Pergamon

Tetrahedron, Vol. 53, No. 8, pp. 2767-2774, 1997

0040-4020/97 $17.00 + 0.00

PII: S0040-4020(97)00004-5

MM3 Parameters for Carbocations

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Abstract: Based on the experimental heats of formation and, in part, the geometries of 44 aliphatic and alicyclic carbocations including cyclopropyl, cyclobutyl and cyclopentyl cations, a set of 94 cation parameters has been developed for MM3. © 1997 Elsevier Science Ltd. All rights reserved.

Introduction

Cationic rearrangements are a potentially valuable means for the construction of a desired carbon framework.[1] To check their applicability, a program based on force field calculations and allowing an automated educt- and/or product oriented search for favorable rearrangement paths would be helpful. For such a program (CARESY), which just has been completed,[2] we needed parameters for carbocations. Such parameters exist for MM2[3] and MMP2,[4] but not for MM3.[5] We therefore developed a parameter set for aliphatic and alicyclic carbocations for MM3.

For calculations on carbocations with MM3, parameters for bond lengths, bond angles, out of plane angles and torsion angles of the most important combinations of the atom type 30 (C^+) with the atom types 1 (sp^3 carbon), 5 (hydrogen), 22 (cyclopropane carbon) and 56 (cyclobutane carbon) had to be developed. This was done on the basis of the experimental heats of formation[6] and, in part, the geometries of 44 aliphatic and alicyclic carbocations including cyclopropyl, cyclobutyl and cyclopentyl cations (Figure 1) and resulted 94 cation parameters for MM3.

Methods

In all cases where the starting parameters were generated by calculations, we used force field methods and proceeded as follows: After a model cation had been chosen, this cation was optimized using the conformational search program HUNTER[7] in connection with MM2[3a] and the parameter set UNICAT2.[3b-d] Then a series of perturbations of the structural unit to be parametrized (bond length, bond angle or torsion angle) was carried out, while all other structural data were held constant. Subsequently, the differences of the heats of formation of the perturbed structures as calculated with MM2 and MM3 were subjected to an iteration procedure based on the program PAPQMD[8] (bond lengths, bond angles), or a regression analysis according to Hopfinger and Pearlstein[9] (torsion angles). To simplify the iteration procedure and the regression analysis, respectively, all parameters were determined one by one, beginning with the parameters of lowest complexity (bond lengths), and ending with the parameters of highest complexity (torsion angles).

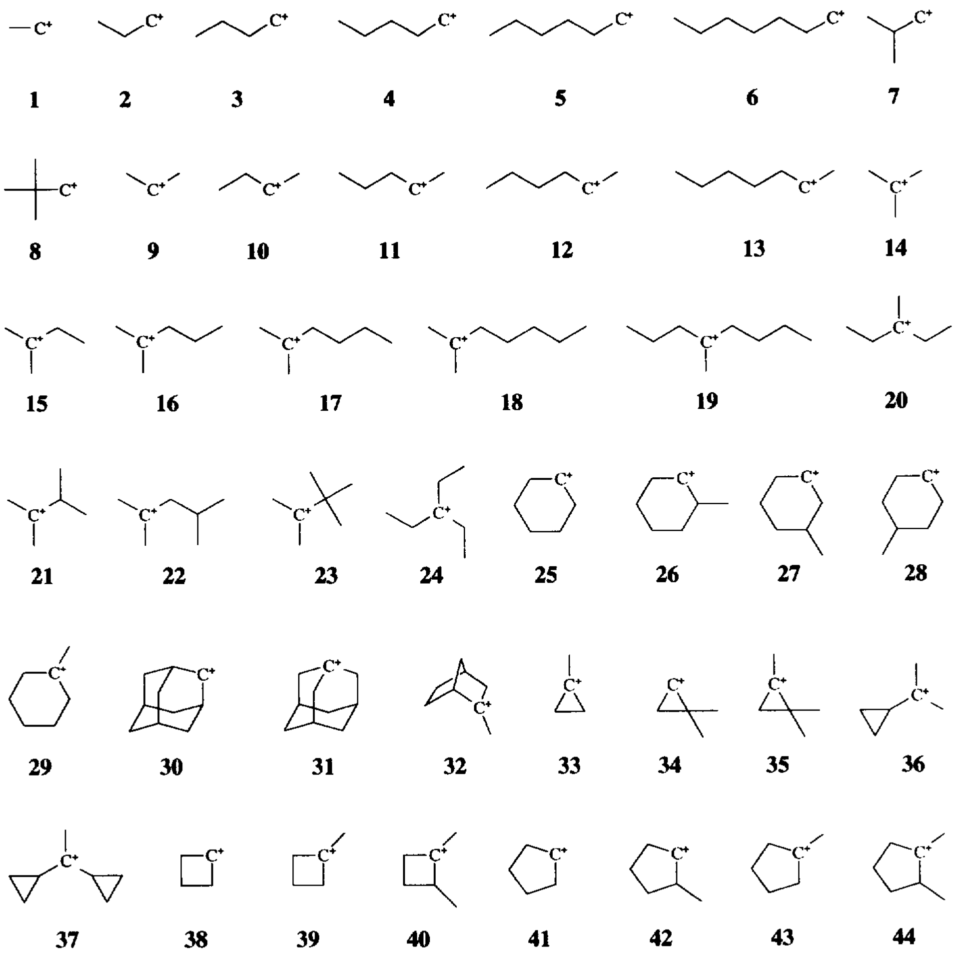


Figure 1. Reference cations for the parametrization of MM3

Concerning the model cations, three cases had to be distinguished and treated differently: (1) The model cation contained only one unknown parameter, i.e. the parameter to be determined. In this case the cation could be used as such. This was also true for cases, where the parameter to be determined was present several times but could be perturbed independently. (2) The model cation contained more than one unknown parameter, including the parameter to be determined. In this case the constants of all additional unknown parameters were set to zero in order to eliminate their influence in both MM2 and MM3. Albeit only correct for parameters with eventually identical constants in both force fields, the results proved acceptable. (3) The model cation contained the parameter to be determined several times, and an independent perturbation was impossible. In this case the structure of the model cation was modified such, that it contained the parameter to be determined only a single time. In general, this was done by substitution.

Illustrative for the three different cases and their treatment is the use of the ethyl cation (**1**) as model cation for the parametrization of (1) the bond lengths 1-30 and 5-30, (2) the bond angles 1-30-5 and 5-30-5, and (3) the torsion angle 5-1-30-5 (Figure 2). In the first case the cations could be treated as such, in the second case the constants of the unknown parameters for the bond angle 5-30-5 and 5-30-1, respectively, were set to zero, and in the third case three of the five hydrogens were replaced by fluorine and the constants of the resulting new torsion angle parameters 5-1-30-11, 11-1-30-5 and 11-1-30-11 set to zero.

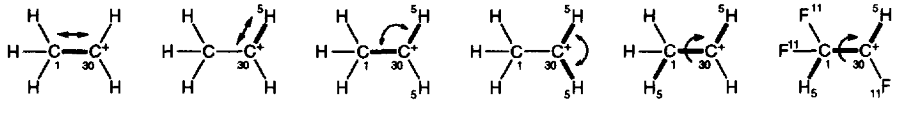


Figure 2. The use of the ethyl cation (**1**) as model cation for the generation of different starting parameters

With the exception of the bond lengths 1-30 (cyclopentane)[4b,10] and 30-56 (cyclobutane),[11] which were taken from ab initio calculations, the starting values for the missing parameters were either developed from parameters of similar atom type combinations as described by Schnur,[12] or taken from MMX.[13] The starting parameters for the out of plane angles were taken from UNICAT2.[3b-d] After the first parameter set was complete, all parameters were optimized by „trial and error" until the fit of the calculated and experimental heats of formation of the 44 aliphatic and alicyclic cations given in Figure 1 could no longer be improved. It was only with the 1-adamantyl (**31**),[4b] cyclobutyl (**38**),[11] 1-methylcyclobutyl (**39**)[10] and cyclopentyl cation (**41**)[4b,10] that several parameters were refined with respect to ab initio geometries.

All heats of formation were calculated using a bond energy scheme containing increments for the bonds 1-30, 5-30, 22-30 and 56-30, and correction terms for primary cations and special features like β-branching.[14] The determination of the increments for the bonds 1-30 and 5-30 was based on the averaged heats of formation of all tertiary and secondary cations, respectively, and not only on a single cation like the tert-butyl (**19**) and the sec-propyl cation (**9**), respectively.[15] The increments for the bonds 22-30 and 56-30 were derived analogously using the averaged heats of formation of the cations **33-37** and **38-40**, respectively. To account for stabilizing β-effects, for every carbon atom in β-position of a secondary (tertiary) carbocation 3.0 (1.5) kcal/mol were subtracted.[14] The correction term for primary cations amounted to +5.34 kcal/mol and was chosen such, that the average deviation of the calculated heats of formation of the reference cations (**1-8**) was zero.

All calculations were performed with the conformational search program HUNTER in connection with MM3 and are valid for the conformation of lowest energy, i.e. the global minimum. The cation type (primary, secondary, tertiary) and the number of ß-alkyl substituents are recognized automatically. No changes in the original MM3 program were necessary; only a separate parameter file had to be created.

Results and Discussion

Our final MM3 parameters for aliphatic and alicyclic carbocations are listed in Table 1. The experimental and calculated heats of formation of the reference cations **1-44** are listed in Table 2, and a comparison of selected bond lengths, bond angles and torsion angles of the 1-adamantyl (**31**), cyclobutyl (**38**), 1-methylcyclobutyl (**39**) and cyclopentyl cation (**41**) as determined with MM3 and ab initio calculations is given in Table 3.

Table 1. MM3 Parameters for Carbocations

Ring	Atom types	Torsional angle constants			Ring	Atom types	Torsional angle constants		
		V_1	V_2	V_3			V_1	V_2	V_3
	1 1 1 30	0.085	0.160	-0.070		5 30 56 5	0.050	0.000	0.220
	5 1 1 30	-0.040	0.077	0.141		5 30 56 56	0.000	0.000	0.250
	1 1 30 1	0.013	0.043	0.104		56 1 30 5	0.000	0.000	0.250
	1 1 30 5	-2.500	0.026	0.956	4	30 56 56 56	0.000	0.000	5.000
	5 1 30 1	-0.054	0.252	0.079	4	56 30 56 56	0.000	0.000	5.000
	5 1 30 5	1.070	2.090	-0.510		1 1 22 30	0.000	0.000	0.300
5	1 1 1 30	2.200	1.100	1.650		5 1 22 30	0.000	0.000	0.300
5	1 1 30 1	1.000	1.500	-4.000		1 22 22 30	0.200	0.270	0.093
	1 1 56 30	0.150	0.150	0.080		5 22 22 30	0.200	0.270	0.093
	5 1 56 30	0.000	0.000	0.300		22 22 22 30	0.200	0.270	0.093
	1 56 56 30	0.150	0.150	0.080		30 1 22 1	0.000	0.000	0.300
	5 56 56 30	0.000	0.000	0.300		30 1 22 5	0.000	0.000	0.300
	30 56 56 56	0.150	0.150	0.080		30 1 22 22	0.000	0.000	0.300
	30 1 56 1	0.150	0.150	0.080		22 1 1 30	0.150	0.150	0.080
	30 1 56 5	0.000	0.000	0.300		1 1 30 22	0.250	0.050	0.400
	30 1 56 56	0.150	0.150	0.080		5 1 30 22	0.050	0.000	0.320
	30 1 1 56	0.150	0.150	0.080		22 1 30 22	0.250	0.050	0.400
	1 1 30 56	0.250	0.050	0.400		1 22 30 22	0.000	3.300	0.000
	5 1 30 56	0.050	0.000	0.320		5 22 30 22	0.000	6.000	0.000
	56 1 30 56	0.250	0.050	0.400		22 22 30 22	0.500	6.000	0.985
	56 30 56 1	0.050	0.050	0.300		1 22 30 1	0.150	0.400	0.150
	56 30 56 5	0.050	0.000	0.320		5 22 30 1	0.500	6.000	0.000
	56 30 56 56	0.250	0.050	0.400		22 22 30 1	0.000	4.000	0.000
	1 30 56 1	0.100	-4.150	0.100		22 1 30 1	0.250	0.050	0.400
	1 30 56 5	0.050	1.000	0.320		1 22 30 5	0.000	0.150	0.150
	1 30 56 56	0.250	0.050	0.400		5 22 30 5	0.000	6.000	1.000
	56 1 30 1	0.250	0.050	0.400		22 22 30 5	0.000	0.500	0.000
	5 30 56 1	0.000	0.000	0.250		22 1 30 5	0.000	0.000	0.250

Ring	Atom types	Bond length constants		Atom types	Out of plane constants	Atom types	Heat of formation increments (kcal/mol)
		k_s	r_o		k_Φ		
	1 30	7.455	1.471	30 1	0.500	1 30	65.976
5	1 30	9.500	1.439	30 5	1.500	5 30	74.623
	30 56	7.400	1.435	30 22	0.500	22 30	47.510
	5 30	7.516	1.085	30 56	0.500	30 56	67.130
	22 30	7.000	1.400				

Ring	Atom types	Bond angle constants		Ring	Atom types	Bond angle constants	
		k_Φ	Φ_o			k_Φ	Φ_o
	1 1 30	0.050	109.540		56 30 56	2.000	120.000
	5 1 30	0.835	109.500	4	56 30 56	2.000	107.000
	1 30 1	2.299	120.000	4	56 56 30	2.000	72.000
	1 30 5	2.277	120.000		1 30 22	0.450	120.000
	5 30 5	0.527	119.000		1 22 30	0.450	116.000
5	1 1 30	2.800	105.600		5 30 22	0.572	120.000
5	1 30 1	2.800	105.700		5 22 30	0.450	120.000
	1 30 56	2.000	120.000		30 1 22	0.450	109.500
	1 56 30	0.520	109.500		30 22 22	0.450	120.000
	5 30 56	2.149	109.500		22 30 22	0.450	120.000
	5 56 30	0.520	109.500	3	22 30 22	0.299	70.000
	30 1 56	0.520	109.500	3	22 22 30	0.299	92.000
	30 56 56	0.520	109.500				

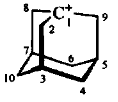
Table 2. Experimental and Calculated Heats of Formation of **1**-**44**

No	Carbocation	Type	ΔH_f°exp[a] (kcal/mol)	ΔH_f°calc (kcal/mol)	$\Delta\Delta H_f^\circ$ (kcal/mol)	β-Alkyl branches[b]
1	ethyl	prim	215.6	217.7	+ 2.1	
2	1-propyl	prim	211	207.1	− 3.9	
3	1-butyl	prim	203	201.4	− 1.6	
4	1-pentyl	prim	194	195.7	+ 1.7	
5	1-hexyl	prim	191	190.0	− 1.0	
6	1-heptyl	prim	183	184.3	+ 1.3	
7	*iso*-butyl	prim	199	198.5	− 0.5	
8	2,2-dimethyl-1-propyl	prim	190	192.0	+ 2.0	
9	2-propyl	sec	190.9	189.5	− 1.4	0
10	2-butyl	sec	183	179.4	− 3.6	1
11	2-pentyl	sec	175	173.7	− 1.3	1
12	2-hexyl	sec	168	168.0	± 0.0	1
13	2-heptyl	sec	162	162.3	+ 0.3	1
14	*tert*-butyl	tert	165.8	163.5	− 2.3	0
15	2-methyl-2-butyl	tert	158	156.8	− 1.2	1
16	2-methyl-2-pentyl	tert	152	151.1	− 0.9	1
17	2-methyl-2-hexyl	tert	147	145.4	− 1.6	1
18	2-methyl-2-heptyl	tert	139	139.7	+ 0.7	1
19	4-methyl-4-octyl	tert	133	133.2	+ 0.2	2
20	3-methyl-3-pentyl	tert	152	150.4	− 1.6	2
21	2,3-dimethyl-2-butyl	tert	150	151.6	+ 1.6	2
22	2,4-dimethyl-2-pentyl	tert	148.4	144.3	− 4.1	1
23	2,3,3-trimethyl-2-butyl	tert	144.5	147.7	+ 3.2	3
24	3-ethyl-3-pentyl	tert	147.7	144.2	− 3.5	3
25	cyclohexyl	sec	175	178.2	+ 3.2	2
26	2-methyl-cyclohexyl	sec	169	167.8	− 1.2	3
27	3-methyl-cyclohexyl	sec	173	170.9	− 2.1	2
28	4-methyl-cyclohexyl	sec	172	171.0	− 1.0	2
29	1-methyl-cyclohexyl	tert	157	156.9	− 0.1	2
30	2-adamantyl	sec	168	173.5	+ 5.5	4
31	1-adamantyl	tert	159	165.9	+ 6.9	3
32	2-methyl-2-norbornyl	tert	171	174.0	+ 3.9	3
33	1-methyl-cyclopropyl	tert	218	218.0	± 0.0	0
34	2,2-dimethyl-cyclopropyl	sec	213	213.0	± 0.0	2

Table 2. Continued

No	Carbocation	Type	ΔH_f°exp[a] (kcal/mol)	ΔH_f°calc (kcal/mol)	$\Delta\Delta H_f$° (kcal/mol)	β-Alkyl branches[b]
35	1,2,2-trimethyl-cyclopropyl	tert	193	193.0	± 0.0	2
36	dimethylcyclopropylcarbinyl	tert	179	178.8	− 0.2	2
37	methyldicyclopropylcarbinyl	tert	200	200.0	± 0.0	4
38	cyclobutyl	sec	225.1	225.0	± 0.0	1
39	1-methyl-cyclobutyl	tert	193	193.0	± 0.0	1
40	1,2-dimethyl-cyclobutyl	tert	182	182.0	± 0.0	2
41	cyclopentyl	sec	191.4	191.8	+ 0.4	2
42	2-methyl-cyclopentyl	sec	179	180.1	+ 1.1	3
43	1-methyl-cyclopentyl	tert	167	164.9	− 2.1	2
44	1,2-dimethyl-cyclopentyl	tert	158	158.8	+ 0.8	3

(a) Ref 6. (b) No data quantifying an eventual stabilization of primary cations by β-alkyl branching exist.



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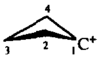

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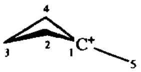

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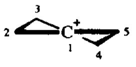

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Table 3. Selected Structural Data of **31**, **38**, **39** and **41** as Determined by MM3 and ab initio Calculations

Carbocation	Bond lengths (Å)			Bond and Torsion angles (°)		
		MM3	ab initio		MM3	ab initio
1-adamantyl (**31**)[a]	C1-C2	1.479	1.448	C2-C1-C9	118.0	118.1
	C2-C3	1.548	1.616	C1-C2-C3	98.2	98.1
	C3-C4	1.545	1.525	C2-C3-C4	109.3	108.3
	out of plane distance of C^+: MM3: 0.21 Å, X-ray:[e] 0.21 Å					
cyclobutyl (**38**)c[b]	C1-C2	1.423	1.424	C4-C1-C2	111.4	112.7
	C1-C3	1.698	1.649	C2-C3-C4	96.9	92.1
	C2-C3	1.571	1.647	C1-C2-C3	68.9	64.5
				C1-C2-C3-C4	−26.0	f
1-methylcyclobutyl (**39**)[c]	C1-C2	1.432	1.435	C1-C2-C3	69.9	68.2[g]
	C1-C3	1.715	1.723	C2-C3-C4	94.7	f
	C2-C3	1.558	1.625	C4-C1-C2	106.4	f
	C1-C5	1.472	1.493	C1-C2-C3-C4	−30.7	f
cyclopentyl (**41**)[d]	C1-C2	1.447	1.439	C1-C2-C3	105.6	105.6
	C2-C3	1.535	1.538	C2-C3-C4	102.5	f
	C3-C4	1.523	1.534	C5-C1-C2	110.5	105.7
				C5-C1-C2-C3	−11.6	−10.9

For ab initio data, see (a) ref 4b, (b) ref 11, (c) ref 10, (d) ref 4b,10. (e) For X-ray data, see ref 16. (f) No data published. (g) Calculated from the bond lengths given in ref 10.

In general, the experimental and calculated heats of formation agree well (Table 2). Exceptions are cations with strong hyperconjugative interactions (**30**, **31**, **32**), whose calculated heats of formation are distinctly too high (+5.5 (**30**), +6.9 (**31**), +3.9 kcal/mol (**32**)). In all other cases, the largest deviations are 3.9 kcal/mol for primary cations (**2**), 3.6 kcal/mol for secondary cations (**10**), and 4.1 kcal/mol for tertiary cations (**22**). Especially the fit of the heats of formation of small ring carbocations (**33-44**) is nearly perfect. This is due to the fact that MM3 differentiates between three-, four- and five-membered rings and uses a parameter set which is extented enough to cover all pecularities.

The constants of the out of plane angles were chosen such, as to reproduce geometries as well as possible. For example, the tert-butyl cation (**14**) was calculated to be planar, as has been found in the crystal state[17] and by ab initio calculations.[18] More significantly, the out of plane distance of the cationic center and the bond angles of the 1-adamantyl cation (**31**), as determined by an X-ray analysis[16] and ab initio calculations,[4b] respectively, were correctly described, as was the nonplanarity of the cyclobutyl (**38**)[11,19] and the 1-methylcyclobutyl cation (**39**)[10,20]. While the elongation of the bond C2-C3 in **31**, **38** and **39** could not be reproduced, the cyclopentyl cation (**41**) was found to be chiral (C_2 symmetry), as shown by ab initio calculations[4b,10] (Table 3).

Summary

Based on the heats of formation and, in part, the geometries of 44 reference carbocations, a MM3 parameter set for aliphatic and alicyclic carbocations has been developed, which includes parameters for three-, four- and five-membered rings. The experimental heats of formation are reproduced well, except for cations with strong hyperconjugative interactions. In these cases, the heats of formation are calculated too high, while the bonds taking part in the hyperconjugation are calculated too short. For the description of all other aliphatic and alicyclic carbocations the present parameter set proved valid. All calculations were done with the conformational search program HUNTER, which analyses the cation type (primary, secondary, tertiary) and the number of ß-alkyl substituents automatically.

Acknowledgment. This work was supported by the Fonds der Chemischen Industrie.

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(*Received in Germany* 8 *December* 1996; *accepted* 30 *December* 1996)