

Figure 9. Zwitterion-tricyclic route for 2-methylthiophene; labels as in Figure 3.

major difference is the unfavorable upward shift of the energy minimum of intermediate I'_1 for the forward reaction and the steeper slope for the backward reaction. A comparison of both mechanisms clearly favors the internal cyclization-isomerization route. This is in agreement with conclusions from experiment.¹⁰ For 2-methylthiophene the situation for the internal cyclization-isomerization mechanism (Figure 8) is closer to the one in parent thiophene than to the one in 2-cyanothiophene. This means it is less favorable than in 2-cyanothiophene. The barrier of TS_{0b} is slightly higher than for TS_{0a} , and the first singlet and the ground state are more separated in the region of TS_1 . Also the energy of TS_1 is already substantially higher than the energy of I_3 . For the zwitterion-tricyclic route of this compound (Figure 9) the curves are again similar to the one in Figures 4 and 7. The efficiency of this mechanism for this compound is enhanced compared to the one for 2-cyanothiophene due to the closeness of the first excited singlet and ground-state surfaces in the vicinity of I'_1 . Also

there is a rather flat profile of the barrier for backward and forward reaction which could mean an equalization in probability for the system to move either way. Altogether, however, we find that the forward reaction is also not very efficient in this case.

Conclusion

We have studied the reaction mechanism of thiophene and two substituted thiophenes, 2-cyanothiophene and 2-methylthiophene, with respect to permutation of the ring atoms. The two most important mechanisms are the internal cyclization-isomerization route and the zwitterion-tricyclic route. It is found that the internal cyclization-isomerization route consists of a sequence of small geometric rearrangements which can either lead to the product or return to the reactant in three regions close to intermediates I_3 and I_{0a} and transition structure TS_1 . From the three systems 2-cyanothiophene is clearly favoring this route for formation of 3-cyanothiophene. But even in this case, the overall efficiency of product formation should be much less than for the internal cyclization-isomerization route of 2-cyanopyrrole to 3-cyanopyrrole,²³ due to the much larger energy gap between S_1 and S_0 in the vicinity of intermediate I_{1b} . The zwitterion-tricyclic route shows a rather large geometric rearrangement in the initiation step, but no branching. Altogether it seems less favorable than the other mechanism. It is conceivable, however, that this mechanism is dominant for 2-methylthiophene. From this investigation no clear decision in favor of the zwitterion-tricyclic mechanism can be made. The latter mechanism involves significant d orbital participation. Without d orbitals no intermediate of the type I'_0 could be found. It is conceivable that this mechanism will be favored in solution with polar solvents.

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AM1, PM3, and MNDO Calculations of Radical Formation Energies in the Gas Phase and in Solution

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The results of the quantum-chemical calculations of radical formation energies from simple organic molecules in gas phase and in dielectric polarizable medium using AM1 and MNDO Hamiltonians with original MNDO and recent MNDO-PM3 parametrizations in combination with self-consistent reaction field procedure are in satisfactory quantitative agreement with experimental data. A solvent-assisted merostabilization effect is observed only in the case of captodative radicals.

The formation of organic radicals is an essential part of many important reactions. The stabilization of radicals by substituents in the molecule, and by the solvent, has therefore been the focus of attention for many years. A specific merostabilization effect at a carbon radical center connected simultaneously with an electron-donor and an electron-acceptor substituent was defined by several au-

thors some time ago.¹⁻⁴ However, quantum-chemical studies at different levels of sophistication did not indicate any substantial additional stabilization in these so-called

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Table I. The AM1, PM3, and MNDO Calculated Heats of Formation ΔH_f° of Some Organic Molecules and Respective Carbon Radicals in Gas Phase and in a Dielectric Medium of $\epsilon = 80$

compound	r_o , Å	ΔH_f° , kcal/mol					
		AM1		PM3		MNDO	
		$\epsilon = 1$	$\epsilon = 80$	$\epsilon = 1$	$\epsilon = 80$	$\epsilon = 1$	$\epsilon = 80$
1. CH_3OH	2.39	-58.03	-58.51	-51.88	-53.12	-57.35	-58.58
2. CH_2OH	2.17	-26.52	-28.06	-23.49	-24.78	-31.70	-33.21
3. $\text{CH}_3\text{CH}_2\text{OH}$	2.76	-64.21	-65.24	-58.72	-59.61	-62.99	-63.71
4. CH_3CHOH	2.61	-36.67	-37.82	-35.23	-36.04	-42.97	-43.74
5. $(\text{CH}_3)_2\text{CHOH}$	3.08	-69.54	-70.25	-65.76	-66.41	-65.41	-65.96
6. $(\text{CH}_3)_3\text{COH}$	2.96	-43.71	-44.33	-44.85	-44.36	-51.43	-51.92
7. $(\text{CH}_3)_3\text{COH}$	3.33	-71.60	-72.02	-71.28	-71.74	-64.27	-64.65
8. $(\text{CH}_3)_2(\text{CH}_2)\text{COH}$	3.25	-34.28	-34.78	-33.96	-34.44	-32.57	-33.04
9. CH_3OH	2.46	19.28	15.29	23.29	18.39	19.50	16.23
10. CH_2CN	2.46	57.31	52.62	62.00	56.21	53.49	49.13
11. CH_3COO^-	2.60	-115.41	-180.29	-119.65	-185.42	-110.02	-174.87
12. CH_2COO^-	2.45	-76.70	-149.59	-81.29	-154.78	-76.54	-149.43
13. $(\text{CH}_2\text{OH})_2$	2.88	-110.08	-111.56	-98.20	-99.57	-106.10	-107.26
14. $\text{CH}_2(\text{OH})\text{CHOH}$	2.77	-78.79	-82.89	-74.66	-75.57	-85.69	-87.79
15. $\text{CH}_2(\text{CN})\text{OH}$	2.76	-23.94	-26.33	-14.49	-19.01	-22.45	-26.88
16. $\text{CH}(\text{CN})\text{OH}$	2.66	7.09	-0.96	12.75	3.00	-1.07	-8.78

Table II. The AM1, PM3, and MNDO Calculated Experimental Bond Dissociation Energies of Some Organic Molecules in Gas Phase and in Aqueous Solution^a

compound	bond dissociation energy, kcal/mol								
	$\epsilon = 1$				$\epsilon = 80$				
	AM1	PM3	MNDO	exp ^b	exp ^c	AM1	PM3	MNDO	exp ^b
1. $\underline{\text{C}}\text{H}_3\text{OH}$	91.3	88.2	84.9	91.9 ± 1.7	94.0 ± 2.0	91.2	88.7	85.2	90.9 ± 1.7
2. $\text{C}\underline{\text{H}}_3\text{CH}_2\text{OH}$	87.3	83.3	79.2	92.2 ± 2.2	93.0 ± 1.0	87.2	83.2	79.7	91.2 ± 2.2
3. $(\text{CH}_3)_2\underline{\text{C}}\text{HOH}$	85.6	81.3	73.8	89.3 ± 1.7	91.0 ± 1.0	85.7	81.9	73.8	88.3 ± 1.7
4. $(\text{CH}_3)_3\underline{\text{C}}\text{OH}$	97.1	97.1	91.5	99.1 ± 2.0	100.0 ± 2.0	97.0	97.1	91.4	98.1 ± 2.0
5. $\underline{\text{C}}\text{H}_3\text{CN}$	97.8	98.5	93.8	95.5 ± 1.7	93.5 ± 2.5	97.1	97.6	92.8	94.5 ± 1.7
6. $\underline{\text{C}}\text{H}_3\text{COO}^-$	98.5	97.3	93.6	91.9 ± 1.7		90.7	90.4	85.2	90.9 ± 1.7
7. $(\underline{\text{C}}\text{H}_2\text{OH})_2$	91.1	83.3	80.2	89.6 ± 2.2		88.4	83.8	79.5	88.6 ± 2.2
8. $\underline{\text{C}}\text{H}_2(\text{CN})\text{OH}$	90.8	87.1	81.4			85.1	81.8	77.9	

^aC-H bond is dissociated at the underlined carbon atom. $\Delta H_f^\circ = 59.8$ kcal/mol was used for the H atom both in gas phase and in dielectric medium. ¹Ref. 11. ²Ref. 20.

captodative radicals if compared to the energies of formation of the corresponding dihomosubstituted species (cf. ref 5 references therein). A recent study at the ROHF 4-31G level⁶ confirms this conclusion in general, since only a small effect was obtained for some substituted methyl radicals. Some years ago we proposed on the basis of INDO UHF calculations including reaction field perturbation, a solvent-assisted merostabilization mechanism,⁵ i.e. the additional stabilization of captodative radicals by a polarizable environment. A similar effect was observed by using AM1⁷ and MNDO⁸ Hamiltonians in combination with self-consistent reaction field (SCRf) procedure.⁹ Some controversial ideas based on the experimental measurements of radical formation energies in condensed media have been published recently^{10,11} as no substantial radical stabilization in polarizable solvent was found. However, these experimental data do not refer to captodative radicals but to simpler mono- or disubstituted carbon radicals. Therefore, in order to validate our previous theoretical work it was important to perform the

calculations of the radical formation energies in solution for the compounds for which the recent experimental data¹¹ are available.

We have chosen again the SCRf LCAO MO method, which in combination with AM1 Hamiltonian has given a good quantitative description of the tautomeric equilibrium constants of various heterocyclic compounds.^{12,13} MNDO and MNDO-PM3¹⁴ parametrizations were also used for comparative calculations. The essence of the SCRf method is summarized in the use of reaction field modified Hamiltonian H' in the Schroedinger equation

$$H' = H_o + \Gamma \langle \Phi | \mu | \Phi \rangle \mu \quad (1)$$

where H_o is the Hamiltonian for the isolated molecule, Φ is its wavefunction, and μ is the dipole moment operator. The factor Γ is the reaction field tensor which is a function of the dielectric properties of the medium and the shape of the molecule. In the case of spherical cavity for the solute molecule in solution this factor has the following simple form

$$\Gamma = \frac{2(\epsilon - 1)}{(2\epsilon + 1)r_o^3} \quad (2)$$

where ϵ denotes the macroscopic dielectric permittivity of solvent and r_o is the cavity radius. The electronic energy

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Table III. The AM1, PM3, and MNDO Calculated Dipole Moments of Some Organic Molecules in Different Media

compound	dipole moment, D					
	AM1		PM3		MNDO	
	$\epsilon = 1$	$\epsilon = 80$	$\epsilon = 1$	$\epsilon = 80$	$\epsilon = 1$	$\epsilon = 80$
1. CH ₃ OH	1.621	1.753	1.487	1.593	1.479	1.595
2. CH ₂ OH	1.385	1.515	1.278	1.402	1.388	1.496
3. CH ₃ CH ₂ OH	1.685	1.836	1.561	1.684	1.400	1.511
4. CH ₃ CHOH	1.554	1.671	1.384	1.500	1.405	1.522
5. (CH ₃) ₂ CHOH	1.691	1.831	1.574	1.689	1.434	1.545
6. (CH ₃) ₂ COH	1.412	1.546	1.308	1.404	1.326	1.426
7. (CH ₃) ₃ COH	1.618	1.768	1.539	1.652	1.464	1.584
8. (CH ₃) ₂ (CH ₂)COH	1.521	1.698	1.437	1.566	1.431	1.546
9. CH ₃ CN	2.894	3.650	3.206	3.722	2.630	3.022
10. CH ₂ CN	2.721	3.422	3.004	3.809	2.672	3.313
11. (CH ₂ OH) ₂	2.025	2.816	2.049	2.533	0.003	2.860
12. CH ₂ (OH)CHOH	0.435	2.750	1.385	1.885	0.361	2.678
13. CH ₂ (CN)OH	2.189	4.027	2.525	4.771	2.287	4.135
14. CH(CN)OH	4.177	5.155	4.556	5.667	4.147	5.051

of the solute molecule is then found by the solution of the resulting Fock equations until self-consistency of electronic field is achieved.^{15,16}

The results of the AM1 and MNDO calculations of heats of formation of eight compounds and the respective carbon radicals resulting from the following homolytic bond cleavage reaction



are given in Table I. The calculations refer to the isolated forms of molecules and radicals, and as in the isotropic polarizable medium with $\epsilon = 80$.¹⁷ Full geometry optimization of every species was carried out in both cases. To be able to calculate the bond dissociation energies, the restricted Hartree-Fock open-shell (ROHF) method was used for the radical species. The calculated bond dissociation energies (BDE), as compared to the experimental data, are given in Table II. For obvious reasons it is not possible to calculate the heat of formation of the hydrogen atom in solution using the SCRF method. The indirectly estimated experimental value of $\Delta H_f^\circ = 59.8$ kcal/mol obtained on the basis of data given in ref 11 was used instead. The results of AM1 calculations of BDE in aqueous solution are in a remarkably good agreement with the data obtained by the experimental photoacoustic calorimetry measurements for seven simple carbon radicals (cf. also Figure 1a). The numerical agreement between MNDO calculated and experimental heats is much worse, but the general tendency of electronic effects on the dissociation energies is described properly (Figure 1b). The quality of MNDO-PM3 results as compared with the experimental data is intermediate of AM1 and MNDO results. For some compounds (methanol, *tert*-butyl alcohol, acetate anion) the calculated MNDO-PM3 heats of formation coincide with experimental values in the limits of experimental error. However, for other compounds the agreement is substantially worse. The overall standard deviation of MNDO-PM3 results from experimental heats of formation is $\sigma_{PM3} = 4.3$ kcal/mol, whereas the corresponding standard deviation of AM1 results $\sigma_{AM1} = 2.0$ kcal/mol, i.e. just inside the average estimated experimental error (cf. Table II). Thus our results indicate that the AM1 parametrization is superior of the MNDO-PM3

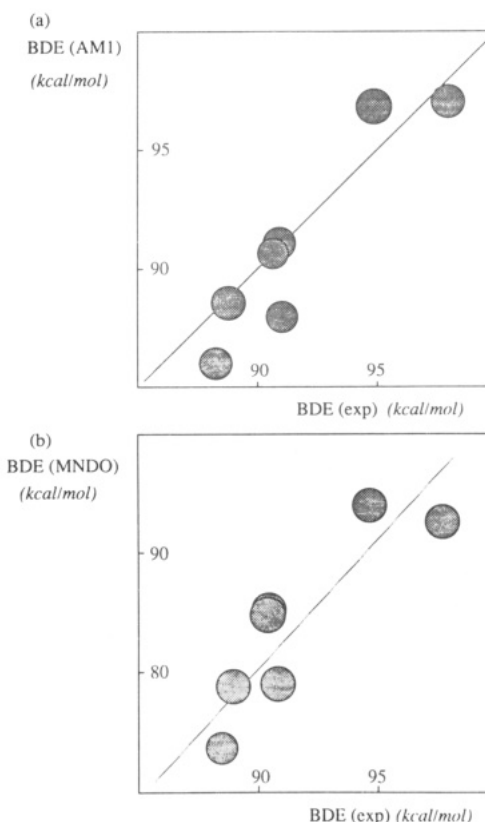


Figure 1. The dependence between AM1 (a) and MNDO (b) calculated and experimental bond dissociation energies in solution. For the AM1 results the line has unit slope and intercepts the origin of coordinates. For the MNDO results the line corresponds to the least-squares fit.

parametrization for the ROHF calculation of carbon radical formation energies.

It should be mentioned that the bond dissociation energies for most compounds are rather insensitive to the solvent polarity—a conclusion which follows from both the experimental and quantum-chemical data. However, in the case of the captodative cyanohydroxymethyl radical a substantial solvent stabilization is predicted by both AM1 and MNDO SCRF calculations resulting also in a corresponding significant change of the C-H bond dissociation energy of cyanomethanol in a different dielectric environment. Unfortunately no experimental data for this compound is available, but the overall agreement of the computational results with experiment for the other compounds sets a sound basis for this prediction. A significant difference between the BDE for acetate ion in gas phase

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(17) The spherical cavity was assumed for solute molecules and radicals in solution. The cavity radius was estimated on the basis of additive bond refractions of molecules as described in ref 9.

and in solution that is due to the small change in molecule size (which is much more important for charged species because of the Born ionic solvation term in total energy) can be noticed. However, this is not observed experimentally¹¹ (cf. Table II), which indicates either that there is practically no change in the volume of the acetate ion due to the C-H bond cleavage or the gas-phase experiment is in error. It is worth while to note in this connection that the AM1 prediction for the solution is in a very good agreement with experimental BDE, whereas the data for the isolated species are more inconsistent (difference between calculated and experimental BDE is 6.6 kcal/mol).

As mentioned before,^{5,9} the additional stabilization of the captodative radicals in solution is supported by the increase of their dipole moments. However, the data presented in Table III on the calculated dipole moments of molecules and radicals do not stress the specifically enhanced dipole moment change of cyanohydroxymethyl radical in comparison with other species.¹⁸ Remarkably enough, the largest change (by 84% as calculated using AM1 parametrization) is obtained for the closed-shell cyanomethanol molecule. The large increase of AM1,

(18) Remarkably enough, the largest change (by 84% as calculated using AM1 parametrization) was obtained for the closed-shell cyanomethanol molecule. The large increase of the AM1, PM3, and MNDO calculated dipole moments of the radical resulting from the C-H bond dissociation of ethylene and MNDO calculated dipole moment of ethylene glycol itself are mainly due to conformational change in these species (from trans conformation of OH groups in gas phase to gauche conformation in solution), but not to the electron redistribution in this radical.

PM3, and MNDO calculated dipole moments of the radical resulting from the C-H bond dissociation of ethylene glycol and MNDO calculated dipole moment of ethylene glycol itself are mainly due to the conformational change in these species (from trans conformation of OH groups in gas phase to gauche conformation in solution), but not to the electron redistribution in this radical. Altogether the calculated dipole moments of the closed-shell molecules are higher than the corresponding radicals (cf. Table III). In part this is caused by significant geometry changes at the carbon atom from a nearly tetrahedral configuration in the molecule to a planar configuration in the radical.

In conclusion, our results show that the AM1 SCRF ROHF method describes satisfactorily the homolytic dissociation energies (however, not the dissociation paths., cf. ref 19) of carbon-hydrogen bonds in polar solvents. More direct experimental data on bond cleavage energies are needed to validate the prediction of the merostabilization of captodative radicals in these media.

Registry No. H₃COH, 67-56-1; HO·CH₂, 2597-43-5; H₃CC-H₂OH, 64-17-5; H₃CC·CHOH, 2348-46-1; (H₃C)₂CHOH, 67-63-0; (H₃C)₂C·OH, 5131-95-3; (H₂C)₂COH, 75-65-0; (CH₃)₂(C·H₂)COH, 5723-74-0; CH₃CN, 75-05-8; ·CH₂CN, 2932-82-3; H₃CCO₂⁻, 71-50-1; H₂C·CO₂⁻, 19513-45-2; (CH₂OH)₂, 107-21-1; H₂C·(OH)CHOH, 36730-46-8; H₂C·(CN)OH, 107-16-4; (CN)C·HOH, 27924-05-6.

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Electrolytic Reactions of Fluoro Organic Compounds. 7.¹ Anodic Methoxylation and Acetoxylation of 2,2,2-Trifluoroethyl Sulfides. Preparation of Highly Useful Trifluoromethylated Building Blocks

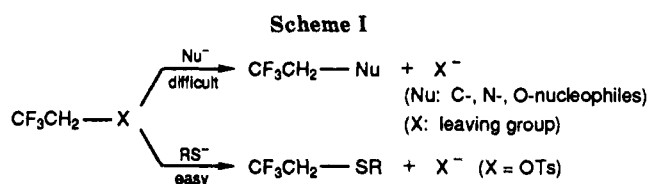
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Anodic methoxylation and acetoxylation of 2,2,2-trifluoroethyl sulfides and the corresponding nonfluorinated sulfides were comparatively studied. It was found that a trifluoromethyl group remarkably promoted anodic substitution and methoxy and acetoxy groups were introduced adjacent to the trifluoromethyl group of the sulfides. Longer perfluoroalkyl groups also promoted these anodic substitutions. These products were shown to be highly useful building blocks for the synthesis of fluoro organic compounds.

Recently, a great deal of interest has been focused on trifluoromethylated compounds because of their possible biological activities.² However, methods for their synthesis are limited in many cases.³ For example, nucleophilic substitution hardly occurs at the position α to a trifluoromethyl group due to its strong electron-withdrawing effect,^{4,5} although sulfur nucleophiles undergo such sub-



stitution efficiently (Scheme I).⁶ Therefore, the realization of substitution at the α -position is one of the most important subjects in modern organo fluorine chemistry. Electrochemical reactions have recently been shown to be

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