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Formal Steric Enthalpies of Crowded Methyl Esters[1]

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We have defined formal steric enthalpies of esters and acids and have calculated FSE values for the major conformers of the set of 15 esters $R_1R_2CHCOOMe$ in which R_1 and R_2 are H, Me, Et, *i*-Pr, and *t*-Bu. This is the first quantitative study of comparative steric effects for these classes of compounds. We have also examined the relationships between single conformer FSE's and the population FSE's.

The first quantitative studies of steric effects on chemical reactivity were those of Taft.[2-4] The Taft E_s values are based on esterification and on ester hydrolysis. They have long provided a useful guide to steric effects in additions to carbonyl groups and other reactions. There has been considerable interest in the dissection of E_s values in order to gain a better understanding of these effects and with a view to predicting them directly from structure by additivity.[5-7] The procedures have met with some success but are not general. This outcome is not surprising in view of the known tendency of steric effects to become nonadditive as soon as crowding exceeds some minimum level.[8-12]

E_s values do not provide a direct measure of steric properties of esters, but rather they provide relative measures of the steric difference between a transition state and the respective reactant state. In the past there has been no general way to calculate the steric properties of acids or of esters.

With the development of formal steric enthalpy it now becomes possible to make the desired direct comparisons.[11,12] In the present study we have defined formal steric enthalpies for esters and for acids and have calculated FSE values for all staggered conformers of a series of 15 esters having the structure $R_1R_2CHCOOMe$ with R_i-H, Me, Et, *i*-Pr, and *t*-Bu. In addition to their use in relating steric properties to structures, the data provide a basis for the quantitative theoretical prediction of steric effects on reaction rates and equilibria, based directly on molecular structure and otherwise independent of availability of experimental rates or equilibria.[10,13-15]

A given FSE value applies to a specific single conformer. In studies of alkanes we have calculated the statistical mechanical correction that relates the steric properties of a mixture of conformers to the steric properties of the single conformer of lowest energy.[11] This has utilized an empirical extrapolation based on additive gauche interactions. In the present study we have more complete information on enthalpies of the conformers and have been able to compare values of population FSE values of esters obtained by additivity of gauche enthalpies with those derived by direct calculations.

Table I. Group Increments for Esters, Acids, and Tetrahedral Intermediates

gp	DETSB corrns, d_i (eq 2)	gp	DETSB corrns
CH_3	0.134	α-CH_3	0.14
CH_2	0.815	α-CH_2	0.56
CH	2.272	α-CH	1.65
C	4.855		
CH_3O	0.584	COO	0.0
CH_2O	0.675	OH (acid)	0.0
CHO	1.432	$C(OH)_2O$	2.21
CO	3.265		

Results. To define FSE values for esters we first specify the structural units necessary to define the formal bond enthalpy components; these include the structural units already defined for alkanes and alcohols[11,12] plus the following new units: COO, acid OH, α-CH_3, α-CH_2, α-CH, and α-C. The next steps are to select standard molecules that contain the new units and to specify what FSE values are to be assigned to selected conformers of the new standard molecules. The selected standards, the specific conformers, and the formally assigned FSE values are as follows:[16] $MeCH_2COOMe$ (0.85), R-$EtCH_2COOMe$ (0.85), R-$EtCH_2COOMe$ (1.00), $Me_2CHCOOMe$ (0.85), R-EtMeCHCOOMe (1.00). The basis for selecting these particular FSE values is discussed below when we consider the calculation of formal gauche enthalpies. We postpone the calculation of the α-C correction term.

We also assign a correction (*d* value) of 0 for COO and 0 for carboxyl OH. There are not enough thermodynamic data to permit calculation of the *c* values.[11,12] Application of eq 1 and 2 of the cited references and use of the steric energies listed in Table II result in the *d* correction increments shown in Table I. Relevant correction terms from preceding studies are also included, as is the *d* value for $C(OH)_2O$, the unit for a tetrahedral intermediate. This will be needed in subsequent reports; the value is based on the standard conformers $CH_3C(OH)_2OCH_3$ (0), $CH_3CH_2C(OH)_2OCH_3$ (0.30), and R-$CH_3CH_2CH_2C(OH)_2OCH_3$ (0.30).

Table II summarizes the formal steric enthalpies derived for the 43 staggered conformers of the esters $R_1R_2CHCOOMe$; cf. Figure 1 and Appendix. The global minima are flagged with an asterisk, the others with a plus sign. Several of the unflagged conformers illustrate the effect of rotating the COOMe group by 180° to interchange the carbonyl oxygen and the alkoxy oxygen. The significance of formal gauche enthalpies and of excess steric crowding is described below. Details of the geometries are given in Table III.[17] Formal steric enthalpies of acids are

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[1] Definitions: SE, steric energy derived from a molecular mechanics calculation; FSE, formal Steric Enthalpy. See Appendix for definition of conformations.

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[16] See Appendix for definition of conformations.

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Table II. Formal Steric Enthalpy for Conformations of Esters $R_1R_2CHCOOMe$

	R_1	R_2	conformn[a]		attitude[b] of COOMe	SE[c]	FSE[d]	gauche[e] enthal	steric[f] crowding	run ID[g]
1*	H	H	H	H	120	1.76	0.85	0.85	0.00	BIN7001E
2*	Me	H	Me	H	266	2.17	0.86	0.85	0.01	BIN7002E
3A*	Et	H	T	H	94	2.97	0.84	0.85	−0.01	B7E20311
3B$^+$	Et	H	R	H	255	3.11	0.98	1.00	−0.02	BIN7103e
4A$^+$	*i*-Pr	H	TBAR	H	270	4.85	1.13	1.15	−0.02	BIN7102e
4B	*i*-Pr	H	RBAR	H	283	4.74	1.02	1.00	0.02	B7E20411
4B*	*i*-Pr	H	RBAR	H	107	4.73	1.01	1.00	0.01	BIN7102e
5*	*t*-Bu	H	*t*-Bu	H	90	7.72	1.28	1.15	0.13	B7E20511
6*	Me	Me	Me	Me	62	3.38	0.84	0.85	−0.01	B7E20611
6	Me	Me	Me	Me	243	3.38	0.84	0.85	−0.01	BIN7204E
7A$^+$	Et	Me	T	Me	63	4.80	1.45	1.55	−0.10	B7E20711
7B*	Et	Me	R	Me	62	4.36	1.01	1.00	0.01	BIN7S05E
7C$^+$	Et	Me	L	Me	93	4.96	1.61	1.70	−0.09	B7E20721
7C	Et	Me	L	Me	268	5.06	1.71	1.70	0.01	B7E20731
8A*	*i*-Pr	Me	TBAR	Me	262	7.02	2.08	1.85	0.23	B7E20821
8B$^+$	*i*-Pr	Me	RBAR	Me	94	7.23	2.29	2.40	−0.11	BT70I12E
8C$^+$	*i*-Pr	Me	LBAR	Me	241	7.05	2.11	1.70	0.41	B7E20811
8C	*i*-Pr	Me	LBAR	Me	63	7.05	2.11	1.70	0.41	B7E20831
9	*t*-Bu	Me	*t*-Bu	Me	262	11.01	3.35	2.55	0.80	B7E20911
9*	*t*-Bu	Me	*t*-Bu	Me	83	10.90	3.24	2.55	0.69	B7E20922
10A	Et	Et	T	T	57	7.69	3.52	3.50	0.02	B7E21041
10A$^+$	Et	Et	T	T	233	7.66	3.49	3.50	−0.01	B7E21052
10B$^+$	Et	Et	T	R	39	6.37	2.20	2.40	−0.20	B7E21053
10C$^+$	Et	Et	T	L	64	5.82	1.65	1.70	−0.05	B7E21011
10C	Et	Et	T	L	245	5.87	1.70	1.70	0.00	B7E21021
10D$^+$	Et	Et	R	R	40	6.00	1.83	1.85	−0.02	B7E21061
10E*	Et	Et	R	L	243	5.39	1.22	1.15	0.07	B7E21071
10F$^+$	Et	Et	L	R	262	8.36	4.19	3.80	0.39	B7E21031
11A$^+$	*i*-Pr	Et	TBAR	T	261	8.50	2.74	2.55	0.19	B7E21161
11B$^+$	*i*-Pr	Et	TBAR	R	87	10.35	4.59	3.95	0.64	B7E21121
11C*	*i*-Pr	Et	TBAR	L	261	8.05	2.29	2.00	0.29	B7E21131
11D$^+$	*i*-Pr	Et	RBAR	T	85	10.00	4.24	4.35	−0.11	B7E21171
11E$^+$	*i*-Pr	Et	RBAR	R	100	10.47	4.71	4.50	0.21	B7E21181
11F$^+$	*i*-Pr	Et	RBAR	L	268	8.42	2.66	2.55	0.11	B7E21151
11G$^+$	*i*-Pr	Et	LBAR	T	243	10.08	4.32	3.65	0.67	B7E21191
11H$^+$	*i*-Pr	Et	LBAR	R	228	8.74	2.98	2.55	0.43	B7E21141
11I$^+$	*i*-Pr	Et	LBAR	L	243	8.25	2.49	1.85	0.64	B7E21111
11I	*i*-Pr	Et	LBAR	L	63	8.25	2.49	1.85	0.64	BIN7N22E
12A$^+$	Et	*t*-Bu	T	*t*-Bu	84	14.30	5.83	4.50	1.33	B7E21231
12B*	Et	*t*-Bu	R	*t*-Bu	50	12.13	3.66	2.70	0.96	B7E21211
12B	Et	*t*-Bu	R	*t*-Bu	260	12.24	3.77	2.70	1.07	B7E21221
12C$^+$	Et	*t*-Bu	L	*t*-Bu	240	14.61	6.14	4.65	1.49	B7E21241
13A$^+$	*i*-Pr	*i*-Pr	TBAR	TBAR	233	12.73	5.38	4.10	1.28	B7E21331
13B	*i*-Pr	*i*-Pr	TBAR	RBAR	258	10.87	3.52	2.70	0.82	B7E21321
13B*	*i*-Pr	*i*-Pr	TBAR	RBAR	78	10.79	3.44	2.70	0.74	B7E21322
13C$^+$	*i*-Pr	*i*-Pr	TBAR	LBAR	133	12.98	5.63	4.65	0.98	B7E21311
13D$^+$	*i*-Pr	*i*-Pr	RBAR	RBAR	259	12.74	5.39	4.50	0.89	B7E21341
13E	*i*-Pr	*i*-Pr	RBAR	LBAR	225	14.06	6.71	6.45	0.26	B7E21363
13E$^+$	*i*-Pr	*i*-Pr	RBAR	LBAR	98	13.88	6.53	6.45	0.08	B7E21362
13F$^+$	*i*-Pr	*i*-Pr	LBAR	RBAR	235	13.55	6.20	3.80	2.40	B7E21351
14A*	*i*-Pr	*t*-Bu	TBAR	*t*-Bu	58	16.92	6.85	4.80	2.05	B7E21411
14A	*i*-Pr	*t*-Bu	TBAR	*t*-Bu	240	17.12	7.05	4.80	2.25	B7E21421
14A	*i*-Pr	*t*-Bu	TBAR	*t*-Bu	261	17.05	6.98	4.80	2.18	B7E21496
14B$^+$	*i*-Pr	*t*-Bu	LBAR	*t*-Bu	55	18.27	8.20	6.60	1.60	B7E21442
14B	*i*-Pr	*t*-Bu	LBAR	*t*-Bu	238	18.44	8.37	6.60	1.77	B7E21472
14C$^+$	*i*-Pr	*t*-Bu	RBAR	*t*-Bu	60	17.82	7.75	4.65	3.10	B7E21451
14C	*i*-Pr	*t*-Bu	RBAR	*t*-Bu	241	17.88	7.81	4.65	3.16	B7E21481
14C	*i*-Pr	*t*-Bu	RBAR	*t*-Bu	71	17.88	7.81	4.65	3.16	B7E21461
15*	*t*-Bu	*t*-Bu	*t*-Bu	*t*-Bu	61	23.80	11.02	6.75	4.27	B7E21512
15	*t*-Bu	*t*-Bu	*t*-Bu	*t*-Bu	244	23.96	11.18	6.75	4.43	B7E21524

[a] FSE(RCOOH) = FSE(RCOOMe) − 0.85. See Appendix for definition of *T*, *T*-BAR, etc. Conformations marked with asterisk are global minima. These and the conformers marked with plus are included in the figures. [b] "Attitude" is the torsion for the sequence CCC′=O based on the R_i of highest priority, the group in the 12 o'clock position in Figure 1. [c] Steric energy calculated with the DETSB force field. [d] Formal steric enthalpy. [e] Formal gauche enthalpy. [f] FSE, formal gauche enthalpy. [g] Identifies the corresponding entries in Table III.[17]

given by the relationship FSE(acid) = FSE(methyl ester) − 0.85.

Additional local minima may arise from alternative "attitudes" of the carbomethoxyl group. For example, if two alkyl groups are present, as for methyl isobutyrate (**6**), then the local minimum having the carbomethoxyl group in the 150–330° "attitude" is of higher energy by 0.67 kcal/mol than is the minimum having the 60–240° "attitude" shown.

As in previous studies we have based the FSE assignments for the standard conformers on estimates of formal gauche enthalpies; the specific increments used in defining formal steric enthalpy values are arbitrary, but reasonable. Different choices would lead to somewhat different definitions of FSE, but the values of FSE obtained for crowded

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(17) Supplementary material. See paragraph at end of this paper.

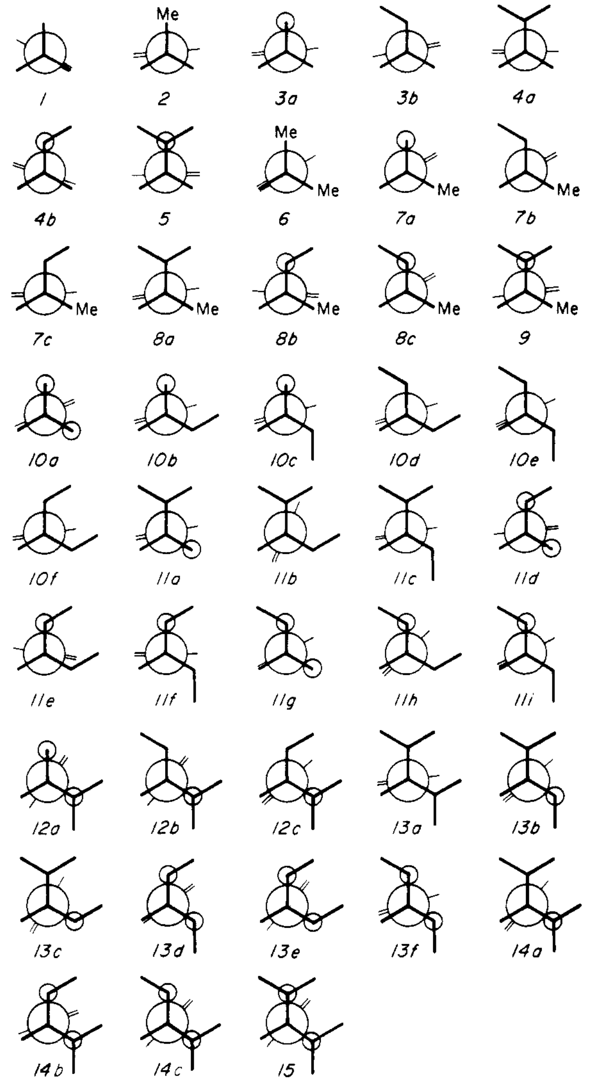

Figure 1. Newman projections of esters $R_1R_2CHCOOMe$ looking at the C carbon atom and along the C–C′ bond. β-Me groups are labeled, Et groups are represented by a line as in **3b** or as a small circle as in **3a** (to indicate projection toward the viewer), *i*-Pr groups are marked as in **4a** and **4b**, *t*-Bu groups as in **5**. Hydrogen atom positions are indicated by lines having no terminating symbols. A representative approximate "attitude" of the COOMe group is shown; the correct torsion for the group is defined in Table II. Representative torsions and complete data for heavy atoms are listed in Table III.[17]

molecules are not very sensitive to the choices.[11] The correspondence between the formal gauche enthalpy and the FSE is expected to be very close for conformers that are not too crowded. On the other hand, steric effects are not additive for crowded molecules, and for these the FSE's will exceed the formal gauche enthalpies.

We use the following assignments of gauche enthalpy increments: CCCC, 0.7 per gauche interaction; CCCCC, g^+g^- 1.25 additional; CCCC′, 0.15 per interaction; CCCO, 0.15 per interaction; CCCCO, g^+g^- 0.0 additional; CCCCC′, g^+g^- 1.25 additional; CCCOC, g^+g^- 1.25 additional; COOR′ group, 0.85; $R_1R_2R_3C$ interaction with COO, 0.70. These are consistent with our earlier assignments. The assignment of 0.85 to the FSE of methyl acetate and all other esters reflects the nonbonded interaction of the Me group of the OMe with the carbonyl carbon of the ester and represents an attempt to keep all definitions of FSE on a consistent basis. Comparisons within esters are unaffected by the choice, and comparisons with other classes of molecules are affected only by a constant additive term.

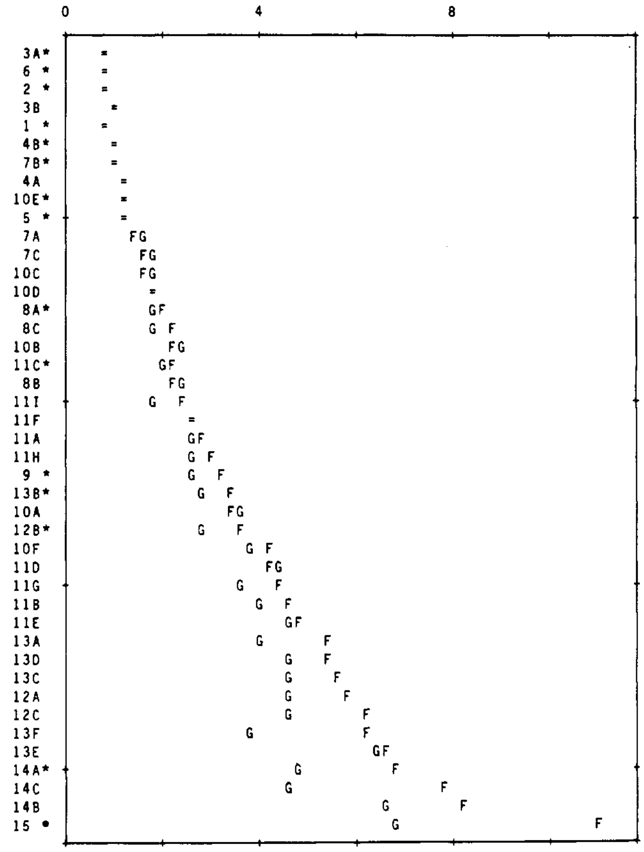

Figure 2. For each conformer indicated on the vertical axis the symbols indicate the formal gauche enthalpy *G* and the formal steric enthalpy *F*. The identifications correspond to those used in Figure 1 and in Table II.

The treatment of gauche interactions has been discussed by many workers.[18-21]

Figure 2 provides a graphical comparison of the FSE values (indicated as "*F*") and the formal gauche enthalpies (indicated as "*G*"). If the two are sufficiently close, then the combined point is shown as "=". Of the five esters used in defining the FSE scale only two are actually needed, the rest providing a redundant check. Therefore, the closeness of agreement for some 19 additional esters shows that the FSE values have been consistently defined for the esters in the set.

Discussion. In using molecular mechanics for the interpolation and the extrapolation of the steric component of thermodynamic and structural data we are concerned with the accuracy that may be attainable. While the best experimental enthalpies of formation of individual alkanes have estimated uncertainties of the order of 0.2–0.4 kcal/mol, certain relative values have much lower tolerances.[22,23] In the references, progressions of enthalpies of formation have been reported for several series Y-$(CH_2)_mH$ having Y = methyl, vinyl, cyclopentyl, cyclohexyl, and phenyl and for certain other series. In all series, addition of a CH_2 group eventually leads to the constant increment of −4.926 for the gas-phase enthalpy of forma-

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(18) Reference 22, p 548.

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tion at 298 K, a value that seems to be reliable to a few thousandths kilocalorie/mole. It thus appears possible to develop procedures for interpolating and extrapolating relative enthalpies of formation for some types of compounds that are reliable to better that 0.1 kcal/mol.

On the basis of consistencies we believe that the reported FSE values in the present study are correct to within a few tenths of a kilocalorie/mole. In unpublished work we have used the ester data in rate correlations that provide a further verification since resulting log *k*(rel) data are reproduced especially well, with a standard deviation of less than 0.25 kcal/mol for most of the set.

In Table II we report FSE values for some 60 conformers; details of the geometries are presented in Table III.[17] Although FSE values have been calculated for all 43 possible staggered conformers, these do not include all local minima. There may be some 80 more than shown in Table II. The additional local minima are of two types, those involving the R_1R_2CHC' part of the ester and those involving the "attitude" of the COOMe group.

Relative energies of "attitude" pairs differing by 180° in the orientation of the COOMe group are shown for the **4B**, **6**, **7C**, **10A**, **10C**, **11I**, **12B**, and **13B** pairs.[16] For most of these 180° interchanges, the difference in FSE is less than 0.1 kcal/mol. In addition to the 180° interchange there are other possible "attitudes" of higher energy that we have explored in less detail. For example, there is a local minimum for methyl isobutyrate, **9** in Figure 1, having the carbonyl group at about 150° instead of at about 240°. In an example calculation based on carboxylic acids the energy, of the 150° conformer is some 0.67 kcal/mol higher than that of the 60° conformer.

We looked for additional local minima. Except for conformers having g^+g^- interactions there appears to be just the one local minimum for any given staggered conformer. However, a g^+g^- interaction can assume either a right-handed or a left-handed helical conformation. Two such pairs are shown in Table II, both for methyl *i*-Pr-*t*-BuOAc. The structure obtained in run B7E21421 for conformer 14A defines a right-handed helix while that of run B7E21496 defines a left-handed helix. For 14C the corresponding pair is B7E21461 and B7E21451. It should be noted that the output of the MOLMEC runs for compound **14** as listed in Table III[17] corresponds in each case to the mirror image of the "standard" description as given in Table II.

The following staggered conformers have a single local minimum with respect to the R_1R_2CH group: **1**–**10**, **11A**, **11C**, **11F**, **11H**, **11I**, **12B**, **12C**, **13A**, **13B**, **13F**, **15**. Even with a g^+g^- interaction there may be only a single minimum because of symmetry. Staggered conformers expected to have both right-handed and left-handed helical forms include **11B**, **11D**, **11E**, **11G**, **12A**, **13C**, **13D**, **13E**, **14A**, **14B**, and **14C**.

Although it is the FSE values for individual conformers that are subject to direct calculation, the treatment of equilibria or of rates has to be based on an estimate for the population of conformers, on the population FSE. Allinger refers to this as "total strain".[24] The data reported in Table II provide a basis for directly estimating population FSE's. To a first approximation each conformer contributes to the population FSE in accordance with its energy multiplied by its fractional population as determined by the Boltzmann distribution.

Two estimates of population FSE's are presented in Table IV. The first is derived from the limited set of conformers indicated with asterisks and plus signs in Table II. The second is based on an attempt to include all major local minima at least approximately. To do so we doubled the initial set of FSE's so as to represent the presence of 180° "attitude" conformers. We then added FSE's to represent the higher energy "attitude" conformers, using an incremental energy of either 0.7 or 1.0, depending of whether methyl groups extend into the COOMe region. For those staggered conformers having g^+g^- interactions, we added a second FSE of equal value to represent the additional local minimum of the second helical hand. Incidentally the difference between the population FSE and the FSE for the conformer of lowest energy is the SM term in eq 5 of ref 12.

Table IV. Population Formal Steric Enthalpies of Esters $R_1R_2CHCOOMe$

	R_1	R_2	FSE	populn FSE[a]
1	H	H	0.85	0.85
2	Me	H	0.86	0.86–1.08
3	Et	H	0.84	0.90–0.99
4	*i*-Pr	H	1.01	1.24–1.38
5	*t*-Bu	H	1.28	1.28–1.50
6	Me	Me	0.84	0.84–1.00
7	Et	Me	1.01	1.24–1.38
8	*i*-Pr	Me	2.08	2.15–2.24
9	*t*-Bu	Me	3.24	3.24–3.40
10	Et	Et	1.22	1.55–1.63
11	*i*-Pr	Et	2.29	2.60–2.74
12	Et	*t*-Bu	3.66	3.75–3.84
13	*i*-Pr	*i*-Pr	3.44	3.84–3.92
14	*i*-Pr	*t*-Bu	6.85	7.10–7.31
15	*t*-Bu	*t*-Bu	11.02	11.02–11.18

[a] The first value is based on the conformers in Table II marked with either an asterisk or a plus sign. The second is based on a larger population of conformers having various "attitudes" of the COOMe group and with doubling of the g^+g^- conformers since both right- and left-handed helical forms will be present.

These calculations should bracket the correct values of the population FSE's. The largest difference between the two estimates of population FSE's is 0.2 kcal/mol. It therefore appears that the first type of calculation gives a relative population FSE reliable on average to perhaps 0.2 kcal/mol or better.

We turn now to the problem of predicting for a given molecule which conformer or conformers have the lowest FSE's. A successful method could save a great deal of computational time. The numbers in Table II and the plot of Figure 2 show the extent of the scatter between the additive formal gauche enthalpies and the FSE's. It is to be expected that the formal gauche enthalpy will underestimate the FSE for a highly crowded conformer. We have not yet been able to identify structural features that would allow us to make reliable corrections to the gauche estimate. The correspondence between formal gauche enthalpy and FSE is, however, sufficiently good for practical screening out of unprofitable calculations. Thus, for ester **10** we could omit the three high-energy forms with only a minor effect on the estimation of the population FSE.

Calculations. All calculations were performed with the set of programs MOLMEC. The DETSB force field was used throughout.[12] Replicate calculations from different starting data gave results agreeing to 0.01 kcal/mol. We believe that all reported steric energies are converged to at least 0.05 kcal. Most are converged to better than 0.01.

We examined stereo displays and stereo plots of the various conformers treated in the present study, including superposition plots to visualize the differences that occur on progressing through series of increasing methyl substitution.

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(24) Burkert, U.; Allinger, N. L. *ACS Monogr.* **1982**, *177*, 339.

In Table III[17] we list all torsions involving heavy atoms. We also summarize certain dihedral angles. The dihedral angles for a *tert*-butyl group never depart by more than 2 or 3° from 0–120–240. However, the two methyls of an isopropyl usually have a dihedral angle of 125–130°. The R_1R_2 dihedral angle ranges from about 125 to 142° as the size of the groups increases.

In selecting representative standard molecules for making a formal definition of FSE values it must be kept in mind that for any given series the first two or three members may not always be the best candidates since they may show departures of several tenths of a kilocalorie/mole from strict additivity.[25] This is not unexpected; for some series the first member (with $m = 0$) is a special case and cannot be expected to show additivity since the differences with higher homologues lie primarily in the formal bond enthalpy term.

For members having $m > 1$, the bonding perturbation for successive CH_2 units may be expected to be negligible from one series to another, and the effects may be treated as steric in origin. For $m = 1$ the CH_2 group is in a special α-position unless γ = alkyl or cycloalkyl. Similar considerations hold for other units as well. In the definition of the formal steric enthalpy the requirement for special sets of α units is an extnesion of these principles.

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Appendix

For the 15 esters $R_1R_2CHCOOMe$ there are 43 possible staggered conformations as shown in Figure 1. We have devised a nomenclature for these that relies on simplicity rather than generality. Of the R_i groups in the set, only two, Et and *i*-Pr, can adopt more than one staggered conformation. We denote the conformations of the ethyl group in terms of torsions for the sequence CCCC′, designating the three possibilities as $T \cong 180°$, $R \cong 60°$, or $L \cong 300°$. For the *i*-Pr group the unique sequence is HCCC′ with the designations *T*-BAR, *R*-BAR, and *L*-BAR to emphasize that a different sequence is used.

A torsion is defined by looking down a given bond and finding how many degrees in the clockwise direction we must rotate a reference group on the near atom to cause it to eclipse the reference group on the far atom. As an example, for compound **2** of Figure 1 (methyl propionate) the torsion defined by MeCC′═O is about 260°. Although a torsion is geometrically equivalent to a dihedral angle, it is convenient to restrict the term "dihedral angle" to relationships that are not torsions as defined above. An example would be to state that the dihedral angle between two methyl groups of compound **6** of Figure 1 (methyl isobutyrate) is about 130°. The dihedral angle in this example is defined by planes that intersect along the C–C′ bond, one plane passing through each methyl group.

We make use of a "standard" designation for each conformer based on the priority order *i*-Pr, Et, *t*-Bu, Me, H in clockwise sequence, looking from the α-carbon atom toward the carbonyl carbon. This provides a way to keep track of aliases and enantiomers. Since we are dealing with energies, we consider only one enantiomer. As an illustration, the "standard" designation *L*(Et,Me,H) (Figure 1 compound **7C**) is the mirror image of the nonstandard designation *R*(Et,H,Me) while *L*(Et,H,Me) denotes a different conformation, viz. *R*(Et,Me,H), compound **7B**. The sets of torsion values presented in Table III in the supplementary material are not necessarily in the "standard" form. The discrepancies arise from a decision to avoid transcription errors by reporting raw output data. The protocol we have chosen for preparing input data for the molecular mechanics computations was designed to minimize chances of errors; it does not necessarily yield the "standard" sequences.

Registry No. **1**, 79-20-9; **2**, 554-12-1; **3**, 623-42-7; **4**, 556-24-1; **5**, 10250-48-3; **6**, 547-63-7; **7**, 868-57-5; **8**, 30540-29-5; **9**, 19910-30-6; **10**, 816-11-5; **11**, 32444-33-0; **12**, 88246-54-2; **13**, 94991-59-0; **14**, 54461-01-7; **15**, 10250-50-7.

Supplementary Material Available: Table III (formal steric enthalpies of conformations of methyl esters [methyl acetate ... methyl di-*tert*-butylacetate] and Appendix II (specification of conformation) (13 pages). Ordering information is given on any current masthead page.

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(25) An excellent summary is given in Reference 23, p 238. The original work is that of Prosen, Johnson, and Rossini.[26]

(26) Prosen, E. J.; Johnson, W. H.; Rossini, F. D. *J. Res. Natl. Bur. Stand.* 1946, *37*, 51.

Tandem Alkylation–Reduction. Highly Stereoselective Synthesis of (*E*)-1-Hydroxymethyl Methyl Propenyl Ethers from Aldehydes Using 1-Lithio-1-methoxyallene[1,2]

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Tandem alkylation–reduction of a series of aldehydes, by alkylating with 1-lithio-1-methoxyallene followed by reducing with lithium–ammonia, regiospecifically and highly stereoselectively affords the 1-hydroxymethyl methyl propenyl ether in which the alkene geometry is exclusively *E*. Aldehydes that have been subjected to this convenient procedure include aromatic, aliphatic, and heterocyclic aldehydes. Subsequent hydrolysis, in the aromatic and aliphatic cases, affords the corresponding α-hydroxy ethyl ketones. The stereochemistry of the propenyl ethers was established by ^{13}C NMR spectroscopy. A mechanism for the selective reduction of the methoxyallene system is proposed.

In ongoing studies extending the utility of tandem alkylation–reductions of carbonyl compounds,[2] we have demonstrated the usefulness of the method for rapid assembly of complex aromatic alkanes,[4a] aromatic alkenes,[4b]