aryl ring. It is suggested that polar interactions between the carbonyl oxygen and the *ortho*-aryl carbons (with respect to the side-chain) might be important for the conformational distribution in such compounds.

THIS paper describes the conformational analysis of a series of 3-arylpropanoic acids and their methyl esters by ¹H n.m.r. spectroscopy. The main purpose was to study the effect of the Ar substituent upon the conformational equilibrium as well as to compare the results obtained by use of different methods [1-3] for treatment of the n.m.r. data.

$$ArCH_2CH_2CO_2R$$

	(1a)	(1b)	(2b)	(3b)	(4a)
Ar =	Ph	Ph	$4-O_2NC_6H_4$	$4-ClC_6H_4$	$4-MeC_6H_4$
R =	H	Me	Me	Me	H

	(4b)	(5a)	(5b)	(6b)
Ar =	$4-MeC_6H_4$	$4-MeOC_6H_4$	$4-MeOC_6H_4$	1-Naphthyl
R =	Me	H	Me	Me

	(7a)	(7b)	(8a)	(8b)
Ar =	2-Furyl	2-Furyl	2-Thienyl	2-Thienyl
R =	H	Me	H	Me

RESULTS AND DISCUSSION

The spectra of the CH_2CH_2 fragment were of the AA'BB'-type with the low-field half broadened by long-range coupling to the aromatic protons. The preliminary analysis was carried out according to the literature [4,5] and the values thus obtained were further

investigation are shown below together with the appropriate coupling constants.[1] The two *gauche*-forms are mirror images and hence of equal energy.

At fast exchange, the constants J_{AB} and $J_{AB'}$ are averaged as follows:

$$J_{AB} = n_tJ_t^g + n_g(J_g^t + J_g^{g'})/2 \qquad (1)$$

$$J_{AB'} = n_tJ_t^t + n_gJ_g^g \qquad (2)$$

Here n_t and n_g are the populations of the *trans*- and *gauche*-conformers, respectively $(n_t + n_g = 1)$. The couplings in the individual rotamers were calculated according to the method of Abraham and Gatti,[1] assuming the following values of substituent electronegativities: [9] Ph, 2.75; CO_2H, 2.60. Thus, the values obtained for the couplings were: $J_t^g = 4.75$ Hz, $J_t^t = 13.36$ Hz, $J_g^g = 3.91$ Hz, and $J_g^t + J_g^{g'} = 16.06$ Hz. It is expected that equation (2) will give better results than (1) due to the larger variations of $J_{AB'}$ with the conformer population.[1] The results for n_t calculated on the basis of equation (2) as well as for the corresponding energy difference ΔE_{g-t} are shown in the Table.

trans   *gauche*   *gauche*
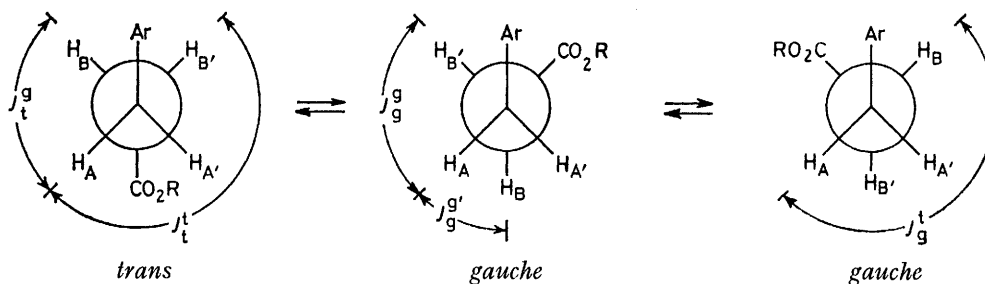
refined using the LAOCOON-3 programme [6] adapted for an ICL-1904A computer. The final parameters for all the compounds studied are collected in the Table. As is frequently the case for systems of this type, the geminal coupling constants $J_{AA'}$ and $J_{BB'}$ could not be determined from the spectra due to partial degeneracy.[7] The assignment of the vicinal couplings J_{AB} and $J_{AB'}$ was based on the approach of Abraham and Pachler.[8]

The staggered conformers of the compounds under

The conformational distribution was estimated also using the methods of Snyder [2] and Lin.[3] The n_t-values obtained were somewhat lower than those given in the Table: by 0—5% (Snyder, $\phi = 65°$, $S = 1/13$), or by 1—13% (Lin). Within the series of compounds however, the trends shown by all three methods were very similar.

The Table shows that the *trans*-conformer is favoured

[1] R. J. Abraham and G. Gatti, *J. Chem. Soc. (B)*, 1969, 961.
[2] E. I. Snyder, *J. Amer. Chem. Soc.*, 1966, **88**, 1165.
[3] Wei-chuwan Lin, *J. Chem. Phys.*, 1970, **52**, 2805.
[4] (a) D. M. Grant, R. C. Hirst, and H. S. Gutowsky, *J. Chem. Phys.*, 1963, **38**, 470; (b) R. C. Hirst and D. M. Grant, *ibid.*, 1964, **40**, 1909.
[5] E. W. Garbish, *J. Chem. Educ.*, 1968, **45**, 480.

[6] S. M. Castellano and A. A. Bothner-By, ' Computer Programs in Chemistry ', ed. D. F. DeTar, W. A. Benjamin, New York, 1968, vol. 1, p. 10.
[7]. R J. Abraham, 'The Analysis of High-Resolution NMR Spectra', Elsevier, Amsterdam, 1971.
[8] R. J. Abraham and K. G. R. Pachler, *Mol. Phys.*, 1964, **7**, 165.
[9] J. R. Cavanaugh and B. P. Dailey, *J. Chem. Phys.*, 1961, **34**, 1099.

in both solvents for all compounds studied. Assuming the *gauche–trans* energy difference ΔE_{g-t} to be a measure

N.m.r. parameters [a] and conformational populations of the compounds $ArCH_2{}^ACH_2{}^BCO_2R$

| Compound	Solvent [b]	δ_A	δ_B	J_{AB}	$J_{AB'}$	n_t, %	ΔE_{g-t}, kJ/mol [c]
(1a)	C	2.950	2.676	6.53	9.13	55.2	2.24
	N	2.907	2.661	6.73	8.72	50.9	1.81
(1b)	C	2.917	2.593	6.62	9.11	55.0	2.22
	N	2.952	2.659	6.79	8.51	48.7	1.59
(2b)	C	3.065	2.690	7.40	7.57	38.7	0.58
	N	3.061	2.707	7.38	7.67	39.8	0.69
(3b)	C	2.905	2.603	6.64	8.43	47.8	1.50
	N	2.896	2.614	6.92	8.10	44.3	1.15
(4a)	C	2.912	2.648	6.17	9.11	55.0	2.22
(4b)	C	2.806	2.506	6.35	9.16	55.5	2.27
	N	2.809	2.523	6.63	8.68	50.5	1.77
(5a)	C	2.889	2.673	6.74	8.63	49.9	1.71
	N	2.873	2.656	6.78	8.37	47.2	1.44
(5b)	C	2.886	2.591	6.99	8.75	51.2	1.84
	N	2.849	2.588	6.89	8.51	48.7	1.59
(6b)	C	3.400	2.745	6.03	9.58	60.0	2.72
(7a)	C	2.966	2.709	6.65	8.52	48.8	1.60
(7b)	C	2.961	2.651	6.72	8.48	48.4	1.56
(8a)	C	3.153	2.730	6.59	8.53	48.9	1.61
(8b)	C	3.142	2.670	6.61	8.49	48.5	1.57

[a] Chemical shifts (δ) in p.p.m. relative to internal $SiMe_4$, J values in Hz. [b] C = $CDCl_3$; N = CD_3NO_2. [c] $\Delta E_{g-t} = RT \ln 2n_t/(1 - n_t)$, calculated from the data in the preceding column.

of the Ph/CO_2R nonbonded interaction, one can see that the results for (1a) and (1b) correspond well to those obtained earlier [10] on the basis of conformational studies of $PhCH_2CH(Ph)CO_2R$ ($Ph/CO_2H = 2.51$ kJ/mol, and $Ph/CO_2Me = 1.67$ kJ/mol). Thus, the additivity of the conformational effects in trisubstituted ethanes of the above-mentioned type discussed before [10] is supported by the present results.

For all compounds except (2b), the population of the *trans*-conformer is higher in the less polar solvent ($CDCl_3$) in accordance with expectations. In most cases n_t is higher for the acids as compared to the corresponding esters.

It is generally accepted at present that the conformational equilibria in substituted ethanes are affected by both steric and polar factors. The highest n_t value observed for (6b) could be attributed solely to the steric influence of the bulky naphthyl group. Comparison of the results obtained for the five *p*-phenyl substituted esters in a given solvent reveals the following order of n_t values: Me > H > McO > Cl > NO_2. Considering simply the opposite directions of the $4-O_2NC_6H_4$ and the

averaged $4-MeOC_6H_4$ group dipoles, one might expect to find the n_t value for the Ph compound (1b) to be between those for (2b) and (5b): this is contrary to experiment. On the other hand, the observed n_t order shown above correlated very well with the Hammett σ_m values of the substituents [11] (correlation coefficient $r = 0.986$ in $CDCl_3$ and $r = 0.992$ in CD_3NO_2). On this basis, one might assume that the stability of the *gauche*-form is affected by a polar interaction between the negative carbonyl oxygen and the induced electric charges at the *ortho*-aryl carbons (with respect to the side chain and hence *meta* to phenyl group substituent):
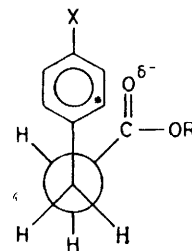
The lower n_t values for the heteroaromatic compounds (7) and (8) as compared to their Ph analogues could be explained similarly, remembering that in furan and thiophen the carbons represent the positive dipole end.[12]

EXPERIMENTAL

The compounds were prepared according to the following scheme:
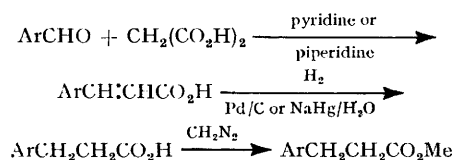
All compounds were characterized by their m.p., i.r., and n.m.r. spectra, details of which are listed in Supplementary Publication No. SUP 22422.*

The n.m.r. spectra were taken on JEOL PS-100 (100 MHz) and TESLA BS-487C (80 MHz) spectrometers at normal probe temperature, using *ca.* 0.5 molar solutions. Care was taken to obtain spectra of adequate quality for the analysis.[7] It is believed that the uncertainties in the n.m.r. parameters are no more than 0.001 p.p.m. for the chemical shifts and 0.1 Hz for the coupling constants.

The authors are indebted to Mr. V. Hitov (Medical Academy, Sofia) for some of the n.m.r. measurements.

[10] S. L. Spassov, A. S. Orahovats, S. M. Mishev, and J. Schraml, *Tetrahedron*, 1974, **30**, 365.

[11] H. H. Jaffé, *Chem. Rev.*, 1953, **53**, 191.

[12] J. A. Joule and G. F. Smith, ' Heterocyclic Chemistry ', Van Nostrand Reinhold London, 1972.