priate set of structural elements may be described in terms of a main atom plus atoms in the first rank out, the ligands. In particular it is assumed that a single c[C_H_H_H_O_], etc., will be sufficient to correlate enthalpies of formation data for both alcohols and ethers. I mention this point because at least one force field, MM2(85), uses different reference bond lengths for the set of groups, depending on whether the groups occur in alcohols or in ethers, and still different reference values for the set if they occur in glycols. This implies that a more complex set of structural groups has been used, some of which depend on atoms in the second rank out.

The last column indicates the number of instances available for each group. The available data are insufficient to provide definitive values for c[C_H_O_O_O_], c[C_C_O_O_O_], and c[C_O_O_O_O_].

Tables II–V list the compounds used to derive the c increments reported in Table I. The differences between the assigned FSE values and the experimental FSE values calculated by eq 1 and using the c increments of Table I have standard deviations of about 0.4 kcal/mol. Data for the compounds of the acetal and orthoester families (Table V) are less certain.

The FSE values were assigned to the standards as follows: A molecule of a straight-chain compound in the extended form is assumed to have a FSE of 0. For other molecule energies due to gauche interactions were based on the values listed above and were summed for the conformer of lowest energy.

Table VI reports experimental FSE values for most of the other alcohols and ethers for which enthalpy of formation data for the gas phase are available. On the basis of the generalities observed for alkanes and cycloalkanes, FSE values for the cyclohexanols should correspond to those found for the acyclic alcohols. The relatively large negative values suggest that the experimental enthalpies of formation may be in serious error. The data for some of the glycols are also strongly negative and are in error; other glycol enthalpy values are inconsistent in that additions of successive methylene groups do not produce the expected increments in the enthalpies of formation. The expected increment is −4.926 kcal/mol per added CH_2 increment as summarized in ref 4 (p 240); cf. Benson value in Table I.

The standard deviations of the several correlations are given in the footnotes of the tables.

Experimental Formal Steric Enthalpy. 4. Aldehydes, Ketones, Acids, and Esters

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This study is a critical evaluation of experimental values of formal steric enthalpies derived from published values of enthalpies of formation of aldehydes, ketones, esters, and acids, gas phase, 25°C. These data may be useful for calibration of force fields.

As discussed in the first paper in this series,[1] eq 1 defines the relationship between the observed enthalpy of formation and the formal steric enthalpy.[2,3] The left-hand side is the enthalpy of formation of the single conformer of lowest energy; SM corrects for the contribution due to multiple conformers of higher energy. The first term on the right-hand side is the formal bond enthalpy expressed as a sum of group increments; FSE is the formal steric enthalpy. In this study I derive the c increments from appropriate standards having defined FSE values and from them calculate FSE values for the remaining compounds. The data come from refs 4 and 5.

$$\Delta H_f - \mathrm{SM} = \sum n_i c_i + \mathrm{FSE} \qquad (1)$$

The SM values of all compounds are based on assigning the energies of staggered conformations as follows: C_C_C_C═O trans 0, gauche 0.30, and g^+g^- as 1.90 plus the sum of the gauche interactions.

Table I lists the structural elements needed to describe monofunctional aldehydes, ketones, esters, and acids. c increments for alkane structural elements[1] and for alkoxyl groups[6] are also included. Since the c increments for each set are underdetermined, it is necessary to make one arbitrary assignment for each. I have chosen to set c[C_C_CKH_H_] and c[C_C_CEH_H_] equal to c[C_C_C_H_H_]. For many of the structural elements, it is necessary to go to the second rank out in making the definition. This is effected by defining three types of sp^2 carbon atoms, CD for olefins (treated elsewhere, ref 7), CE

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Table I. *c* Increments for Aldehdyes, Ketones, and Esters

structural[a] element (increment)	definition[b] of structural element	value[c] of *c* increment	no.[d]	Benson values[e,f]	structural[a] element (increment)	definition[b] of structural element	value[c] of *c* increment	no.[d]	Benson values[e,f]
c[C_C_H_H_H_]	$CH_3(C)$	-10.033		-10.20	*c*[C_CKH_H_H_]	$CH_3(CK)$	-10.16	9	-10.08
c[C_C_C_H_H_]	$(C)CH_2(C)$	-5.147		-4.93	*c*[C_C_CKH_H_]	$(C)CH_2(CK)$	(-5.147)		-5.2
c[C_C_C_C_H_]	$(C)CH(C)_2$	-2.258		-1.90	*c*[C_C_C_CKH_]	(C)CH(C)(CK)	-1.62	3	-1.7
c[C_C_C_C_C_]	$(C)C(C)_3$	-0.217		0.50	*c*[C_C_C_C_CK]	$(C)C(C)_2(CK)$	2.14	2	1.4
c[C_H_H_H_O_]	$CH_3(O)$	-6.819		-10.08	*c*[CEC_OEOH]	(C)CE(OE)(OH)	-92.78	9	-93.2
c[C_C_H_H_O_]	$(C)CH_2(O)$	(-5.147)		-8.1	*c*[CEC_OCOE]	(C)CE(OE)(OC)	-81.52	8	-78.2
c[C_C_C_H_O_]	(C)CH(C)(O)	-4.34		-7.2	*c*[C_CEH_H_H_]	$CH_3(CE)$	-10.55	6	-10.08
c[C_C_C_C_O_]	$(C)C(C)_2(O)$	-3.87		-6.6	*c*[C_C_CEH_H_]	$(C)CH_2(CE)$	(-5.147)		-5.2
c[CKC_H_OK]	(C)CK(H)(OK)	-29.22	9	-29.1	*c*[C_C_C_CEH_]	(C)CH(C)(CE)	-4.66	2	-1.7
c[CKC_C_OK]	(C)CK(OK)(C)	-31.61	4	-31.4	*c*[C_C_C_C_CE]	$(C)C(C)_2(CE)$	-1.99	3	1.4

[a] C_ is sp^3 carbon, CE is sp^2 carbon of an ester or an acid, CK is sp^2 carbon of an aldehyde or a ketone, H_ is hydrogen attached to carbon, O_ is sp^3 oxygen, OC denotes the alkoxy oxygen of esters, OE denotes the sp^2 oxygen of esters and acids, OH denotes the carboxylic OH group, OK denotes the sp^2 oxygen of aldehydes and ketones. [b] Attached groups are indicated in parentheses. [c] Values in parentheses are defined values. [d] Number of occurrences of the element in the data set. [e] Reference 8. [f] The Benson values are based on setting *c*[C_H_H_H_O_] equal to *c*[C_C_H_H_H_]; values in this study are based instead on setting *c*[C_C_H_H_O_] equal to *c*[C_C_C_H_H_].

Table II. Compounds Used To Calculate *c*[CKC_C_OK] and *c*[CKC_H_OK]

compound	formula	ΔH_f(exptl)	ref[b]	ΔH_f(strain free)[c]	SM	ΔH_f(calcd)[d]	FSE(exptl)[e]	FSE(expected)[f]
propanal	C_3H_6O	-44.36	P	-44.40	0.00	-44.40	0.04	0.00
butanal	C_4H_8O	-48.95	P	-49.55	0.16	-49.39	0.44	0.00
butanal	C_4H_8O	-49.00	S	-49.55	0.16	-49.39	0.39	0.00
3-pentanone	$C_5H_{10}O$	-61.64	P	-61.97	0.18	-61.79	0.15	0.00
pentanal	$C_5H_{10}O$	-54.61	P	-54.69	0.37	-54.32	-0.29	0.00
pentanal	$C_5H_{10}O$	-54.45	S	-54.69	0.37	-54.32	-0.13	0.00
3-hexanone	$C_6H_{12}O$	-66.52	P	-67.12	0.40	-66.72	0.20	0.00
hexanal	$C_6H_{12}O$	-59.37	S	-59.84	0.59	-59.25	-0.12	0.00
octanal	$C_8H_{16}O$	-69.23	S	-70.14	1.02	-69.12	-0.12	0.00
2-nonanone	$C_9H_{18}O$	-81.43	P	-82.56	0.80	-81.76	0.33	0.00
5-nonanone	$C_9H_{18}O$	-82.43	P	-82.56	0.80	-81.76	-0.67	0.00
nonanal	$C_9H_{18}O$	-74.16	S	-75.28	1.23	-74.05	-0.11	0.00
decanal	$C_{10}H_{20}O$	-79.09	S	-80.43	1.45	-78.98	-0.11	0.00

[a] Kcal/mol at 25 °C. [b] S is ref 4, P is ref 5. [c] Calculated from c increments of Table I. [d] Value in column 5 plus value in column 6. [e] Value in column 3 minus value in column 7 (eq 1). [f] Standard deviation of FSE(expt) - FSE(expected) is 0.4.

Table III. Compounds Used To Calculate *c*[C_CKH_H_H_], *c*[C_C_C_CKH_], and *c*[C_C_C_C_CK]

compound	formula	ΔH_f(exptl)[a]	ref[b]	ΔH_f(strain free)[c]	SM	ΔH_f(calcd)[d]	FSE(exptl)[e]	FSE(expected)[f]
acetaldehyde	C_2H_4O	-39.70	P	-39.36	0.00	-39.36	-0.34	0.00
acetaldehyde	C_2H_4O	-39.63	S	-39.36	0.00	-39.36	-0.27	0.00
acetone	C_3H_6O	-51.94	P	-51.88	0.00	-51.88	-0.06	0.00
acetone	C_3H_6O	-52.00	S	-51.88	0.00	-51.88	-0.12	0.00
2-butanone	C_4H_8O	-57.05	P	-56.93	0.00	-56.93	-0.12	0.00
2-butanone	C_4H_8O	-56.97	S	-56.93	0.00	-56.93	-0.04	0.00
2-methylpropanal	C_4H_8O	-51.58	P	-50.90	0.00	-50.90	-0.68	0.00
2-pentanone	$C_5H_{10}O$	-61.90	P	-62.07	0.16	-61.91	0.01	0.00
2-pentanone	$C_5H_{10}O$	-61.82	S	-62.07	0.16	-61.91	0.09	0.00
3-methyl-2-butanone	$C_5H_{10}O$	-62.74	P	-63.43	0.00	-63.43	0.69	0.00
2-hexanone	$C_6H_{12}O$	-66.87	P	-67.22	0.37	-66.85	-0.02	0.00
2-methyl-3-pentanone	$C_6H_{12}O$	-68.38	P	-68.47	0.10	-68.37	-0.01	0.00
3,3-dimethyl-2-butanone	$C_6H_{12}O$	-69.48	P	-69.71	0.00	-69.71	0.23	0.00
2,2-dimethyl-3-pentanone	$C_7H_{14}O$	-74.98	P	-74.75	0.00	-74.75	-0.23	0.00

[a-e] See Table II. [f] Standard deviation of FSE(exptl) - FSE(expected) is 0.3.

for esters, and CK for aldehydes and ketones. CD has CD plus either sp^3 C_, H_, or CD attached, the CK has sp^3 C_ and sp^2 OK plus either sp^3 C_ or H_ attached; CE has sp^3 C_, sp^2 OE, and sp^3 O_ with either sp^3 C_ (ester) or H_ (acid) on sp^3 O_. These definitions include second rank atoms for such structural elements as [C_C_C_CD-H_] and C_C_C_CEH_]. The values differ in minor respects from those given in an earlier reference.[2]

The entries in Table I summarize the atoms implied by the definitions of the structural elements. Tables II and III list the compounds used to derive the *c* increments reported in Table I for aldehydes and ketones. Table IV shows the available data for these compounds; relatively few compounds of these classes have been studied.

Tables V–VII provide the corresponding data for acids and for esters. All simple esters have been assigned a FSE value of 0.85 kcal/mol to reflect the steric interaction of the alkoxyl carbon atom with the carbonyl group of the ester. This value is expected to be valid for all primary and secondary alkoxyl groups. For the esters and acids in Tables VI and VII the R group of the ester is expected

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Table IV. Experimental Formal Steric Enthalpies of Aldehyde and Ketones

compound	formula	ΔHf-(exptl)[a]	ref[b]	ΔH_f-(strain free)[c]	SM	ΔH_f-(calcd)[d]	FSE-(exptl)[e]	FSE-(expected)
propanal	C_3H_6O	−44.36	P	−44.40	0.00	−44.40	0.04	0.00
cyclopentanone	C_5H_8O	−45.91	P	−52.20	0.00	−52.20	6.29	
cyclohexanone	$C_6H_{10}O$	−54.04	P	−57.35	0.00	−57.35	3.31	
cyclohexanone	$C_6H_{10}O$	−55.00	S	−57.35	0.00	−57.35	2.35	
cycloheptanone	$C_7H_{12}O$	−59.15	P	−62.49				
2,4-dimethyl-3-pentanone	$C_7H_{14}O$	−74.40	P	−74.97	0.00	−74.97	0.57	
heptanal	$C_7H_{14}O$	−63.05	P	−64.99	0.81	−64.18	1.13	0.00
heptanal	$C_7H_{14}O$	−63.10	S	−64.99	0.81	−64.18	1.08	0.00
2-ketobicyclo[2.2.2]octane	$C_8H_{12}O$	−53.11	P	−61.22	0.00	−61.22	8.11	
cis-3-ketobicyclo[3.3.0]octane	$C_8H_{12}O$	−55.00	P	−61.86	0.00	−61.86	6.86	
trans-3-ketobicyclo[3.3.0]octane	$C_8H_{12}O$	−49.40	P	−61.86	0.00	−61.86	12.46	
cyclooctanone	$C_8H_{14}O$	−64.91	P	−67.64				
2,2,4-trimethyl-3-pentanone	$C_8H_{16}O$	−80.86	P	−81.25	0.00	−81.25	0.39	
2-ethylhexanal	$C_8H_{16}O$	−71.61	P	−71.49	0.81	−70.68	−0.93	
cis-8-ketobicyclo[4.3.0]nonane	$C_9H_{14}O$	−59.66	P	−67.01	0.00	−67.01	7.35	
trans-8-ketobicyclo[4.3.0]nonane	$C_9H_{14}O$	−59.56	P	−67.01	0.00	−67.01	7.45	
2,2,4,4-tetramethyl-3-pentanone	$C_9H_{18}O$	−82.65	P	−87.53	0.00	−87.53	4.88	
2,6-dimethyl-4-heptanone	$C_9H_{18}O$	−85.47	P	−86.55	0.37	−86.18	0.71	
cis-8-keto-1-methylbicyclo[4.3.0]nonane	$C_{10}H_{16}O$	−68.59	P	−75.00	0.00	−75.00	6.41	
trans-8-keto-1-methylbicyclo[4.3.0]nonane	$C_{10}H_{16}O$	−65.77	P	−75.00	0.00	−75.00	9.23	
2-keto-1,7,7-trimethylbicyclo[2.2.1]heptane	$C_{10}H_{16}O$	−63.93	P	−77.49	0.00	−77.49	13.56	
2,2,5,5-tetramethyl-3-hexanone	$C_{10}H_{20}O$	−94.14	P	−95.04	0.00	−95.04	0.90	
2,2,6,6-tetramethyl-4-heptanone	$C_{11}H_{22}O$	−100.67	P	−102.54	0.00	−102.54	1.87	
6-undecanone	$C_{11}H_{22}O$	−92.59	P	−92.85				
2-dodecanone	$C_{12}H_{24}O$	−96.63	P	−98.10	1.66	−96.44	−0.19	0.00

[a–e] See Table II.

Table V. Compounds Used To Calculate *c*[CEC_OEOH] and *c*[CEC_OCOE]

compound	formula	ΔH_f(exptl)[a]	ref[b]	ΔH_f(strain free)[c]	SM	ΔH_f(calcd)[d]	FSE(exptl)[e]	FSE(expected)[f]
propanoic acid	$C_3H_6O_2$	−108.39	P	−107.96	0.00	−107.96	−0.43	0.00
butanoic acid	$C_4H_8O_2$	−113.72	P	−113.11	0.16	−112.95	−0.77	0.00
ethyl propionate	$C_5H_{10}O_2$	−110.80	P	−111.88	0.00	−111.88	1.08	0.85
pentanoic acid	$C_5H_{10}O_2$	−117.57	P	−118.25	0.37	−117.88	0.31	0.00
hexanoic acid	$C_6H_{12}O_2$	−122.35	P	−123.40	0.59	−122.81	0.46	0.00
methyl pentanoate	$C_6H_{12}O_2$	−112.62	P	−113.81	0.37	−113.44	0.82	0.85
ethyl pentanoate	$C_7H_{14}O_2$	−121.15	P	−122.17	0.37	−121.80	0.65	0.85
heptanoic acid	$C_7H_{14}O_2$	−128.15	P	−128.55	0.80	−127.75	−0.40	0.00
methyl hexanoate	$C_7H_{14}O_2$	−117.73	P	−118.96	0.59	−118.37	0.64	0.85
octanoic acid	$C_8H_{16}O_2$	−132.48	P	−133.70	1.02	−132.68	0.20	0.00
methyl octanoate	$C_9H_{18}O_2$	−127.58	P	−129.25	1.02	−128.23	0.65	0.85
nonanoic acid	$C_9H_{18}O_2$	−137.98	P	−138.84	1.13	−137.71	−0.27	0.00
decanoic acid	$C_{10}H_{20}O_2$	−142.18	P	−143.99	1.45	−142.54	0.36	0.00
methyl nonanoate	$C_{10}H_{20}O_2$	−132.39	P	−134.40	1.13	−133.27	0.88	0.85
methyl decanoate	$C_{11}H_{22}O_2$	−137.14	P	−139.55	1.45	−138.10	0.96	0.85
undecanoic acid	$C_{12}H_{22}O_2$	−146.89	P	−149.14	1.67	−147.47	0.58	0.00
methyl undecanoate	$C_{12}H_{24}O_2$	−141.92	P	−144.70	1.67	−143.03	1.11	0.85

[a–e] See Table II. [f] Standard deviation of FSE(exptl) − FSE(expected) is 0.4.

Table VI. Compounds Used To Calculate *c*[C_CEH_H_H_], *c*[C_C_C_CEH_], and *c*[C_C_C_C_CE]

compound	formula	ΔH_f-(exptl)[a]	ref[b]	ΔH_f-(strain free)[c]	SM	ΔH_f-(calcd)[d]	FSE-(exptl)[e]	FSE-(expected)[f]
acetic acid	$C_2H_4O_2$	−103.44	P	−103.33	0.00	−103.33	−0.11	0.00
acetic acid	$C_2H_4O_2$	−103.93	S	−103.33	0.00	−103.33	−0.60	0.00
methyl acetate	$C_3H_6O_2$	−98.45	P	−98.89	0.00	−98.89	0.44	0.85
ethyl acetate	$C_4H_8O_2$	−106.14	P	−107.25	0.00	−107.25	1.11	0.85
ethyl acetate	$C_4H_8O_2$	−105.86	S	−107.25	0.00	−107.25	1.39	0.85
butyl acetate	$C_6H_{12}O_2$	−116.06	P	−117.54	0.33	−117.21	1.15	0.85
methyl 2,2-dimethylpropanoate	$C_6H_{12}O_2$	−119.40	O	−120.43	0.00	−120.43	1.03	0.85
methyl 2-methylbutanoate	$C_6H_{12}O_2$	−117.71	P	−118.18	0.23	−117.95	0.24	0.85
ethyl 2,2-dimethylpropanoate	$C_7H_{14}O_2$	−128.11	P	−128.79	0.00	−128.79	0.68	0.85
ethyl 2-methylbutanoate	$C_7H_{14}O_2$	−124.86	P	−126.54	0.23	−126.31	1.45	0.85

[a–e] See Table II. [f] Standard deviation of FSE(exptl) − FSE(expected) is 0.5.

to make no contribution to the FSE value. Again the values are limited, and values for key compounds are discordant.

There is some question about best values for the pairs *c*[C_C_C_CKH_], *c*[C_C_C_CEH_] and *c*[C_C_C_C_CK], *c*[C_C_C_C_CE]. On the basis of the

Table VII. Experimental Formal Steric Enthalpies of Esters and Acids Based on Gas-Phase Enthalpies of Formation at 25 °C

compound	formula	ΔH_f (exptl)[a]	SD	ref[b]	ΔH_f (strain free)[c]	SM	ΔH_f (calcd)[d]	FSE-(exptl)[e]	FSE-(expected)
succinic acid	$C_4H_6O_2$	-196.70	0.8	P	-195.85	0.00	-195.85	-0.85	0.00
2,2-dimethylpropanoic acid	$C_5H_{10}O_2$	-117.42	1.6	P	-124.87	0.00	-124.87	7.45	0.00
3-methylbutanoic acid	$C_5H_{10}O_2$	-121.89	1.5	P	-120.25	0.09	-120.16	-1.73	0.00
isopropyl acetate	$C_5H_{10}O_2$	-115.13	0.2	P	-116.48	0.00	-116.48	1.35	0.85
methyl bicyclo[1.1.0]butane-1-carboxylate	$C_6H_8O_2$	-39.34	0.2	P	-102.88	0.00	-102.88	63.54	
methyl cyclobutanecarboxylate	$C_6H_{10}O_2$	-84.92	0.3	P	-108.41	0.00	-108.41	23.49	
adipic acid	$C_6H_{10}O_4$	-206.74	0.6	P	-206.15	0.43	-205.72	-1.02	0.00
methyl 2,2-dimethylpropanoate	$C_6H_{12}O_2$	-122.80	0.3	P	-120.43	0.00	-120.43	-2.37	0.85
methyl 3-methylbutanoate	$C_6H_{12}O_2$	-119.00	1.7	P	-115.81	0.09	-115.72	-3.28	0.85
ethyl 3-methylbutanoate	$C_7H_{14}O_2$	-125.96	2.0	P	-124.17	0.09	-124.08	-1.88	0.85
octanedioic acid	$C_8H_{14}O_4$	-213.89	1.0	P	-216.44	0.86	-215.58	1.69	0.00
2-ethylhexanoic acid	$C_8H_{16}O_2$	-133.72	0.4	P	-138.06	0.81	-137.25	3.53	0.00
isopropyl pentanoate	$C_8H_{16}O_2$	-130.23	0.8	P	-131.40	0.37	-131.03	0.80	0.85
methyl heptanoate	$C_8H_{16}O_2$	-123.30	0.3	P	-124.11	0.80	-123.31	0.01	0.85
propyl pentanoate	$C_8H_{16}O_2$	-127.53	0.4	P	-127.32	0.80	-126.52	-1.01	0.85
sec-butyl butyrate	$C_8H_{16}O_2$	-130.33	1.0	P	-131.40	0.75	-130.65	0.32	0.85
butyl pentanoate	$C_9H_{18}O_2$	-133.89	0.5	P	-132.47	0.97	-131.50	-2.39	0.85
isobutyl pentanoate	$C_9H_{18}O_2$	-135.90	0.9	P	-134.47	0.70	-133.77	-2.14	1.05
sec-butyl pentanoate	$C_9H_{18}O_2$	-137.00	0.5	P	-136.55	0.97	-135.58	-1.42	1.05
homocubane-1-carboxylic acid	$C_{10}H_{10}O_2$[f]	0.60	0.0	O	-115.72	0.00	-115.72	116.32	
methyl homocubane-1-carboxylate	$C_{11}H_{12}O_2$[f]	6.26	1.3	O	-111.28	0.00	-111.28	117.54	
dodecanedioic acid	$C_{12}H_{22}O_4$	-233.48	0.5	P	-237.03	1.29	-235.74	2.26	0.00
dodecanoic acid	$C_{12}H_{24}O_2$	-153.44	0.5	P	-154.28	1.88	-152.40	-1.04	0.00
methyl dodecanoate	$C_{13}H_{26}O_2$	-146.94	0.5	P	-149.84	1.88	-147.96	1.02	0.85
tridecanoic acid	$C_{13}H_{26}O_2$	-157.79	0.6	P	-159.43	2.10	-157.33	-0.46	0.00
methyl tridecanoate	$C_{14}H_{28}O_2$	-151.86	0.7		-154.99	2.10	-152.89	1.03	0.85
tetradecanoic acid	$C_{14}H_{28}O_2$	-165.80	1.0	p	-164.58	2.31	-162.27	-3.53	0.00
methyl tetradecanoate	$C_{15}H_{30}O_2$	-156.91	0.7	P	-160.14	2.31	-157.83	0.92	0.85
pentadecanoic acid	$C_{15}H_{30}O_2$	-167.07	1.1	P	-169.72	2.53	-167.19	0.12	0.00
hexadecanoic acid	$C_{16}H_{32}O_2$	-176.17	1.1	P	-174.87	2.74	-172.13	-4.04	0.00
methyl pentadecanoate	$C_{16}H_{32}O_2$	-162.52	0.7	P	-165.28	2.53	-162.75	0.23	0.85
nonadecanoic acid	$C_{19}H_{38}O_2$	-187.69	1.3	P	-190.31	3.39	-186.92	-0.77	0.00
eicosanoic acid	$C_{20}H_{40}O_2$	-194.17	1.8	P	-195.46	3.70	-191.76	-2.41	0.00

[a-e] See Table II. [f] Reference 9.

equality of *c*[C_CKH_H_H_] and *c*[C_CEH_H_H_] and the defined equality of *c*[C_C_CKH_H_] and *c*-[C_C_CEH_H_], the above pairs might be presumed to be equal also, and Benson does use equal values. However, the rather meager data seem to fit the assigned values better than equal values.

Synthesis of (±)-11-Nor-9-carboxy-Δ^9-tetrahydrocannabinol: New Synthetic Approaches to Cannabinoids[†,1]

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A completely regioselective synthesis of (±)-11-nor-9-carboxy-Δ^9-tetrahydrocannabinol (**1**), a principal human metabolite of Δ^9-tetrahydrocannabinol (**2**), has been carried out in seven steps and 14% overall yield from apoverbenone (**9**) and the bis-MOM ether of olivetol. Condensation of **9** with the aryllithium derived from the bis-MOM ether of olivetol gives an unstable tertiary allylic alcohol that undergoes oxidative rearrangement to give enone **42**. Reaction of **42** with acid results in hydrolysis of the MOM ethers and cyclization to benzopyranone **21**. Conversion to MOM ether **39** followed by Li/NH_3 reduction and trapping of the enolate with *N*-phenyltriflimide gives vinyl triflate **40** plus the isomer with a cis ring fusion. Palladium-catalyzed carboxylation, hydrolysis of the MOM ether, and separation from cis acid **41** gives pure **1**. Model experiments employing unsubstituted resorcinol derivatives that lead to ester **27** are described, as are a number of alternative approaches to acid **1**.

Introduction

Cannabis sativa (marijuana) has been employed for many centruies as a medicinal agent and in social and religious rituals.[3] In contemporary society the illicit use of marijuana as a recreational drug has led to the development of methods to ascertain if an individual has been using the drug. The most widely used test procedures

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[†] Dedicated to the memory of Dr. Ulrich Weiss.

(1) For a preliminary communication describing the synthesis of acid 1, see: Huffman, J. W.; Zhang, X.; Wu, M.-J., Joyner, H. H. *J. Org. Chem.* 1989, *54*, 4741.

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