# Triflic-Acid-Mediated Polycondensation of Carbonyl Compounds with Aromatic Hydrocarbons – A Theoretical Study

Alfredo López Lira, Mikhail G. Zolotukhin, Lioudmila Fomina,
Sergei Fomine*

Mono- and diprotonated reaction intermediates involved in the acid-catalyzed polyhydroxy-alkylation of aldehydes and ketones of the general formula R_1COR_2, ($R_1 =$ H, CH_3, CF_3 and $R_2 =$ Ph, CH_3, CF_3) with benzene and biphenyl, were studied theoretically at PBE0/aug-cc-PVTZ//PBE0/6-31$+$G** level of theory. The calculations performed for sulfuric acid and TFSA-catalyzed reactions showed that for all studied reactions the enhancement of the reactivity of diprotonated species is not sufficient to compensate for the large positive Gibbs energy of second protonation. An alternative mechanism has been proposed for the reaction between benzene and benzaldehyde in TFSA involving only monoprotonated species.

The low reactivity of carbonyl compounds with electron donating substituents is due to excessive stabilization of monoprotonated species rendering the reaction thermodynamically impossible.
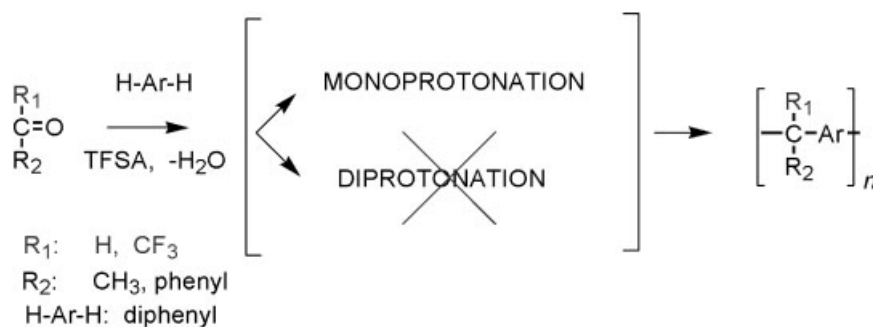
Introduction

Friedel-Crafts aromatic substitution reactions – alkylation and acylation – are some of the most fundamental reactions in organic chemistry, and they have been widely explored in the polymer chemistry.[1,2] It is important to mention that, so far, only traditional types of electrophiles have been used in Friedel-Crafts polymer preparations.

A. L. Lira, M. G. Zolotukhin, L. Fomina, S. Fomine
Instituto de Investigaciones en Materiales, Universidad Nacional Autónoma de México, Apartado Postal 70-360, CU, Coyoacán, México DF 04510, México
E-mail: fomine@servidor.unam.mx

Obviously, the design of monomers bearing new types of electrophilic functional groups is of great importance for the advancement of Friedel-Crafts polymer chemistry.

In this respect, the theory of superelectrophilic activation, suggested by Olah to explain high reactivity of some electrophiles in superacid solutions, presents a promising challenge.[3] Superelectrophiles have since been proposed or studied in numerous superacid-catalyzed reactions.[3–6]

Recently we have found that superacid catalyzed polyhydroxyalkylation reactions of aldehydes and ketones containing electron-withdrawing substituents with non-activated aromatic hydrocarbons adjacent or relatively close to a carbocation center afford linear, high-molecular-weight polymers (Figure 1)[7,8] Thus, simple, practical,
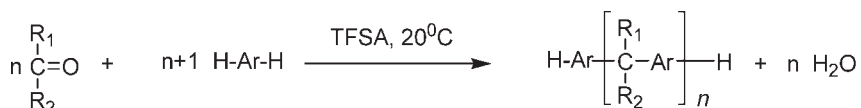
Figure 1. Superacid-catalyzed polyhydroxyalkylation reactions of aldehydes and ketones with non-activated aromatic hydrocarbons. Here, R_1 is H or CF_3; R_2 is CH_3, phenyl or perfluorophenyl; and H–Ar–H is biphenyl, phenyl ether, fluorene, terphenyl, or 4,4'–diphenoxybenzophenone.

metal-free, one-pot reactions of fluorinated aldehydes and ketones with non-activated aromatic hydrocarbons open up wide possibilities for constructing new fluorinated aromatic polymers using commercially available monomers.

It has been shown that the reactivity enhancement of the carbonyl compounds bearing electron-withdrawing groups is due to their lowest unoccupied molecular orbital (LUMO) stabilization.[9] An important question, however, remains open; whether mono- or diprotonated species are responsible for increased reactivity of carbonyl compounds in case of the superacid mediated polycondensation with aromatic hydrocarbons. Although the existence of diprotonated carbonyl molecules in superacids has been proved experimentally[10] the second protonation always occurs at an alternative protonation site (heteroatom or electron rich double bond). Even in the case of the relatively simple reaction between benzaldehyde and benzene in superacid media the nature of active electrophiles is not yet fully understood. Thus, in HSO_3F–SbF_5 mixtures, no dication of benzaldehyde was detected,[11] and, moreover, 4-methoxybenzaldehyde is protonated only at the carbonyl and methoxy groups.[12] Evidently, diprotonation of carbonyl compounds having electron-withdrawing substituents is even more difficult. In a recent paper[13] an alternative explanation of enhanced reactivity of benzaldehyde with benzene in superacid media was suggested where diprotonated benzaldehyde was no longer considered as the reactive species. However, neither experimental nor theoretical evidence was given to favor this mechanism. All this motivated us to study theoretically the reaction of different carbonyl compounds with aromatic hydrocarbons in trifluorosulfonic (triflic) acid (TFSA) as a model reaction for superacid mediated polycondensation to obtain deeper insight into the nature of the reactive species.

Computational Details and Methods Used

The prediction of reliable reaction energies in solution where ionic species are involved is a challenging task for modern computational chemistry. The model selection was based on its ability to reproduce experimentally determined the pK_a of different acids, since exact pK_a determination implies accurate calculation of the Gibbs energies of solvated ionic species. Density functional theory (DFT), in combination with continuum solvation models, has been proven to be a reliable tool to calculate the pK_a of carboxylic acids with chemical precision comparable with that of CBS, G2 and G3 methods.[14] We applied a modified model described in [14] for the calculations.

The total Gibbs solution energies of all molecules (G_s) were calculated as follows: $G_s = E_s + \Delta G_g$, where E_s is the total electronic energy in solution calculated at PBE0/aug-cc-PVTZ level using PBE0/6-31 + G**[15] solution phase optimized geometry and ΔG_g is the Gibbs energy correction calculated as the difference between the total electronic energy and the Gibbs energy in gas phase estimated at PBE0/6-31 + G** level using PBE0/6-31 + G** optimized geometry. Solution phase optimizations were carried out with the Poisson-Boltzmann solver[16,17] implemented in the Jaguar v 6.0 program,[18] using dielectric constant and the solvent probe radii of 77.4 and 2.60, 101 and 2.19, and 80.4 and 1.40Å for triflic acid, sulfuric acid, and water, respectively. The use of different basis sets for gas and solution state optimization greatly reduces computational times without significant loss of accuracy since the calculation of the Gibbs energy correction (the most time-consuming step) representing only a small part of total energy is calculated using reduced basis set. pK_a was calculated according the Equation (1):

$$pK_a = [G_s(A^-) - G_s(AH) + G_s(H^+)]/1.3644 \qquad (1)$$

where $G_s(A^-)$, $G_s(AH)$ and $G_s(H^+)$ are the Gibbs solution energies of the anion, acid and proton, respectively.[20] Two first terms were calculated according to the method described above. For the proton solvation Gibbs energy in water the experimental value of -269.0 kcal · mol^{-1} was used.[20]

The PBE0 function used for the calculations was proven to outperform the popular B3LYP function in thermochemistry and calculations of the barrier heights.[19] All calculations were carried out with the Jaguar 6.0 suite of programs. Since the PBE0 functional is not implemented directly in Jaguar 6.0 it was defined using following keywords; idft = −1, xhf = 0.25, xexnl9 = 0.75, xcornl9 = 1.0, xcorl4 = 1.0, that corresponds to the definition of PBE0 functional in the original paper[15] as follows: 25% of exact HF exchange, 75% of PBE local and nonlocal exchange functional, Perdew-Wang GGA-II 1991 local correlation functional, and PBE local and nonlocal correlation functional. The PBE0 function used in this work can be reproduced in

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Acid	Theoretical[a)]	Experimental	Absolute Error	
			ΔpK_a	ΔG
				kcal · mol^{-1}
CH$_3$COOH	5.81	4.75[21]	1.06	2.4
CF$_3$SO$_3$H	−13.4	−13.6[22]	0.2	0.5
CF$_3$COOH	−1.10	−0.26[21]	0.84	1.9
HCOOH	3.54	3.77[23]	0.23	0.5

[a)]See Section on Computational Details and Methods Used.

Gaussian 03 package with PBE1PBE or in PC-GAMESS using the DFTTYP = PBE0 keywords, respectively.

Table 1 shows calculated and experimentally available pK_a data of different acids. As seen from the Table 1 the adopted model reproduces the pK_a of selected acids with maximum error of about 1 pK_a unit, which corresponds to the error in the Gibbs energy of 2.4 kcal · mol^{-1}.

Results and Discussion

Monoprotonated Species

Figure 2 and Table 3 show the monoprotonation reactions and the corresponding Gibbs energies of monoprotonation for different carbonyl compounds in TFSA. Table 2 shows the Gibbs solution energies of studied molecules.

Among all tested carbonyl compounds in TFSA mediated polycondensation with biphenyl only **1b** and **1e** did not afford polymers.[8] Benzaldehyde (**1a**) was not tested, however, it is well known that benzaldehyde reacts smoothly with benzene in TFSA at room temperature to give triphenylmethane.[11] It is noteworthy, that **1b**, showing the most negative, and **1e**, the most positive Gibbs protonation energies, do not afford polymers with biphenyl. In the case of hexafluoroacetone (**1e**), the protonation reaction in TFSA is an extremely endergonic process requiring 32.4 kcal · mol^{-1} to generate monoprotonated species. The equilibrium concentration of protonated **1e**

must be extremely low in TFSA explaining its poor reactivity. As seen from Table 3, the Gibbs protonation energies of carbonyl compounds are in line with the electronic properties of substituents. One can order the groups adjacent to carbonyl according to their electron-withdrawing ability as CF$_3$, H, CH$_3$, and Ph based on the monoprotonation reaction energies.

Diprotonated Species

Figure 3 and Table 3 shows the Gibbs reaction energies of second protonation for carbonyl compounds: diprotonation at oxygen (O,O); at oxygen and carbon (O,C); and at oxygen and fluorine (O,F). As can be seen, compared to the first protonation, second protonation is extremely energetically unfavorable.

Even in the case of the most basic carbonyl molecule such as acetophenone (**1b**); the second protonation in TFSA requires 27.1 kcal · mol^{-1} for the formation of the most stable dication. In all cases O,O diprotonated species are clearly less stable compared to O,C or O,F ones. The energy difference between O,O and O,C diprotonated species is about 10 kcal · mol^{-1}. To understand the nature of this difference, one can compare the contributions to the total energy for **3c** and **4c–m**; O,O and O,C diprotonated trifluoroacetophenone **1c**. The total electronic energies difference between **3c** and **4c–m** is −576.8 kcal · mol^{-1} at PBE0/6-31 + G** level, while the nuclear repulsion energy difference is 602.2 kcal · mol^{-1}. The total energies represent a sum of total electronic energy and nuclear repulsion. As seen from this example the destabilization of O,O diprotonated species compared to O,C one is due to additional electrostatic repulsion introduced by two closely located protons.

It is noteworthy that in earlier work on the diprotonation of benzaldehyde[11] a similar conclusion about the relative stability of O,O and O,C diprotonated benzaldehyde was made. According to our calculations the most
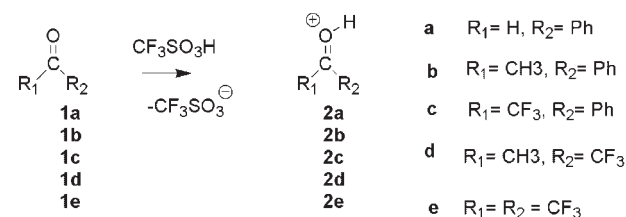

Figure 2. Reactions of protonation of different carbonyl compounds in TFSA with the corresponding Gibbs energies of reaction (kcal · mol^{-1}).

Table 2. Calculated total Gibbs energies (G_s) of reaction intermediates in solution (1 Hartree = 627.509 5 kcal · mol^{-1}).

Table 2. Continued

Molecule	G_{s1} (in TFSA)	G_{s2} (in H_2SO_4)
	Hartree	Hartree
1a	−345.218 292	−345.218 485
1b	−384.479 431	−
1c	−682.072 709	−
1d	−490.549 631	−
1e	−788.130 054	−
2a	−345.621 623	−345.622 345
2b	−384.890 918	−
2c	−682.461 036	−
2d	−490.929 821	−
2e	−788.479 115	−
3a	−345.965 787	−
3b	−385.231 695	−
3c	−682.786 966	−
3d	−491.241 249	−
3e	−788.756 124	−
5d	−491.226 767	−
5e	−788.761 249	−
4a−o	−345.975 009	−
4b−o	−385.241 993	−
4c−o	−682.799 475	−
4a−m	−345.980 084	−
4b−m	−385.248 436	−
4c−m	−682.805 596	−
4a−p	−345.966 180	−
4b−p	−385.238 429	−
4c−p	−682.791 462	−
15o	−501.564 603	−
15m	−501.566 522	−
15p	−501.560 870	−
16b	−771.627 309	−
16c	−1 069.202 364	−
17b	−771.628 020	−
17c	−1 069.202 402	−
6a	−577.550 804	−577.551 344
7a	−577.551 216	−577.550 763
8a	−577.179 488	−577.179 774
9a	−577.577 006	−577.581 222
10a	−577.572 678	−
11a	−501.209 398	−501.209 904
12a	−733.136 505	−733.137 336
13a	−733.150 722	−733.151 651

Molecule	G_{s1} (in TFSA)	G_{s2} (in H_2SO_4)
	Hartree	Hartree
14a	−732.782 868	−732.783 365
19a−m	−577.918 168	−
21m	−733.504 369	−
6b	−847.590 028	−
7b	−847.593 200	−
8b	−847.216 837	−
9b	−847.612 790	−
11b	−771.254 325	−
12b	−1 233.953 543	−
13b	−1 233.967 944	−
14b	−1 233.593 353	−
17b	−771.628 020	−
18b	−771.614 422	−
20b	−1 234.331 833	−
21b	−1 234.315 961	−
19b−m	−847.957 843	−
6c	−1 145.177 803	−
7c	−1 145.190 831	−
8c	−1 144.822 184	−
9c	−1 145.201 106	−
11c	−1 068.834 478	−
12c	−1 531.542 314	−
13c	−1 531.558 207	−
14c	−1 531.195 731	−
17c	−1 069.202 402	−
18c	−1 069.191 534	−
20c	−1 531.919 651	−
21c	−1 531.899 490	−
benzene	−231.972 968	−231.973 061
biphenyl	−462.758 237	−
water	−76.389 897	−76.389 981
CF_3SO_3H	−961.620 691	−
$CF_3SO_3^-$	−961.219 975	−
H_2SO_4	−	−699.974 863
HSO_4^-	−	−699.565 492

stable are O,C-*meta*-diprotonated carbonyl compounds followed by O,C-*ortho* ones with a difference of 3–4 kcal · mol^{-1}. The least stable O,C-diprotonated dications are O,C-*para* ones. This is true for all dications formed from **1a**, **1b** or **1c**. It is interesting to note that, on the basis of NMR spectroscopy, O,C-diprotonated species were

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Table 3. Calculated Gibbs energies[a)] of protonation (ΔG_p) of different molecules in TFSA.

Reaction	ΔG_p
	kcal · mol^{-1}
First protonation	
1a → 2a	−1.6
1b → 2b	−6.8
1c → 2c	7.8
1d → 2d	12.9
1e → 2e	32.4
2d → 5d	65.1
2e → 5e	74.4
11a → 15o	28.8
11b → 15m	27.4
11c → 15p	30.9
11a → 16b	17.4
11b → 16c	19.3
11c → 17b	17.0
Second protonation	
2a → 3a	35.5
2b → 3b	37.6
2c → 3c	46.9
2d → 3d	56.0
2e → 3e	77.6
2d → 5d	65.1
2e → 5e	74.4
2a → 4a–o	29.7
2b → 4b–o	31.4
2c → 4c–o	39.3
2a → 4a–m	26.5
2b → 4b–m	27.1
2c → 4c–m	35.5
2a → 4a–p	35.2
2b → 4b–p	33.4
2c → 4c–p	44.4

[a)]ΔG_p is calculated as the Gibbs energy of the reaction $A + CF_3SO_3H \rightarrow AH^+ + CF3SO_3^-$ in solution of TFSA, where A is a neutral, monoprotonated molecule or carbocation.

discarded as active intermediates in TFSA mediated reaction between benzene and benzaldehyde even though these are the most stable among dications.[5] Unlike monoprotonation, the CH$_3$ group does not stabilize dications compared to H, while CF$_3$ fragments definitely destabilize diprotonated molecules compared to H and CH$_3$ groups, owing to the strong electron-withdrawing character of this substituent. For trifluoracetone (**1d**) and hexafluoracetone (**1e**) second protonation is especially unfavorable, achieving 77.6 kcal · mol^{-1} for O,O-diprotonated molecule (**3e**). As seen from Figure 3 and Table 3 even O,F-diprotonation is more favorable than the O,O-one for **3d–e**.

Reaction Profiles

Although diprotonated species are very unstable they cannot be immediately discarded as possible reaction intermediates since there is a possibility that a decrease of the Gibbs activation energy due to their enhanced reactivity will overcompensate for the unfavorable thermodynamics of diprotonation. To answer this question, the reaction energy profiles were calculated for the reactions of **1b** and **1c** with biphenyl and **1a** with benzene considering mono- and diprotonated species as active electrophilic intermediates.

The reaction of aromatic electrophilic substitution has been a subject of intensive theoretical studies.[24–26] It is well established that the reaction steps involve a complex formation between the electrophile and aromatic hydrocarbon, which is transformed into the σ intermediate. The σ intermediate loses proton to recover the aromaticity. It is suggested that the rate determining step is the formation of the σ intermediate[27] and therefore the transition state search was carried out only for the σ intermediate formation. However, for the reaction of benzaldehyde with benzene an exhaustive search was performed to ensure the locations of all stationary points. The π adduct formation previous to the σ intermediate was not taken into account for the following reasons:

1. The formation of weak complexes is governed by dispersion interactions which are described incorrectly by modern DFT theory.[28] The high level theories correctly describing dispersion interactions are prohibitive due to size of the treated molecules.
2. The available calculated binding energies for π adducts for the reaction of proton exchange and methylation of benzene do not exceed 4 kcal · mol^{-1}.[26] Moreover, when comparing the difference of activation energies, the formation of π adducts will have even less effect due to the partial compensation effect.

Figure 7–10 show the Gibbs reaction energy profiles for the reactions shown in Figure 4 and 5.

Reaction of Benzaldehyde (1a) with Benzene

The energy profiles for the reaction of benzaldehyde with benzene were studied in two solvents, TFSA (Figure 7) and
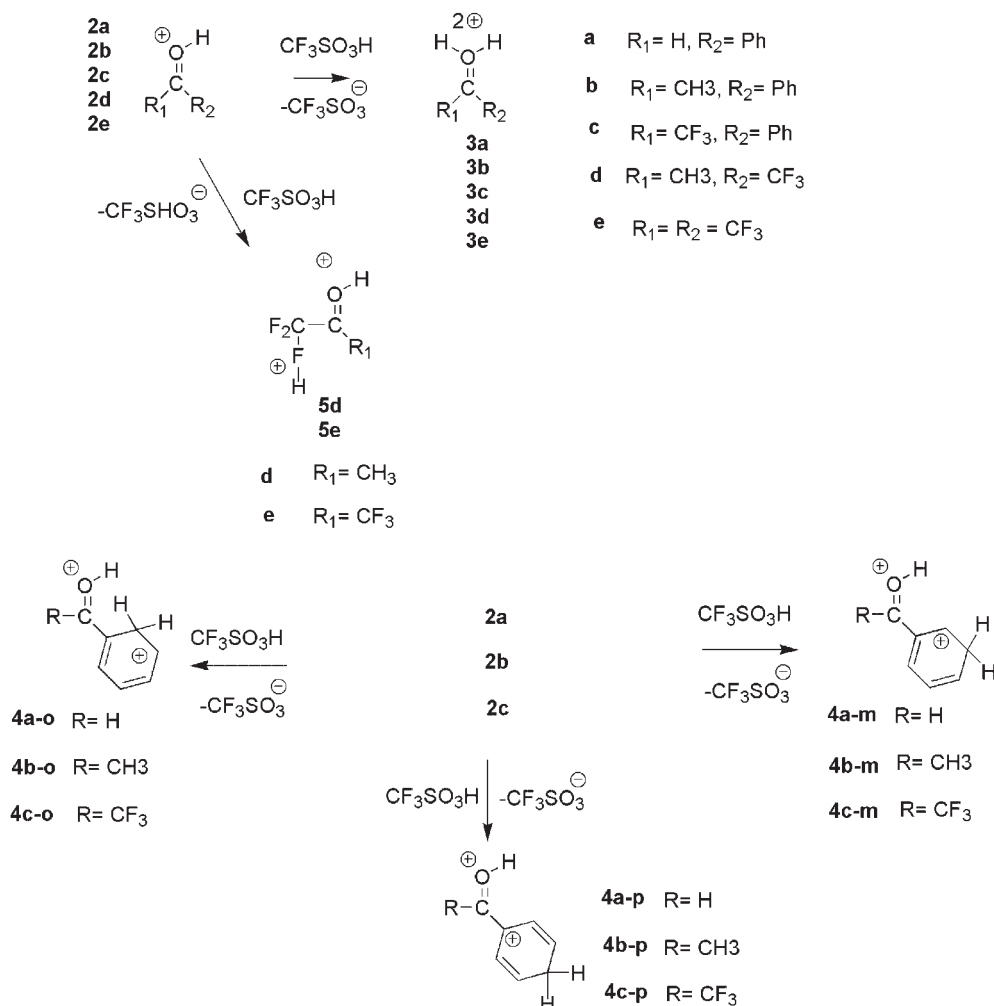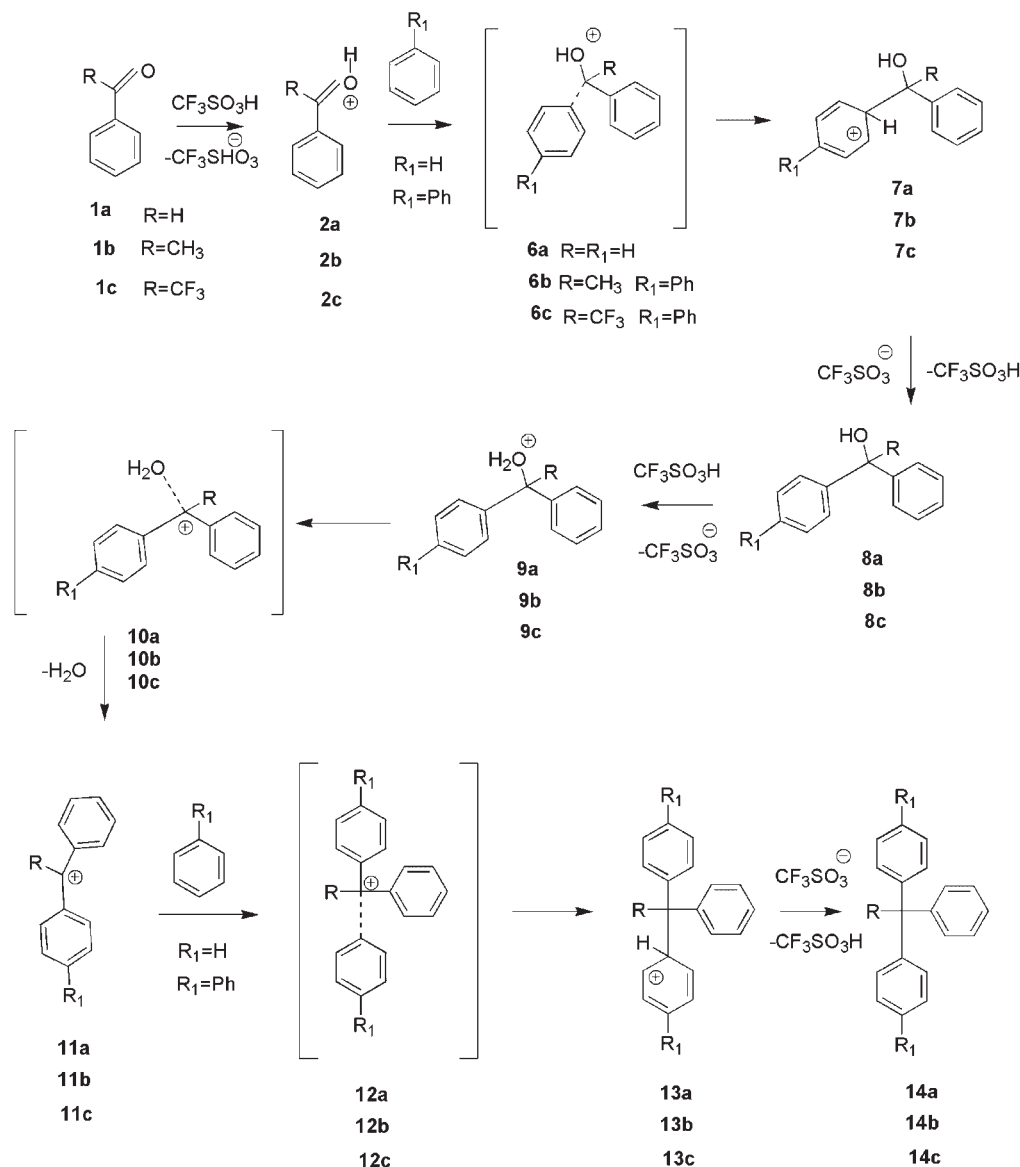
Figure 3. Reactions of protonation of different monoprotonated carbonyl compounds in TFSA.

sulfuric acid (Figure 10). The first step is monoprotonation (**1a** → **2a**). This step is exergonic in TFSA and endergonic in sulfuric acid. After this step the reaction can follow two routes; the monoprotonated species can form the σ complex **7a** passing through a transition state **6a**, or it can form a diprotonated species. As seen from Figure 7, the Gibbs activation energy for **2a** → **7a** reaction is 27.5 kcal·mol^{-1} in TFSA, while among diprotonated species (Figure 3) only **4a–m** has a slightly lower Gibbs energy of second protonation (26.5 kcal·mol^{-1}). All other diprotonated species of **1a** can be ruled out as reaction intermediates due to very high reaction energies. In case of the reaction of dication **4a–m** with benzene (Figure 5) the Gibbs activation energy of this process (Table 4) gives the transition state **19a–m** which is 21.0 kcal·mol^{-1} higher in energy than monoprotonated transition state **6a**.

According to the calculations, dication **4a–m** is more reactive than **2a** judging from the lower Gibbs activation energy of σ complex formation (27.5 vs. 21.9 kcal·mol^{-1}), however, the energy required for the second protonation is

significantly higher than a decrease of the Gibbs activation energy due to the reactivity enhancement. Once the σ complex **7a** is formed, there is a possibility of proton abstraction by triflate anion to produce carbinol **8a**. Another reaction path proposed by the authors[13] to explain the dependence of the reaction rate on the acidity of the medium involves the protonation of **7a** at oxygen to give a dication followed by the proton abstraction from sp^3 carbon to produce monoprotonated carbinol **9a**. The calculations show that the protonation of **7a** is unlikely for two reasons; firstly, this is an endergonic reaction (ΔG = 8.4 kcal·mol^{-1}) and secondly, the transformation of **7a** into **8a** by proton abstraction is a highly exergonic reaction with no detected activation energy.

The formation of carbocation **11a** is essential to form triphenylmethane – the reaction path is then straightforward: the protonation of carbinol **8a** followed by dissociation of protonated carbinol **9a** to give **11a** and a water molecule. As seen from Figure 7 and Table 4, the protonation of **8a** is only slightly endergonic in TFSA
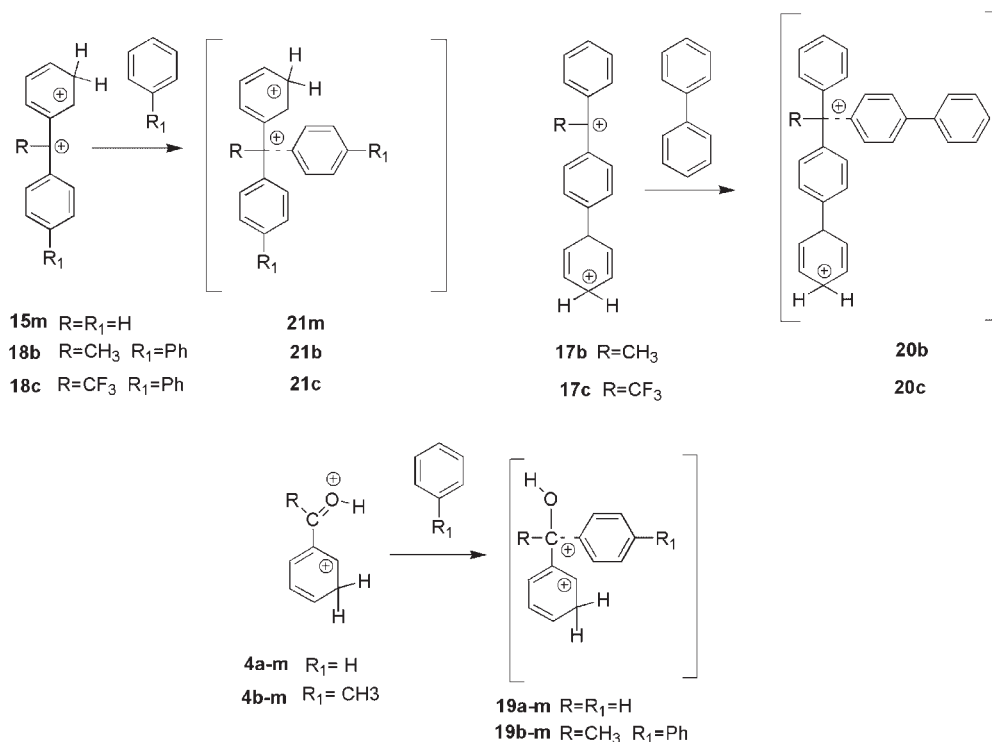
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Figure 4. The reaction path for the aromatic electrophilic substitution reactions of carbonyl compounds with benzene and biphenyl.

(2.0 kcal·mol^{-1}) while the dissociation of intermediate **9a** is exergonic (-14.7 kcal·mol^{-1}) with a very low activation energy of 2.7 kcal·mol^{-1}. We considered dicationic species as possible reaction intermediates for the second part of the aromatic electrophilic substitution of cation **11a** with biphenyl. Figure 4 shows possible protonated structures of cation **11a**. As seen, the formations of all three possible dications are endergonic reactions (Table 3), **15m** being the most stable. However, when comparing the Gibbs activation energy of the σ complex **13a** formation from cation **11a** (28.8 kcal·mol^{-1}, Figure 5) with the protonation energies of **11a** (Figure 6, Table 3), one can see that they are very close. The corresponding transition state **21m** is 20.6 kcal·mol^{-1} higher in energy than the transition state **12a**

as seen from Figure 7, thus discarding the participation of dicationic species in the reaction mechanism. However, according to the report,[11] the reaction rate increases with the acidity of the media. As we mentioned above, the explanations of this fact based on diprotonation of benzaldehyde [13] or protonation of the σ complex **7a** is inconsistent with the calculation results.

To explain the dependence of the reaction rate on the acidity of the media one has to compare the Gibbs reaction energy profile for the reaction of benzaldehyde with biphenyl in TFSA (Figure 7) with that in sulfuric acid (Figure 10). As seen, the two reaction profiles are quite similar except for two details: the protonation energies of **1a** and **8a**. In TFSA the protonation of **1a** is exergonic while

15m R=R₁=H
18b R=CH₃ R₁=Ph
18c R=CF₃ R₁=Ph

21m
21b
21c

17b R=CH₃
17c R=CF₃

20b
20c

4a-m R₁= H
4b-m R₁= CH3

19a-m R=R₁=H
19b-m R=CH₃ R₁=Ph

■ *Figure 5.* Formation of dicationic transition states from protonated carbocations and aromatic hydrocarbons.

in sulfuric acid is endergonic. This fact could explain an increase of the reactivity of benzaldehyde in TFSA compared to sulfuric acid. However, according to the calculations the further increase of the acidity would not change the concentration of **2a** since in TFSA most of benzaldehyde molecules are already protonated. Carbinol **8a** is a weaker base compared to **1a**, as seen from Figure 7 and 10. Even in TFSA the reaction **8a → 9a** is still endergonic with $\Delta G = 2.0$ kcal · mol^{-1}. Therefore, an additional increase in the acidity of the reaction media would increase the equilibrium concentration of **9a**, thus increasing the overall reaction rate. In conclusion, we suggest that the increase of the reaction rate with the acidity of the media can be explained by the involvement of monoprotonated species only. An increase in the acidity from sulfuric to triflic acid raises the concentrations of both **2a** and **9a**, while additional increase of acidity only favors the concentration of **9a**.

Reactions of Acetophenone (1b) and 2,2,2-Trifluoroacetophenone (1c) with Biphenyl

Experiments show that **1c** affords a polymer when reacting with biphenyl in triflic acid while **2b** does not.[7] In fact, acetophenone does not react at all with benzene and toluene in 100 molar excess of TFSA even at 130 °C.[13] Figure 8 and 9 show the Gibbs reaction energy profiles for

the reactions of **1b** and **1c** with biphenyl. **1b** is a much stronger base than **1c** due to the electron-donating effect of CH₃ in **1b**. This is reflected in the differences of the Gibbs energies of monoprotonation for **1b–c** and **8b–c** (Table 3). Thus, the **1b → 2b** reaction is exergonic ($\Delta G = -6.8$ kcal · mol^{-1}), while the **1c → 2c** process is endergonic (7.8 kcal · mol^{-1}). A similar situation holds for the **8b–c → 9b–c** reaction. This means that practically all molecules of **1b** are protonated in triflic acid, while in the case of **1c** only a small fraction of molecules is protonated. As it has been shown before[9] the electron-withdrawing groups adjacent to the carbonyl fragment decrease the activation energy of σ complex formation. This is in line with data shown in Figure 8 and 9. As seen, the Gibbs activation energies of **7b, c** formation are 37.1 and 26.0 kcal · mol^{-1}, respectively. When comparing these values with the energies of second protonation for **2c** (Table 3) all of them are higher than the corresponding activation energies of σ complex formation, thus discarding any of the diprotonated **2c** molecules as the reaction intermediate. For **2b** the situation is similar to **2a** where the O,C-*metha*-diprotonated intermediate **4b–m** has a slightly lower energy compared to transition state **6b**. However, the corresponding diprotonated transition state **19b–m** is 20.6 kcal · mol^{-1} higher in energy than **6b**.

The second reaction step implies the reaction of cations **11b–c** with biphenyl. The most stable dicationic species was found to be **17b–c** (Figure 4), C-protonated at the *para* position of biphenyl fragment. However, similar to the
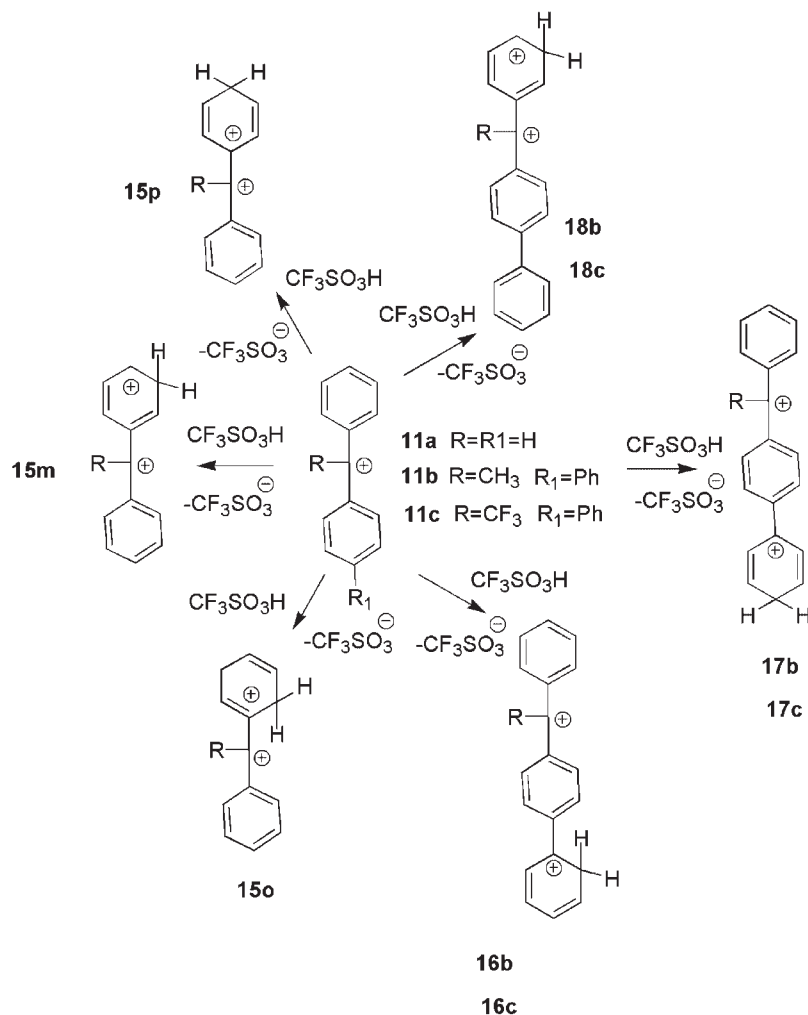
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■ *Figure 6.* Reactions of protonation of different carbocations in TFSA.

reaction of benzaldehyde with benzene, the monocationic species **11b–c** give transition states **12b–c** with much lower energy compared to any of the dications (Figure 8 and 9, Table 4).

The explanation of low reactivity of **1b** is straightforward when inspecting the reaction energy profile (Figure 8). The excessive stabilization of cation **2b** renders the reaction **2b → 14b** thermodynamically impossible with $\Delta G = 14.7$ kcal·mol^{-1}. On the other hand, the reaction path with the participation of diprotonated species **4b–m** will result in very high the Gibbs activation energy of 45.5 kcal·mol^{-1} (**1b → 19b–m**) In the case of **1a** and **1c**, the corresponding reaction energies (**2a, c → 14a, c**) are negative with $\Delta G = -3.7$ and -6.8 kcal·mol^{-1}, respectively.
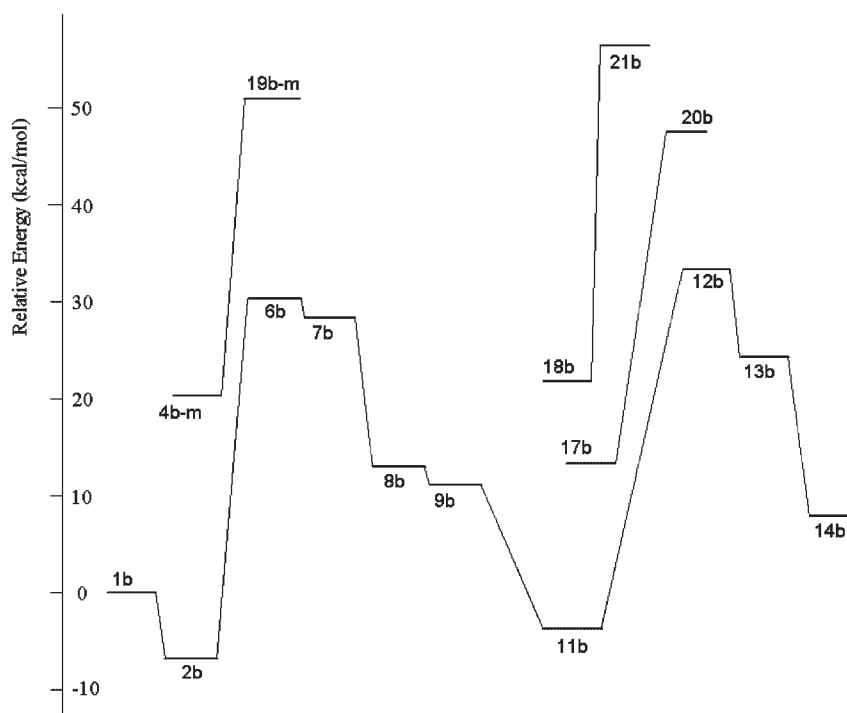
The low reactivity of hexafluoracetone (**1e**) is due to the very strong electron-withdrawing effect of two CF$_3$ substituents resulting in destabilization of monoprotonated species **2e**. On the other hand, very basic carbonyl compounds like acetophenone (**1b**) form very stable monoprotonated intermediates, thus rendering the reaction impossible thermodynamically. Therefore, there is an optimal range for the carbonyl group basicity when the reaction of electrophilic aromatic substitution occurs. The additional increase of the basicity of carbonyl compound could favor the reaction again due to easier access to diprotonated states.
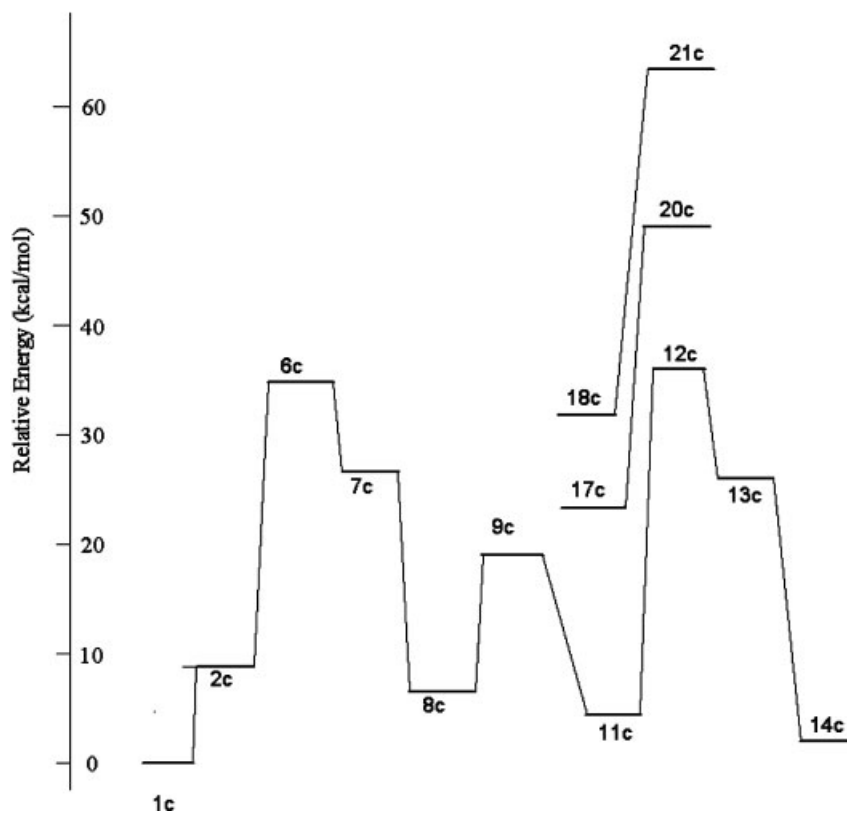
Another factor to consider is steric hindrance. When comparing the reaction energies profiles for **1a–c** (Figure 7–9) one can see that the Gibbs activation energies for the σ complex formation (**7a–c** and **13a–c**) are the lowest for **1a** followed by **1c** and **1b**. As noted above, the electron-withdrawing groups decrease the activation energies of the σ-complex formation.[9] However, the lowest activation energies of the σ complex formations were found for **1a** which is certainly due to steric factor. For CH$_3$ and CF$_3$ groups steric factors are similar and it is the electronic properties of substituents that determine the
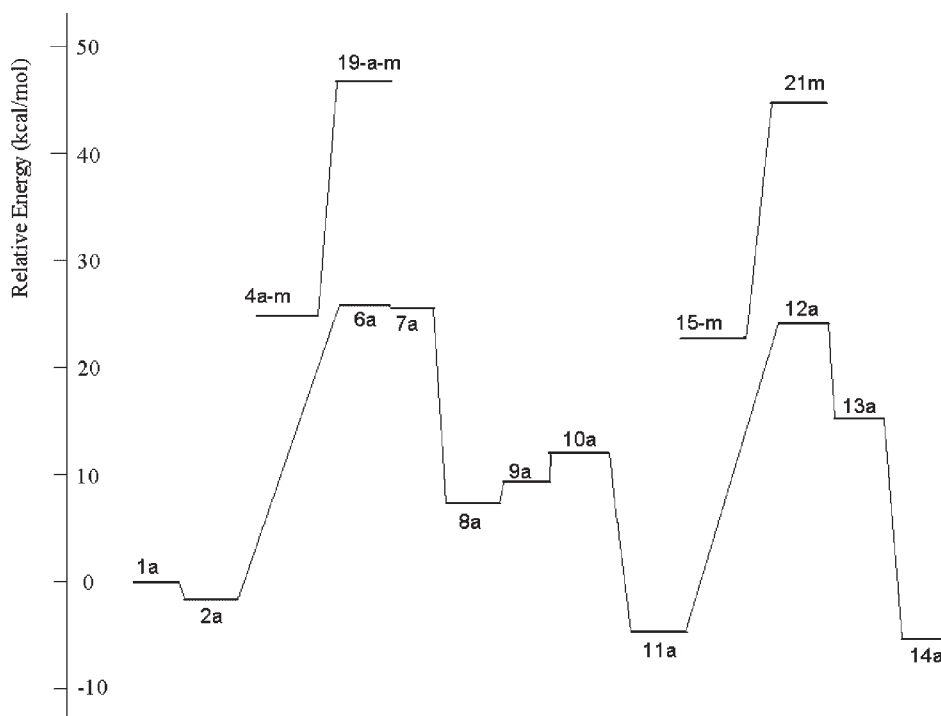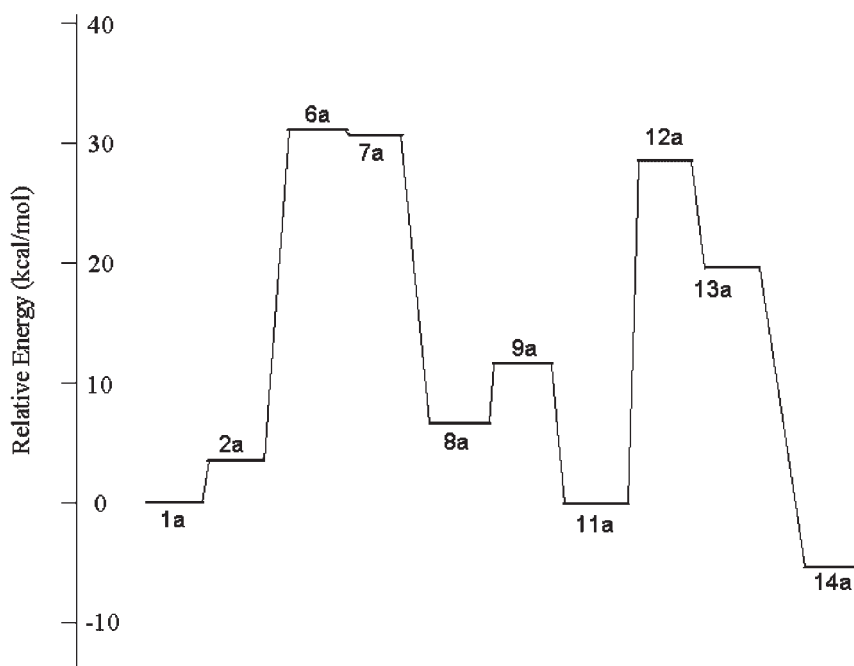
■ *Figure 7.* The Gibbs reaction energy profile for the reaction of **1a** with benzene in TFSA (kcal · mol⁻¹).

■ *Figure 8.* The Gibbs reaction energy profile for the reaction of **1b** with biphenyl in TFSA (kcal · mol⁻¹).

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Figure 9. The Gibbs reaction energy profile for the reaction of **1c** with biphenyl in TFSA (kcal · mol^{-1}).

Figure 10. The Gibbs reaction energy profile for the reaction of **1a** with benzene in H$_2$SO$_4$ (kcal · mol^{-1}).

Table 4. Calculated Gibbs energies of reaction (ΔG) and activation (in brackets) in TFSA and H_2SO_4.

Reaction	ΔG in TFSA	ΔG in H_2SO_4
	$kcal \cdot mol^{-1}$	$kcal \cdot mol^{-1}$
2a → 7a	27.2 (27.5)	27.2 (27.6)
4a–m → 19a–m	(21.9)	–
7a → 8a	−18.2	−24.1
8a → 9a	2.0	5.0
9a → 11a	−14.0 (2.7)	−11.7
11a → 13a	19.9 (28.8)	19.7 (28.6)
13a → 14a	−20.6	−25.0
15m → 21m	(22.0)	–
2b → 7b	35.1 (37.1)	–
4b–m → 19b–m	(30.7)	–
7b → 8b	−15.4	–
8b → 9b	−1.9	–
9b → 11b	−14.8	–
11b → 13b	28.0	–
13b → 14b	−16.4	–
17b → 20b	(34.3)	–
18b → 21b	(34.6)	–
2c → 7c	17.8 (26.0)	–
7c → 8c	−20.1	–
8c → 9c	12.5	–
9c → 11c	−14.6	–
11c → 13c	21.6 (31.6)	–
13c → 14c	−24.0	–
18c → 21c	(31.6)	–
17c → 20c	(25.7)	–

activation energies. In fact, the steric factor is important also for thermodynamics; thus ΔG of the reactions **1a** + 2-biphenyl = **14a** + H_2O and **1b** + 2-biphenyl = **14b** + H_2O in TFSA are of −5.5 and 7.9 kcal $\cdot$ mol^{-1}, respectively, reflecting the destabilizing effect of CH_3 group on the reaction thermodynamics.

Conclusion

According to our calculations, O,O or O,C-diprotonated carbonyl molecules bearing electron-withdrawing and moderately electron donating groups do not participate in the reaction with aromatic hydrocarbons in TFSA due to the extremely positive Gibbs energy of formation. The observed dependence of the reaction rate on the acidity of the media can be explained by a multi-step mechanism

involving only monoprotonated intermediates. Both, strong electron-withdrawing and strong electron-donating groups decrease the reactivity of carbonyl compounds with aromatic hydrocarbons. In the first case, even monoprotonation of the carbonyl group becomes energetically very unfavorable (**1e**); in the second case, the excessively stable monoprotonated carbonyl molecule renders the reaction thermodynamically impossible (**1b**). Steric factor is of importance affecting both thermodynamic and kinetics of the reaction.

[1] C. P. Tsonis, *"Comprehensive Polymer Science"*, G. Allen, J. C. Bevington, Eds., Pergamon, New York 1989, Vol. 5, p. 455.
[2] C. P. Tsonis, *"Polymeric Materials Encyclopedia"*, J. C. Salamone, Ed., CRC Press, Boca Raton 1996, p. 407 ff.
[3] G. A. Olah, *Angew. Chem. Int. Ed. Engl.* **1993**, *32*, 767.
[4] T. Ohwada, *Rev. Heterat. Chem.* **1995**, *12*, 179.
[5] Y. Sato, M. Yato, T. Ohwada, S. Saito, K. Shudo, *J. Am. Chem. Soc.* **1995**, *117*, 3037.
[6] D. A. Klumpp, *Recent Res. Dev. Organic. Chem.* **2001**, *5*, 193.
[7] M. G. Zolotukhin, S. Fomine, R. Salcedo, L. Khalilov, *Chem. Commun.* **2004**, 1030.
[8] A. M. Diaz, M. G. Zolotukhin, S. Fomine, R. Salcedo, O. Manero, G. Cedillo, *Macromol. Rapid Commun.* **2007**, in press.
[9] [9a] E. Ramos Peña, M. G. Zolotukhin, S. Fomine, *Macromolecules* **2004**, *37*, 6227; [9b] E. Ramos Peña, M. Zolotukhin, S. Fomine, *Polymer* **2005**, *46*, 7494.
[10] [10a] D. A. Klumpp, Y. Zhang, J. Patrick, K. S. Lau, *Tetrahedron* **2006**, *62*, 5915;[10b] S. Walspurger, A. V. Vasilyev, J. Sommer, P. Pale, *Tetrahedron* **2005**, *61*, 3559.
[11] G. A. Olah, G. Rasul, C. York, G. K. S. Prakash, *J. Am. Chem. Soc.* **1995**, *117*, 11211.
[12] [12a] G. A. Olah, G. K. S. Prakash, J. Sommer, *"Superacid"* John Wiley and Sons, New York 1985. [12b] J. Sommer, S. Schwartz, P. Pimmelin, P. Canivet, *J. Am. Chem. Soc* **1978**, *100*, 2576.
[13] K. Y. Koltunov, S. Walspurger, J. Sommer, *Catal. Lett.* **2004**, *98*, 89.
[14] G. A. A. Saracino, R. Improta, V. Barone, *Chem. Phys. Lett.* **2003**, *373*, 411.
[15] C. Adamo, V. Barone, *J. Chem. Phys.* **1999**, *110*, 6158.
[16] D. J. Tannor, B. Marten, R. Murphy, R. A. Friesner, D. Sitkoff, A. Nicholls, M. Ringnalda, W. A. Goddard, B. HonigIII, *J. Am. Chem. Soc.* **1994**, *116*, 11875.
[17] B. Marten, K. Kim, C. Cortis, R. A. Friesner, R. B. Murphy, M. N. Ringnalda, D. Sitkoff, B. Honig, *J. Phys. Chem.* **1996**, *100*, 11775.

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Macromolecular
Theory and Simulations

[18] Jaguar 6.0, Schrodinger, LLC, Portland, Oregon 2005.

[19] Y. Zhao, D. G. Truhlar, *J. Phys. Chem. A* **2004**, *10,* 6908.

[20] M. D. Liptak, G. C. Shields, *J. Am. Chem. Soc.* **2001**, *123,* 7314.

[21] J. F. J. Dippy, S. R. C. Hughes, A. Rozanski, *J. Chem. Soc.* **1959**, *81,* 2492.

[22] R. D. Howells, J. D. McCown, *Chem. Rev.* **1977**, *77,* 69.

[23] H. C. Brown, *"Determination of Organic Structures by Physical Methods"*, E. A. Braude, F. C. Nachod, Eds., Academic Press, New York 1955.

[24] P. M. Esteves, J. W. de M. Carneiro, S. P. Cardoso, A. G. H. Barbosa, K. K. Laali, G. Rasul, G. K. Surya Prakash, G. A. Olah, *J. Am. Chem. Soc.* **2003**, *125,* 4836.

[25] K. J. Szabo, A. B. Hornfeldt, S. Gronowitz, *J. Am. Chem. Soc.* **1992**, *114,* 6827.

[26] A. M. Vos, R. A. Schoonheydt, F. de Proft, P. Geerlings, *J. Catal.* **2003**, *220,* 333.

[27] T. W. G. Solomons, *"Fundamentals of Organic Chemistry"*, 5th edition, Wiley, New York 1997.

[28] G. Chalasinski, M. M. Szczesniak, *Chem. Rev.* **2000**, *100,* 4227.