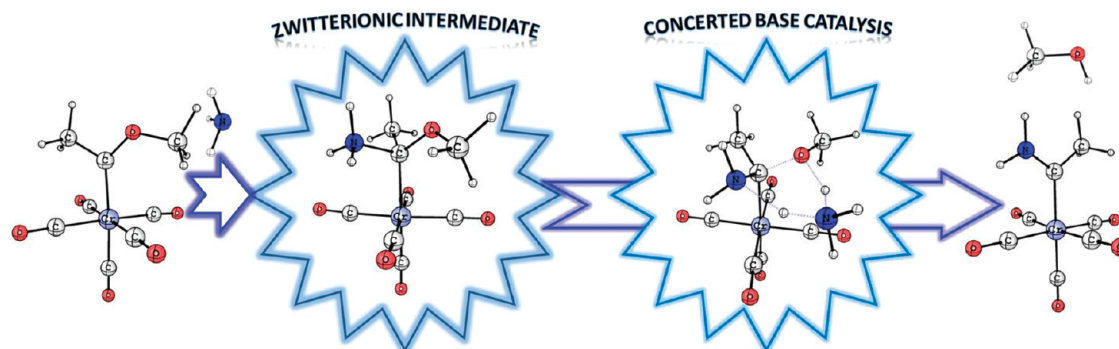


Mechanism of the Aminolysis of Fischer Alkoxy and Thiocarbene Complexes: A DFT Study

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B3LYP calculations have been carried out to study the reaction mechanism of the aminolysis of Fischer carbene complexes of the type $(\text{CO})_5\text{Cr}=\text{C}(\text{XMe})\text{R}$ ($\text{X} = \text{O}$ and S ; $\text{R} = \text{Me}$ and Ph). We have explored different possible reaction mechanisms either through neutral or zwitterionic intermediates as well as a general base catalysis assisted by an ammonia molecule. Our results show that the most favorable pathway for the aminolysis of Fischer carbene complexes is through a stepwise reaction via a zwitterionic intermediate generated by the initial nucleophilic attack. We have found that the ammonia-catalyzed mechanism entails a significantly lower barrier for the rate-determining step than the uncatalyzed one. At lower pressure gas-phase conditions, the rate-determining step corresponds to the concerted proton transfer and MeXH elimination. Thiocarbene complexes show a higher energy barrier for this rate-determining step due to the lower basicity of the MeS^- substituent. At higher pressure or in solution, the rate-determining step corresponds to the initial nucleophilic attack. Our results indicate that the transition state of the nucleophilic attack is more advanced and has a higher barrier for alkoxy carbene than thiocarbene complexes due to the stronger π -donor character of the alkoxy group that reduces the electrophilicity of the attacked carbene atom making the nucleophilic attack more difficult.

Introduction

Since the first targeted synthesis of [methoxy(methyl)-carbenepentacarbonyl]tungsten(0) by Fischer and Maasböl,¹ the chemistry of Fischer carbene complexes has been intensively developed as a new branch of organometallic chemistry.² These compounds have proven themselves to be highly

important building blocks in organic and organometallic synthesis due to their capability to undergo nonconventional, high-yield transformations under mild conditions.³

Typical Fischer carbene complexes usually have a central carbene carbon linked through a formal double bond to a late transition metal (groups VI–VIII) in a low oxidation state. The low-valence metal center generally bears ligands with good π -acceptor properties such as carbon monoxide, phosphine, or nitro groups in the coordination sphere. Typically, in these complexes one substituent of the carbene acts as a π -donor, allowing an electronic stabilization of

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the electron-deficient carbene carbon atom, whereas the other substituent may be either a saturated or unsaturated alkyl or aryl group.

Due to the electrophilic nature of the carbene carbon atom, these compounds undergo nucleophilic additions or substitution reactions at this carbon.⁴ The simplest addition mode of heteroatom nucleophiles to alkoxy-carbene complexes involves the formation of different heteroatom stabilized carbene complexes such as thio- and aminocarbenes complexes.

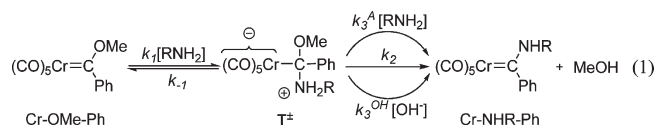
In previous works, reactions of alkoxy-carbenes with amines have been addressed to synthetic applications.^{5,6} For instance, the synthesis of peptides and the α -amino function of amino acids have been protected in the reaction with alkoxy-carbenes to give aminocarbene-labeled peptides.⁷ More recently, this reaction has been used for protein labeling⁸ and design of bioactive surfaces for protein immobilization.⁹ However, most of these studies have been focused on alkoxy-carbene complexes. This is probably because alkoxy-carbenes are prominent according to their synthetic applications. Fischer thiocarbenes, on the other hand, have received much less attention. One of the reasons might be that it appeared that thiocarbene complexes would react following the same patterns of the isostructural alkoxy-carbenes.¹⁰

The first kinetic investigation on these nucleophilic substitution reactions was that of Werner et al.,⁶ who studied the reaction of [methoxy(phenyl)carbene]pentacarbonylchromium(0) (Cr-OMe-Ph), with several primary aliphatic amines (*n*-BuNH₂, C₆H₁₁NH₂, and C₆H₅CH₂NH₂) in *n*-decane, dioxane, methanol, and dioxane–methanol (1:1). In *n*-decane, the rate was found to be third order with respect to amine concentration and in dioxane second order, while in dioxane–methanol mixtures and pure methanol, both first- and second-order dependence on amine were reported. The authors proposed a mechanism where the first amine molecule

activates the substrate by hydrogen bonding to the methoxy group and provides also an acid catalysis to the MeO[−] departure in the product-forming step. The nucleophilic attack occurs with an amine molecule that is hydrogen bonded to a third amine, which presumably helps to stabilize the positive charge positioned at the nitrogen. In more polar solvents, the complex between two amine molecules may be replaced by an amine–solvent complex. Furthermore, in protic solvents the role of activating hydrogen bonds is done by a solvent molecule. Experimental ¹H NMR studies support the presence of association equilibria.¹¹

There have been few other kinetic studies in the early literature; these investigations focused mainly on reactions with amines^{11–13} and phosphines¹⁴ in weakly polar organic solvents. These studies provided no evidence of tetrahedral intermediates. However, this hypothesis is supported by reports postulating that Cr-OMe-Ph forms isolable tetrahedral adducts such as Cr-OMe-Ph-DABCO by reaction with 1,4-diazabicyclo[2.2.2]octane (DABCO) or quinuclidine in ether.¹⁵

More recently, Bernasconi et al.^{16,17} provided additional strong evidence for the presence of tetrahedral intermediates in the reaction of Cr-OMe-Ph with primary amines (*n*-BuNH₂, MeOCH₂CH₂NH₂, ClCH₂CH₂NH₂, H₂NCOCH₂NH₂, and EtO₂CCH₂NH₂) in polar solvents, mainly in water–acetonitrile mixtures, where there are no hydrogen bond associations of the type observed in nonpolar solvents and clearer conclusions could be drawn about mechanistic details. The proposed mechanism is illustrated in eq 1



where k_3^{A} and k_3^{OH} steps refer to the base-mediated catalysis by the amine and by the hydroxide anion, respectively; the k_2 step represents spontaneous, possibly intramolecularly catalyzed conversion of the zwitterionic intermediate T^{\pm} to the product. A detailed analysis of kinetic data provided crucial information about the mechanism of the general base-catalyzed conversion of T^{\pm} to the product. This catalysis involves a fast equilibrium of the proton transfer followed by a general acid-catalyzed loss of methoxide ion by RNH_3^{+} and water, respectively.¹⁶ Furthermore, the most compelling evidence achieved so far for this mechanism has come from the direct detection of the intermediate in the reactions of Cr-OMe-Ph with thiolate ions.¹⁸

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Moreover, different structural features of Fischer carbenes have been tested in order to assess how it affects the reaction mechanism with mainly primary and secondary amines. With respect to such studies, the substituent effects on the aryl group of Fischer alkoxyphenylcarbene Cr(0) and W(0) complexes have been explored^{16,17} as well as the corresponding thiocarbene complexes.^{19,20} In these works, an important role of the π -donor heteroatom has been found. In addition, marked changes on the aminolysis mechanism of $(\text{CO})_5\text{Cr}=\text{C}(\text{OEt})\text{C}_6\text{H}_4\text{X}$ have been reported when $\text{X} = \text{H}$ is changed to $\text{X} = \text{Cr}(\text{CO})_3$. Addition of the $\text{Cr}(\text{CO})_3$ substituent on the phenyl group changes the mechanism of general base catalysis in the rate-limiting step from the leaving group departure for the reaction with $\text{X} = \text{H}$ to the proton transfer for the reaction of $\text{X} = \text{Cr}(\text{CO})_3$.²¹ On the other hand, Ali et al.^{22,23} have reported the kinetic study over [methyl(thiomethyl)carbenepentacarbonyl]Cr(0) and -W(0) complexes. They found that the slightly enhanced electrophilic behavior of tungsten carbene complexes is responsible for the differences in the reactivity observed between chromium and tungsten complexes. Finally, more recently the nucleophilic substitution of imidazolidine and benzimidazolidine ions has been reported.²⁴

In our laboratory, we carried out a kinetic study of the nucleophilic substitution reaction on a series of Fischer thiocarbenes with morpholine as the nucleophile in order to assess the effect of the bulkiness of the alkyl substituent on sulfur atom.²⁵ We observed good correlations between k_1 and k_3^A against the Charton's steric parameter²⁶ (ν_{CH2R}); these results clearly show that the steric volume determines the reactivity of the nucleophilic attack as well as of the general base catalysis. Surprisingly, the morpholine general base catalysis step is two times more sensitive to the bulkiness of the alkyl group than the nucleophilic attachment step. On the other hand, we found that the values of the catalytic rate constants for the general acid-catalyzed one, i.e., k_3^A , are higher for weaker conjugated R_2NH_2^+ ammonia ions. This result could probably indicate that the second step of the proposed mechanism illustrated in eq 1 also involves a

contribution in the rate law of concerted general-base catalyzed leaving group expulsion.²⁷

The aminolysis of carboxylic esters^{28–30} has frequently been compared with the reaction of Fischer carbene complexes and amines.^{2,11,13} It is noteworthy that the nucleophilic substitution of Fischer carbene complexes has generally been assumed to proceed via a stepwise mechanism analogous to that of the reaction of carboxylic esters with nucleophiles.^{5,6,11,16,31} However, with respect to reactivity there are large differences between the Fischer carbene complexes and esters, the former being much more reactive than the latter. This is because the stabilization of the negative charge of T^\pm by delocalization into the CO ligands of the $(\text{CO})_5\text{M}$ moieties is much more effective than the charge stabilization by the oxygen in the corresponding intermediates in ester reactions.

Although several kinetic studies regarding the aminolysis Fischer carbene complexes have been carried out, no computational studies have been reported until now to the best of our knowledge. On the other hand, the analogue organic reaction of the ester aminolysis has been the subject of both experimental kinetic^{32–35} and theoretical studies.^{36–45} Since

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the aminolysis mechanism was found to strongly depend on the nature of ester, amine, and solvent, several studies have been made focusing on different aspects of this reaction. Experimentally, in many of the aminolysis reactions of esters, zwitterionic tetrahedral intermediates are predicted to be involved, and either the formation or breakdown of intermediate can be rate-limiting.^{27,28,30,46} Computational studies have been performed focusing on the understanding of the aminolysis mechanism and the catalytic influence of solvents such as water and alcohol, although general base catalysis by amine/ammonia as well as general acid catalysis has also attracted much attention.^{37,39–42,47} Theoretical calculations are in disagreement with the mechanism of ester aminolysis in the possible formation of zwitterionic intermediates. The possibility for the formation of such an intermediate was discussed in previous computational studies. However, it was recognized that computational calculations fail to identify the zwitterionic intermediates and the corresponding transition states in the gas phase or in aprotic solvents.^{36b,39,41,43,47,48} Thus, some authors have made efforts toward further study on the zwitterionic intermediate by computational means. Singleton and Merrigan³⁸ reported a DFT study on equilibrium isotope effects in the formation of a zwitterionic tetrahedral intermediate between methyl formate and ammonia including 4 to 11 explicit water molecules in combination with Onsager's implicit solvation model. Chalmet et al.⁴⁷ reported a theoretical study on the model reaction of ammonia and formic acid. Their calculations with the continuum model did not predict a stable zwitterionic intermediate, whereas a zwitterionic local minimum was found by explicit consideration of four solvent water molecules. Recently, Sung and co-workers⁴⁴ studied the structure and stability of zwitterionic complexes in the aminolysis of phenyl acetate with ammonia and found that at least five explicit water molecules are needed to stabilize the zwitterions.

In this context, we have carried out the first computational study on the reaction mechanism of the aminolysis of Fischer carbene complexes of the type $(\text{CO})_5\text{Cr}=\text{C}(\text{XMe})\text{R}$ ($\text{X} = \text{O}$ and S ; $\text{R} = \text{Me}$ and Ph). We have examined different possible reaction pathways of the aminolysis of Fischer alkoxy- and thiocarbene complexes with four main aims: first, to study and compare the reaction mechanisms of the uncatalyzed and general base-catalyzed aminolysis of Fischer carbenes; second, to provide insight into the different patterns of reactivity found for alkoxy- and thiocarbenes; third, to discuss the effect of the substitution of R (methyl by phenyl group) in the reaction mechanism; and fourth, to analyze the changes in the thermodynamic and kinetic properties caused by the solvent (50% acetonitrile–50% water).

Computational Details

Theoretical calculations were performed with the GAUSSIAN03 computational package.⁴⁹ All geometry optimizations were computed using the hybrid density functional B3LYP.⁵⁰ The standard 6-31G(d,p) basis set⁵¹ was employed for hydrogen, carbon, oxygen, and sulfur atoms. For the chromium atom we utilized a df-extended (14s9p5d3f/8s4p3d1f) basis set with polarization functions as described by Wachters.⁵² We labeled this mixed basis set as Wachters&6-31G(d,p) throughout this work. In our experience, this level of calculation gives good numerical results comparable to other well-known density functional and MP2 levels that were also tested (see the Supporting Information). Harmonic frequencies were computed to determine the nature of stationary points (one and zero imaginary frequencies for transition states (TS) and minima, respectively)⁵³ and to calculate unscaled zero-point energies (ZPEs) as well as thermal corrections and entropy effects using the standard statistical-mechanics relationships for an ideal gas.⁵⁴ Furthermore, the connectivity between stationary points was unambiguously established by intrinsic reaction path calculations.⁵⁵ For all the stationary points, the electronic energy was improved by adding a set of diffuse functions on the carbon, oxygen, and sulfur atoms. Therefore, all gas-phase relative Gibbs free energies (ΔG_{298}) reported in this work include electronic energies obtained at the B3LYP/Wachters&6-31+G(d,p)//B3LYP/Wachters&6-31G(d,p) level plus ZPE, thermal, and entropy corrections computed at 298.15 K and 1 atm with the B3LYP/Wachters&6-31G(d,p) method.

Nonspecific solvent effects were described by means of the self-consistent reaction field (SCRF) approach in Tomasi's formalism.⁵⁶ Single-point PCM[B3LYP/Wachters&6-31G(d,p)] calculations using the gas-phase optimized geometries, if not stated otherwise, were performed to estimate the change in the Gibbs free energy profile of the reaction in the presence of a

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TABLE 1. Relative Gibbs Free Energies with Respect to Separated Reactants (and Enthalpies in Parentheses) Expressed in kcal mol⁻¹ for Each Reaction Step and Reaction Barriers along the Zwitterionic and Catalyzed Pathway for the Aminolysis of Fischer Alkoxy and Thiocarbene Complexes in the Gas Phase Obtained at the B3LYP/Wachters&6-31+G(d,p)//B3LYP/Wachters&6-31G(d,p) Level of Theory^a

Uncatalyzed Zwitterionic Mechanism				
	R = Me		R = Ph	
	X = OMe	X = SMe	X = OMe	X = SMe
1-anti → 1-syn	1.05 (1.06)	-1.92 (-1.43)	-0.14 (1.20)	-3.47 (-2.25)
1 + NH ₃ → TS(1→3)	22.28 (9.49)	21.32(9.09)	21.68 (10.45)	24.09 (11.75)
1 + NH ₃ → 3	22.13 (9.98)	18.03 (6.03)	21.88 (10.63)	18.10 (6.24)
3 → TS(3→5)	19.41 (19.32)	24.87 (24.71)	18.84 (18.75)	25.24 (25.82)
3 → 5 + MeXH	-34.79 (-20.84)	-32.82 (-19.15)	-35.40 (-22.52)	-30.61 (-18.78)
1 + NH ₃ → TS(3→5)	41.54 (29.31)	42.90 (30.74)	40.72 (29.38)	43.34 (32.06)
Mechanism Catalyzed by Ammonia				
	R = Me		R = Ph	
	X = OMe	X = SMe	X = OMe	X = SMe
1 + 2NH ₃ → TS(2→4)	23.99 (2.97)	22.75 (2.50)	22.85 (2.15)	26.06 (5.23)
1 + 2NH ₃ → 4	20.37 (-2.11)	17.05 (-5.06)	20.11 (-2.38)	17.27 (-5.58)
4 → TS(4→5)	11.84 (9.78)	14.81 (13.94)	10.05 (9.47)	15.12 (15.43)
4 → 5 + NH ₃ + MeXH	-33.03 (-8.74)	-31.84 (-8.06)	-33.49 (-10.72)	-29.78 (-6.95)
1 + 2NH ₃ → TS(4→5)	32.21 (7.68)	31.86 (8.88)	30.16 (7.10)	32.39 (9.85)
	thermodynamics of the reaction			
1 + NH ₃ → 5 + MeXH	-12.66 (-10.85)	-14.79 (-13.12)	-13.52 (-11.89)	-12.51 (-12.54)

^aFor the calculation of relative energies, the most stable conformer in the gas phase was considered, i.e., the *anti* conformation for alkoxy-carbenes and the *syn* conformation for thiocarbenes.

mixture of 50% acetonitrile–50% water. This solvent is commonly chosen in experimental work because it is essentially aqueous but allows the carbene complexes to be soluble enough.⁵⁷ The solvent was modeled with a relative dielectric constant of 58.8 and a density of 0.892 g mL⁻¹.^{24,58}

Results and Discussion

This section is divided as follows: First, the results and discussion of different routes for the uncatalyzed and the general base-catalyzed aminolysis are presented (section A). We then discuss the solvent effects over the reaction mechanism (section B).

Before starting section A, let us briefly mention that each heteroatom-type Fischer carbene complex has two conformations: the *anti* form (an orientation where the heteroatom substituent is directed toward the metal fragment) and the *syn* conformation, interchangeable by rotation through the C_{carb}–X bond (see Figure 1). It has been reported that Fischer alkoxy-carbene complexes show bias for the *anti* conformer in the gas phase, whereas the *syn* conformer is the most stable in solution.^{59–61} In agreement with these predictions, our gas-phase results (see the first entry of Table 1) indicate that the *anti* isomer is the most stable for alkoxy-carbenes, although for thiocarbenes the *syn* is the preferred conformation. In solution, the *syn* conformer is the most stable for both alkoxy- and thiocarbenes (see the

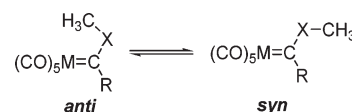


FIGURE 1. *Syn* and *anti* forms of metal Fischer carbene complexes.

first entry of Table 2). In addition, the experimental activation energy for the *anti* to *syn* transformation in the [(methoxymethyl)carbenepentacarbonyl]chromium(0) complex⁶² is 12.4 ± 1 kcal mol⁻¹, while calculations performed by Fernández et al. for the same conformational change predict barriers of 14.3 and 14.6 kcal mol⁻¹ in the gas phase and in methanol, respectively.^{60,61} The small differences between the two conformers (about 1 kcal mol⁻¹)⁶¹ and the relatively low barrier found for the *anti*–*syn* transformation point out that at room temperature Fischer alkoxy-carbene complexes should be present as a mixture of both conformers. For these reasons, the exploration of potential energy surfaces was carried out in both dispositions, and we found small differences between them (less than 1 kcal mol⁻¹) always favoring the *anti* form. On the other hand, Fischer thiocarbene complexes show a clear bias for the *syn* conformer, and the rotation barrier for Fischer thiocarbenes lies in the range of 15–18 kcal mol⁻¹.^{62,63} In this case, only the *syn* conformer was considered for the analysis of the reaction mechanisms.

A. Reaction Mechanisms. A.1. Uncatalyzed Aminolysis.

On the basis of the above-mentioned experimental evidence and previous ester studies, there are three main possible reaction pathways that we have considered (Scheme 1). It is important to note that we use the term “uncatalyzed” for

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TABLE 2. Relative Gibbs Free Energies with Respect to Separated Reactants (and Enthalpies in Parentheses) Expressed in kcal mol⁻¹ for Each Reaction Step and Reaction Barriers along the Zwitterionic and Catalyzed Pathway for the Aminolysis of Fischer Alkoxy and Thiocarbene Complexes in Solution Obtained at the B3LYP/Wachters&6-31+G(d,p)//B3LYP/Wachters&6-31G(d,p) Level of Theory Including Solvent Effects with the PCM[B3LYP/Wachters&6-31G(d,p)] Method^a

Uncatalyzed Zwitterionic Mechanism				
	R = Me		R = Ph	
	X = OMe	X = SMe	X = OMe	X = SMe
1-anti → 1-syn	-1.20 (-1.19)	-3.62 (-3.13)	-1.20 (+0.14)	-4.25 (-3.02)
1 + NH ₃ → TS(1→3)	18.43 (5.64)	21.08 (8.85)	20.21 (8.99)	23.98 (11.65)
1 + NH ₃ → 3	17.00 (4.86)	12.95 (0.95)	17.53 (6.28)	12.51 (0.65)
3 → TS(3→5)	23.07 (22.97)	29.05 (28.89)	22.51 (22.42)	28.34 (28.92)
3 → 5 + MeXH	-36.74 (-22.79)	-31.08 (-17.41)	-37.42 (-24.54)	-28.61 (-16.78)
1 + NH ₃ → TS(3→5)	40.07 (27.83)	42.00 (29.84)	40.04 (28.70)	40.85 (29.56)
Mechanism Catalyzed by Ammonia				
	R = Me		R = Ph	
	X = OMe	X = SMe	X = OMe	X = SMe
1 + 2NH ₃ → TS(2→4)	28.21 (6.93)	29.09 (8.84)	29.46 (8.77)	32.34 (11.51)
1 + 2NH ₃ → 4	20.80 (-1.68)	18.29 (-3.82)	20.72 (-1.76)	17.70 (-5.16)
4 → TS(4→5)	11.62 (9.56)	17.16 (16.29)	9.73 (9.15)	17.67 (17.99)
4 → 5 + NH ₃ + MeXH	-40.54 (-16.25)	-36.42 (-12.64)	-39.42 (-16.65)	-33.80 (-10.97)
1 + 2NH ₃ → TS(4→5)	32.42 (7.89)	35.45 (12.47)	30.45 (7.39)	35.37 (12.83)
	thermodynamics of the reaction			
1 + NH ₃ → 5 + MeXH	-19.74 (-17.93)	-18.13 (-16.46)	-19.90 (-18.26)	-16.10 (-16.13)

^aFor the calculation of relative energies, the most stable conformer in the gas phase was considered, i.e., *anti* conformation for alkoxy-carbenes and *syn* conformation for thiocarbene.

the processes which do not involve additional molecules of base. It is worth noting that in aqueous solution probably additional discrete molecule of solvent might assist the proton-transfer process.^{32,39,64} The first mechanism (route A) is a concerted pathway involving direct nucleophilic substitution coupled with proton transfer from the nucleophile to the leaving group. The second mechanism is a stepwise “addition/elimination” pathway (route B) without zwitterionic intermediates in which the addition and elimination steps are coupled with proton transfer to maintain neutrality in the tetrahedral intermediate. This neutral intermediate with the hydrogen atom on the metal center is postulated on the grounds of experimental works where a similar structure has been identified and even pK_a values have been determined.⁵⁷ The third (route C) is a fully stepwise pathway involving zwitterionic intermediates in which all bond-forming and breaking events occur in separate steps.

We explored these different routes but were unable to find either the neutral intermediate **7** having the hydrogen atom on the metal center or the intermediate **9** where the proton is placed on the leaving group connecting products with the zwitterionic intermediate. Consequently, the stepwise pathway without a zwitterionic intermediate (route B) was discarded as well as those pathways involving the zwitterionic complex **9**. On the other hand, we also failed to find a TS for the concerted mechanism (route A); in fact, all tested structures led to the stepwise pathway with the zwitterionic intermediate **3**.

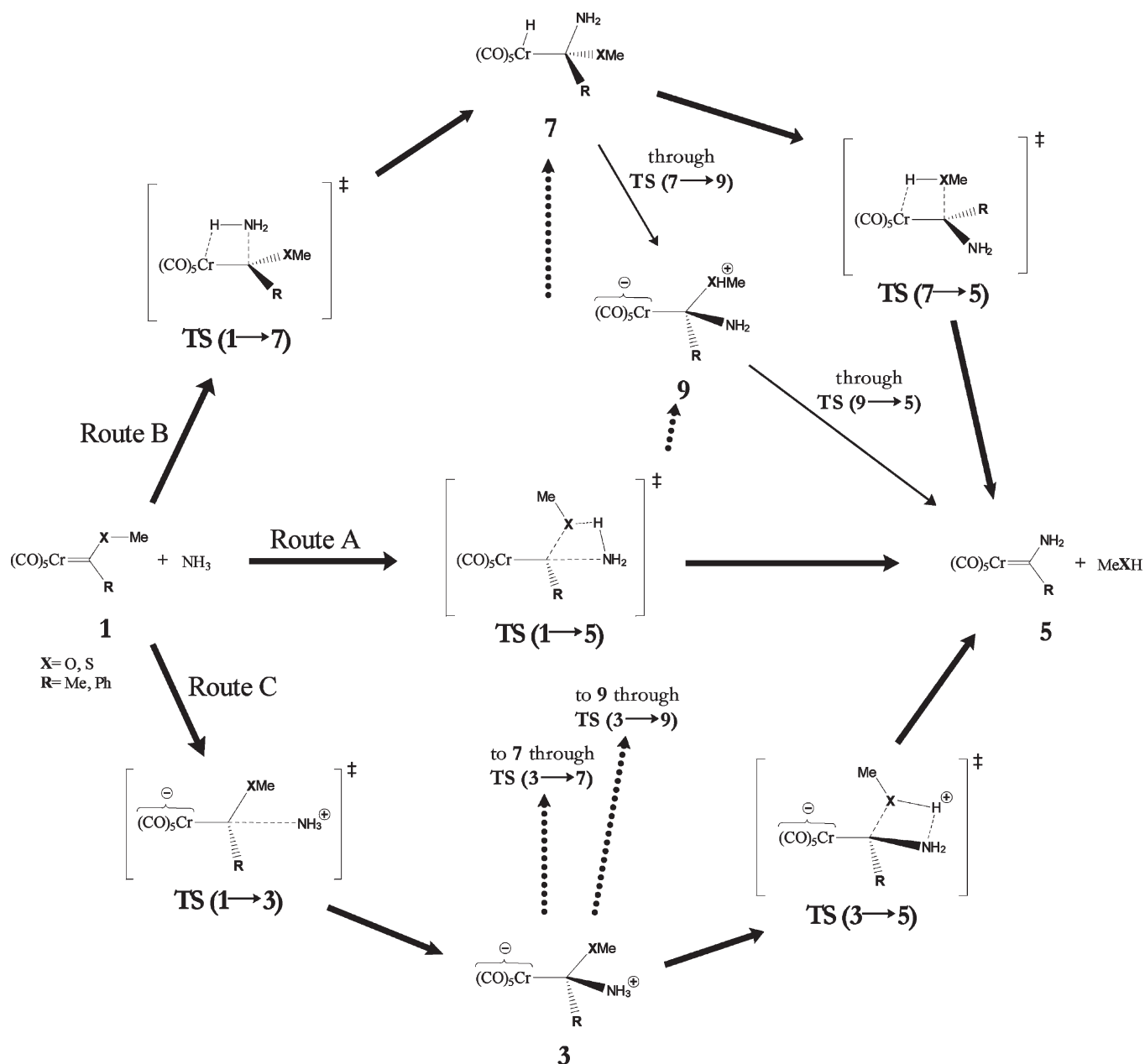
According to our calculations, the stepwise pathway with the zwitterionic intermediate **3** connected to the product **5**

through **TS(3→5)** is the only route available for the uncatalyzed aminolysis mechanism. The structures and related bond lengths along the reaction pathway of Cr-OMe-Me and Cr-SMe-Me are presented in Figures 2 and 3, respectively; the corresponding optimized structures for Cr-OMe-Ph and Cr-SMe-Ph are shown in Figures S1 and S2 of the Supporting Information.

In this stepwise case, the reaction begins with the nucleophilic attack of the ammonia molecule to the carbene carbon atom. Complex **1** and NH₃ are stabilized by an initial interaction of about 2.5 kcal mol⁻¹. However, in terms of relative Gibbs free energy, this prereactive complex is unstable with respect to reactants **1** + NH₃ by ca. 5.5 kcal mol⁻¹. The same happens for a preproduct complex that is unstable with respect to final products according to Gibbs free energies. Because of their lack of stability, these prereactive and product complexes are not particularly relevant; therefore, they are not included in the discussion. The first transition state **TS(1→3)** along the reaction coordinate possesses a tetrahedral carbon atom. As the data in Figures 2 and 3 show, in this TS the C_{carb}-N bond is almost formed (1.756 Å) and the Cr=C_{carb} bond has a length close to that of a single bond (2.257 Å) for X = O and R = Me, whereas for X = O and R = Ph the C_{carb}-N bond is significantly longer (1.930 Å) and Cr=C_{carb} bond is slightly shortened (2.242 Å). This nucleophilic attack is slightly more advanced for R = Me than for R = Ph in line with the somewhat higher π-donor character of Me as compared to Ph. In thiocarbene complexes, this TS is less advanced than in methoxycarbene as expected from the lower π-donor character of the SMe substituent as compared to OMe: the C_{carb}-N bonds are 2.079 Å and 2.139 Å and Cr=C_{carb} bonds are 2.199 Å and 2.194 Å for R = Me and Ph, respectively. The imaginary vibrational frequency

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SCHEME 1. Possible Mechanisms for Aminolysis Reaction of Fischer Thio and Alkoxycarbene Complexes: (A) Concerted Pathway; (B) Stepwise Pathway without Zwitterionic Intermediates; and (C) Stepwise Pathway with Zwitterionic Intermediates



for this TS involves the formation of the $\text{C}_{\text{carb}}-\text{N}$ bond. **TS(1→3)** leads to intermediate **3**, in which the $\text{C}_{\text{carb}}-\text{N}$ is already established (between 1.562 and 1.656 Å) and the carbene carbon is tetrahedral. These $\text{C}_{\text{carb}}-\text{N}$ bond distances are similar to those reported by Sung et al.⁴⁴ for zwitterionic complexes hydrated by five to seven water molecules in the aminolysis of phenyl acetate with ammonia. On the other hand, when the $\text{Cr}=\text{C}_{\text{carb}}$ double bond becomes single, π -back-donation from chromium to carbene carbon vanishes and stronger π -back donation from the metal to carbonyl groups appears. As a consequence, $\text{Cr}-\text{CO}$ bond distances shorten from 1.910 and 1.905 Å in **1** to 1.882 and 1.879 Å in **3** for methyl- and phenylalkoxycarbene complexes, respectively, and from 1.916 and 1.915 Å in **1** to 1.880 and 1.877 Å in **3** for methyl- and phenylthiocarbene complexes, respectively. For

the same reason, $\text{C}=\text{O}$ bond distances of the carbonyl groups lengthen from about 1.155 Å in **1** to 1.159 Å in **3**, on average. The second stage of the process is connected with the concerted proton transfer, breaking of the $\text{C}_{\text{carb}}-\text{X}$ bond, and restoration of the $\text{Cr}=\text{C}_{\text{carb}}$ bond. At the second transition state **TS(3→5)**, the reaction coordinate corresponds mainly to the proton transfer between nitrogen and oxygen or sulfur atoms, recovering the formally $\text{Cr}=\text{C}_{\text{carb}}$ double bond and shortening the $\text{C}_{\text{carb}}-\text{N}$ bond. In the **TS(3→5)** structure, thiocarbene complexes show a less advanced $\text{C}_{\text{carb}}-\text{X}$ bond cleavage than in alkoxycarbene complexes. **TS(3→5)** leads to species **5** + CH_3XH , the products of this reaction.

The computed energies in the gas phase for the stationary points found at every reaction mechanism of all the studied carbene complexes along the zwitterionic pathway are given

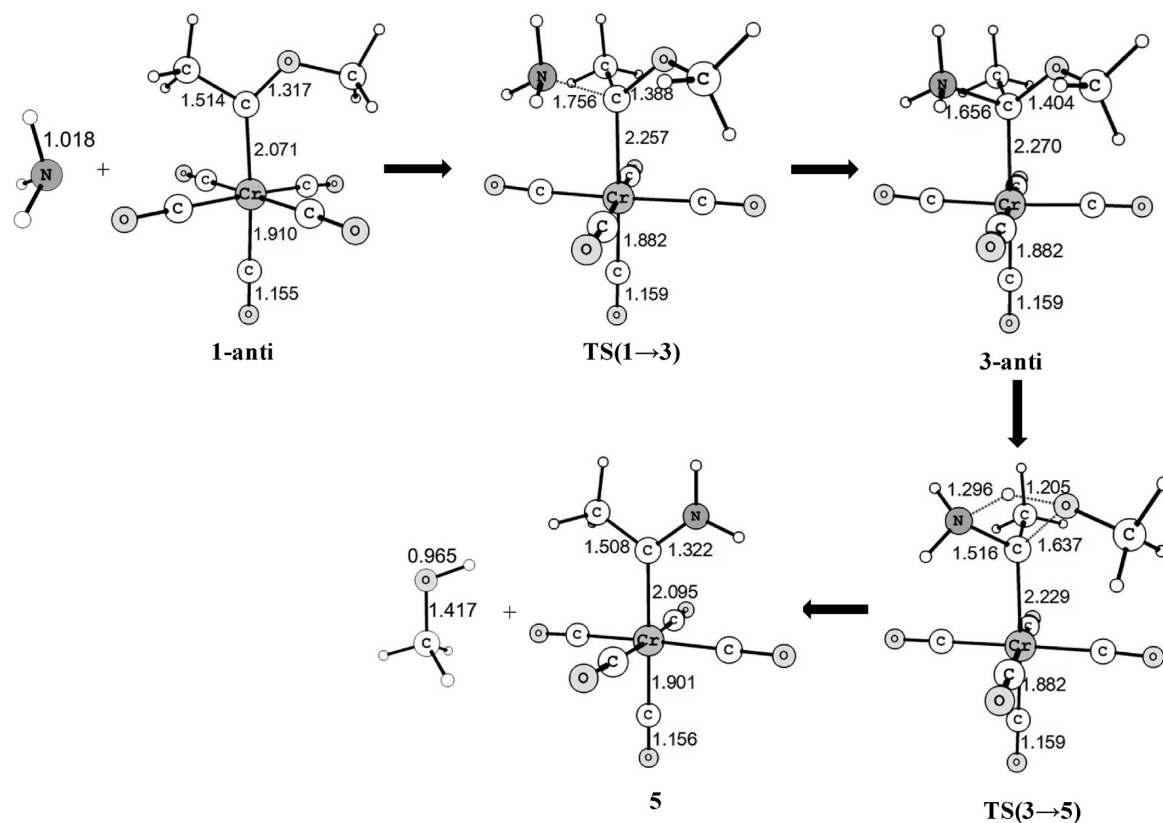


FIGURE 2. B3LYP/Wachters&6-31G(d,p)-optimized structures along the stepwise pathway with the zwitterionic intermediate for the uncatalyzed aminolysis of [methoxy(methyl)carbenepentacarbonyl]chromium(0). Values of bond distances are in angstroms.

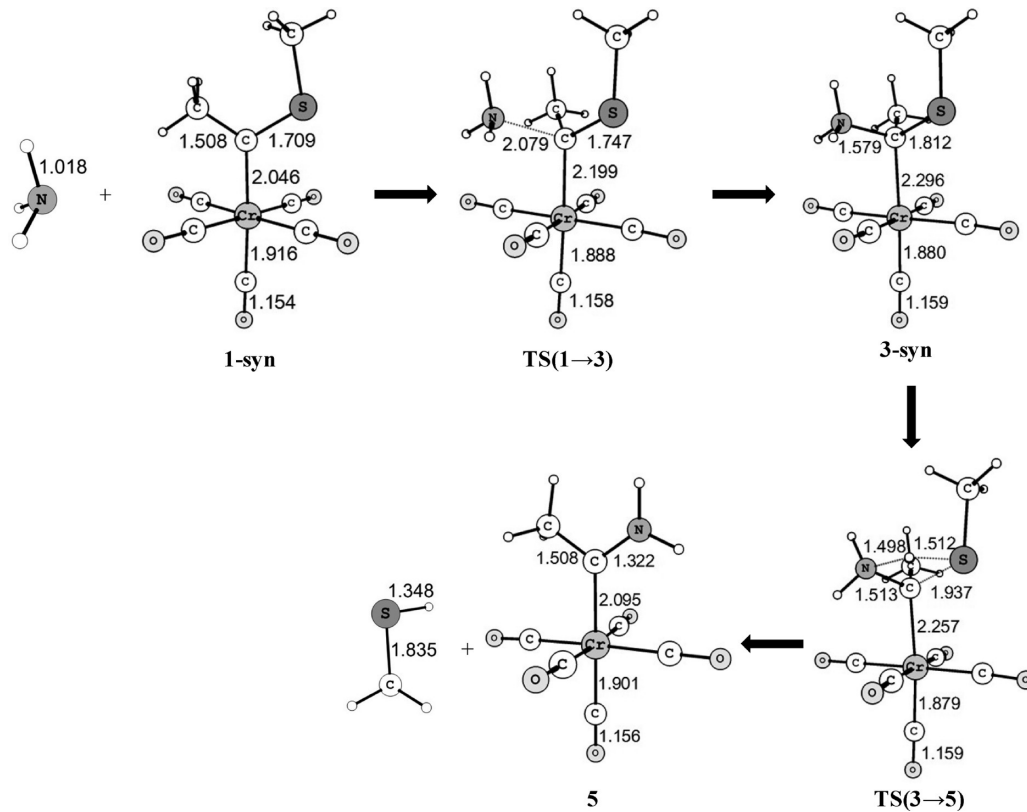


FIGURE 3. B3LYP/Wachters&6-31G(d,p)-optimized structures along the stepwise pathway with the zwitterionic intermediate for the uncatalyzed aminolysis of [thiomethoxy(methyl)carbenepentacarbonyl]chromium(0). Values of bond distances are in angstroms.

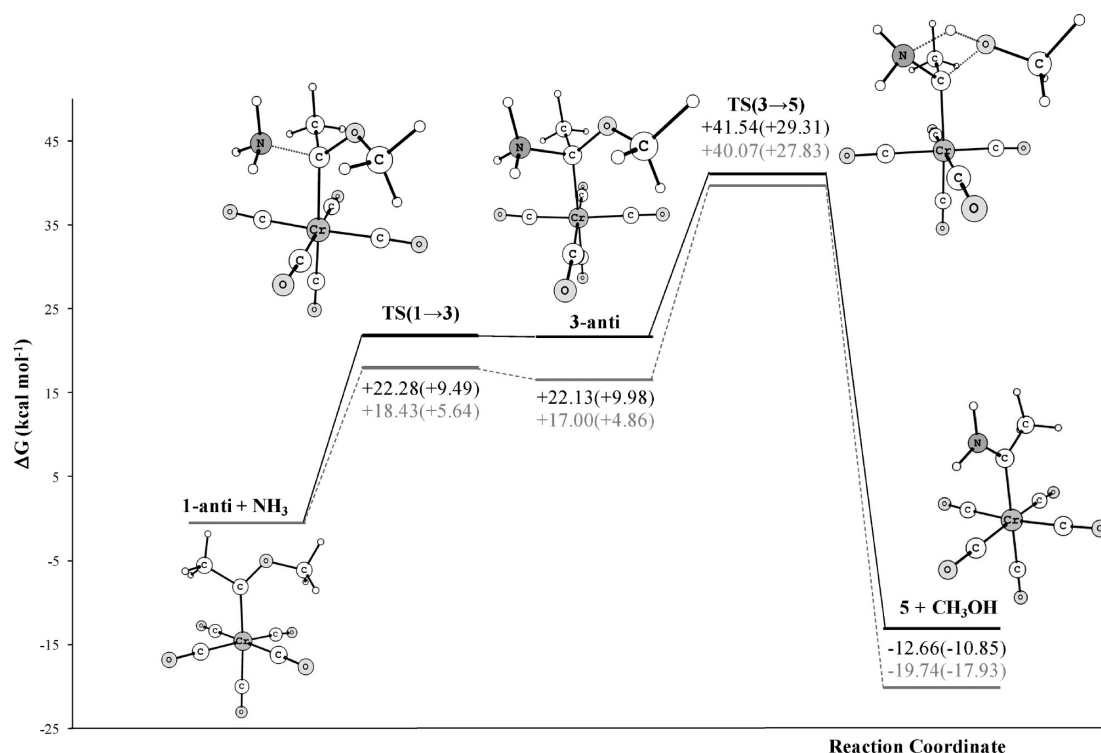


FIGURE 4. Energy profiles for the aminolysis reaction (route C of Scheme 1) of [methoxy(methyl)carbenepentacarbonyl]chromium(0). Black numbers and solid lines point to the gas-phase calculations. Gray numbers and dotted lines show those calculations with the solvent correction. Values are Gibbs free energies (and enthalpies in parentheses) given in kcal mol⁻¹.

in Table 1. We discuss first the energetics obtained in the gas phase. Solvent effects are analyzed in section B. The relative energies of the structures with respect to reactants are depicted in Figure 4 for [methoxy(methyl)carbenepentacarbonyl]chromium(0) complex and in Figure 5 for the thiocarbene analogue. Figures S3 and S4 (Supporting Information) correspond to [methoxy(phenyl)carbenepentacarbonyl]chromium(0) and [thiomethoxy(phenyl)carbenepentacarbonyl]chromium(0), respectively.

The energies of all the structures along the zwitterionic pathway exhibited in Figures 4 and 5 reveal that the first transition state, **TS(1→3)**, is predicted to have a relative Gibbs free energy that ranges from 24.09 to 21.32 kcal mol⁻¹. The Gibbs free energies for intermediate **3** formation from **1** are 22.13 and 21.88 kcal mol⁻¹ for Cr-OMe-Me and Cr-OMe-Ph (in this order), while the values for Cr-SMe-Me and Cr-SMe-Ph are 18.03 and 18.10 kcal mol⁻¹, respectively. The fact that the zwitterionic intermediate is more stable for thiocarbene complexes is a well-known consequence of the stronger π -donor character of alkoxy with respect to thiocarbene substituents: a better π -donor group leads to more effective stabilization of reactants, i.e., Fischer carbenes, which hinders nucleophilic addition.⁴ The second transition state, **TS(3→5)**, is the rate-determining step for this uncatalyzed mechanism because it has a relative Gibbs free energy with respect to separated reactants **1** + NH₃ between 40.72 and 43.34 kcal mol⁻¹. In the gas phase, intermediate **3** is not stable enough to be in thermal equilibrium with the environment. In this situation, the difference in energy between TS and separated reactants is decisive for the rate of chemical reactions. Thiocarbene complexes show a higher energy barrier for this rate-determining step due to lower basicity of the MeS⁻ as compared

to the MeO⁻ substituent. The energy profiles recomputed with the BP86 and PBE functionals as well as with the MP2 method (see Table S1, Supporting Information) show small differences between the different methods, thus providing confidence for the B3LYP results. The high energy of the **3→5** transformation is associated with an unfavorable proton transfer occurring through a TS with a highly strained four-membered ring as was expected on the basis of computational studies of esters.^{36–48} This result agrees fairly well with the experimental notion of negligible contribution of spontaneous conversion of the zwitterionic intermediate to the product (k_2 in eq 1).^{4,16} Since this activation energy is too high to explain the kinetic experiments of reaction rates observed at room temperature, this reaction might be aided by proton transfer from a second molecule of amine, a role which may either be played by a water molecule. For this reason, we decided to undertake calculations including an additional NH₃ molecule that acts as an explicit catalyst molecule.

A.2. General Base-Catalyzed Aminolysis. The experimental aminolysis of Fischer carbene complexes is usually carried out in basic amine solutions. The reaction can take place as a catalyzed process with a catalytic role for a second amine molecule or for a hydroxide anion.¹⁶ Alkoxy carbene complexes always show a general base catalysis, whereas the thiocarbene complexes depend on the amine used.²⁰ The present computational study examines the general base catalysis assisted by an additional ammonia molecule. This represents a simple model for a specific catalyst role, although a reaction mechanism involving multiple water molecules is possible.³⁹ We have analyzed three different routes (A–C) for the reaction mechanism and, also, considered a possible specific-base

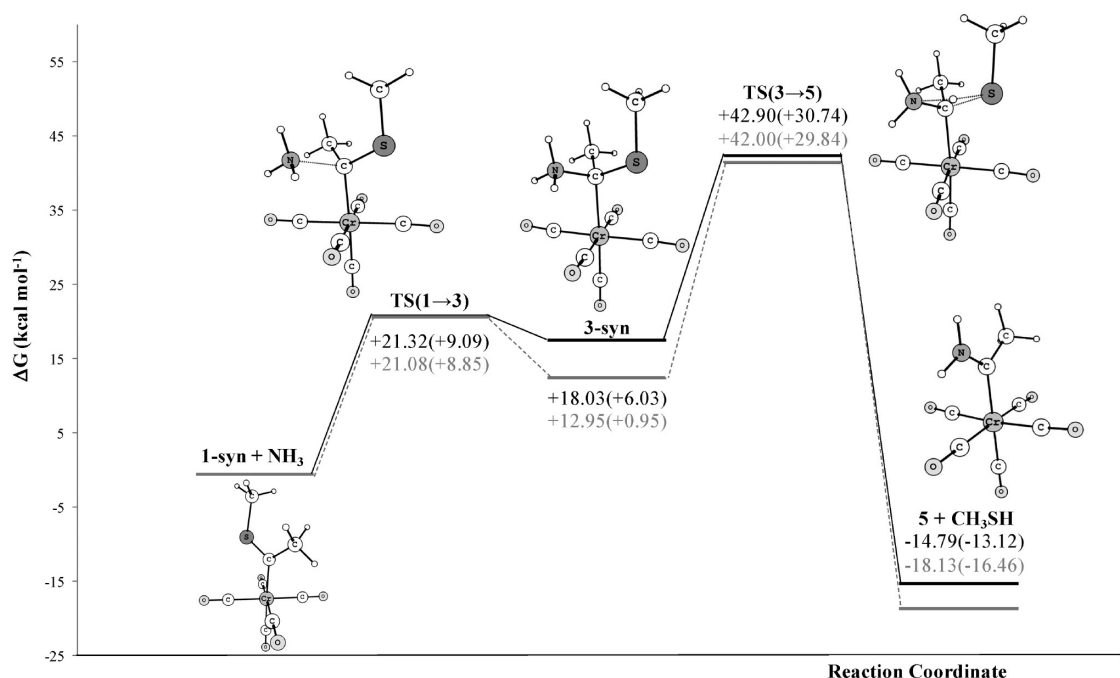


FIGURE 5. Energy profiles for the aminolysis reaction (route C of Scheme 1) of [thiomethoxy(methyl)carbenepentacarbonyl]chromium(0). Black numbers and solid lines point to the gas-phase calculations. Gray numbers and dotted lines show those calculations with the solvent correction. Values are Gibbs free energies (and enthalpies in parentheses) given in kcal mol⁻¹.

general-acid catalyzed mechanism as suggested by Bernasconi et al.¹⁶ (**4**→**11** process as sketched in Scheme 2). We have compared our results with the experimental data mentioned above and theoretical studies of ester aminolysis.⁴²

As in the case of the uncatalyzed mechanism, we were unable to find a concerted or a stepwise pathway involving a neutral species **8**. All of the structures were tested to find an intermediate where the proton is placed either on Cr (**8**) or on the leaving group MeXH (**10**) converged to intermediate **4**. Several attempts were carried out to find a mechanism with specific-base acid-general catalysis through intermediate **11**, but all of the structures converged to the stable intermediate **4**.

In order to estimate the thermodynamics of the proton transfer between zwitterionic intermediate **3** and ammonia molecules, we have performed an optimization of the involved species in the **4**→**11** transformation separately, i.e., NH₃ + **3**→NH₄⁺ + Cr-XMe-R-anion. The Gibbs free energies for this transformation are 108.81 and 102.41 kcal mol⁻¹ for Cr-OMe-Me and Cr-OMe-Ph (in this order), while for Cr-SMe-Me and Cr-SMe-Ph the values are 107.71 and 105.13 kcal mol⁻¹, respectively. These results clearly favor neutral intermediates rather than charged intermediates, as it was expected in the gas phase, and therefore, specific-base acid-general catalysis cannot be observed. This situation could be different in solution due to high stabilization of ionic species, and we have taken it into account in section B.

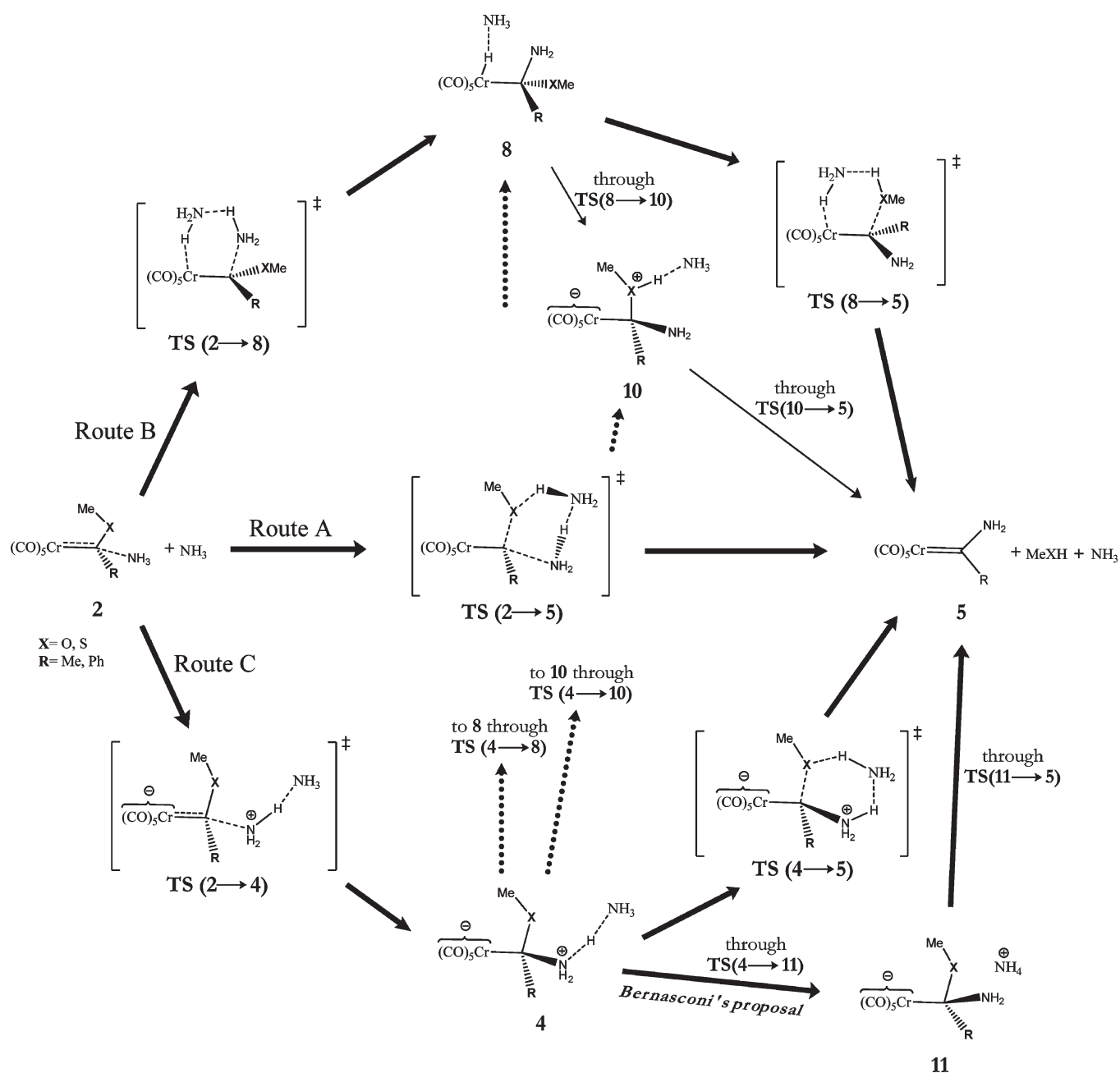
Regarding to the mechanism found, the first transition state, TS(**2**→**4**), has a reaction coordinate involving basically the C_{carb}-N bond formation, formally one of the ammonia molecules can be designated as the nucleophilic agent in the process while the second ammonia serves to assist the first one through the formed hydrogen bond (Figure 6). As discussed previously for the uncatalyzed mechanism, TS(**2**→**4**) is found to be more advanced along the reaction coordinate

in alkoxy-carbenes than in thiocarbenes. In alkoxy-carbenes, the C_{carb}-N bond is 2.134 and 2.155 Å and the Cr=C_{carb} bond is 2.195 and 2.155 Å for R = Me and Ph, respectively, while in thiocarbenes the C_{carb}-N bond is 2.273 and 2.304 Å and the Cr=C_{carb} bond is 2.171 and 2.174 Å for R = Me and Ph, in that order. This result is not unexpected given the fact that the **2**→**4** transformation is more endothermic for alkoxy-carbenes.

TS(**2**→**4**) connects with the stable intermediate **4** where the tetrahedral center of the carbene carbon is formed, i.e., C_{carb}-N bonds are about 1.54 Å. The intermediate **4** has three possible conformations depending on the isomer considered (*anti* or *syn*) and the place where the catalyst is located (*axial* or *equatorial*) that we have designed as **4-axial-anti**, **4-equa-anti**, and **4-equa-syn** (see Figure 7). Note that **4-axial-syn** cannot be obtained because the methoxy or thiomethoxy group hinders this disposition. The equatorial position has a stabilization interaction between the N-H bond of the ammonia catalyst molecule and the equatorial carbonyl group, but it also has a destabilizing steric hindrance between the leaving group and methyl or phenyl group. Which one of these conformations is the lowest in energy depends on a balance of these two effects; for instance, in thiocarbene complexes and in alkoxy-carbenes with R = Ph the intermediate **4-equa-syn** is the preferred isomer, while for alkoxy analogues when R = Me, **4-equa-anti** becomes favored. For all of the carbene complexes considered, the energy barriers for the interchange between these intermediates are about 2 kcal mol⁻¹.

The second step in the stepwise-catalyzed reaction mechanism is a subsequent breaking of the C_{carb}-X bond and simultaneous restoration of the Cr=C_{carb} double bond. The process of breaking/restoring occurs through TS(**4**→**5**), and it is accompanied by a catalyzed transfer of a proton in which the ammonia catalyst molecule takes a proton from

SCHEME 2. Postulated Reaction Mechanisms for Ammonia-Mediated Catalysis of the Aminolysis Reaction of Fischer Thio- And Alkoxycarbene Complexes: (A) Concerted Pathway; (B) Stepwise Pathway without Zwitterionic Intermediates; and (C) Stepwise Pathway with Zwitterionic Intermediates



the nucleophile and simultaneously transfers another one to the leaving group. This double proton transfer is the main component of the transition vector in $TS(4 \rightarrow 5)$. Thiocarbene complexes present $TS(4 \rightarrow 5)$ structures somewhat more advanced than alkoxycarbenes in line with the fact that the $4 \rightarrow 5$ transformation is more exothermic in alkoxycarbenes.

Like intermediate **4**, the $TS(4 \rightarrow 5)$ structure has three possible isomers (depicted in Figure 7): the most stable one depends on the same factors as intermediate **4**. All optimized structures for the most stable intermediates and TSs in the catalyzed stepwise aminolysis of Cr-OMe-Me are shown in Figure 6. The computed gas-phase relative Gibbs free energies and enthalpies for the fully optimized structures along

the stepwise pathways are given in Table 1, and the potential energy profiles are presented in Figures 8 and 9.

The energies of all the structures along the catalyzed pathway C are given in Figures 8 and 9 for $X = O$ and S and $R = Me$ (and Figures S5 and S6, Supporting Information, for $X = O$ and S with $R = Ph$). The first transition state, $TS(2 \rightarrow 4)$, has a relative energy to Fischer carbenes **1** plus two ammonia molecules that ranges from 22.75 to 26.06 kcal mol⁻¹. The relative Gibbs free energy for intermediate **4** formation with respect to separate reactants is 20.37 and 20.11 kcal mol⁻¹ for Cr-OMe-Me and Cr-OMe-Ph (in this order), while for Cr-SMe-Me and Cr-SMe-Ph is 17.05 and 17.27 kcal mol⁻¹, respectively. In the gas phase and under low-pressure

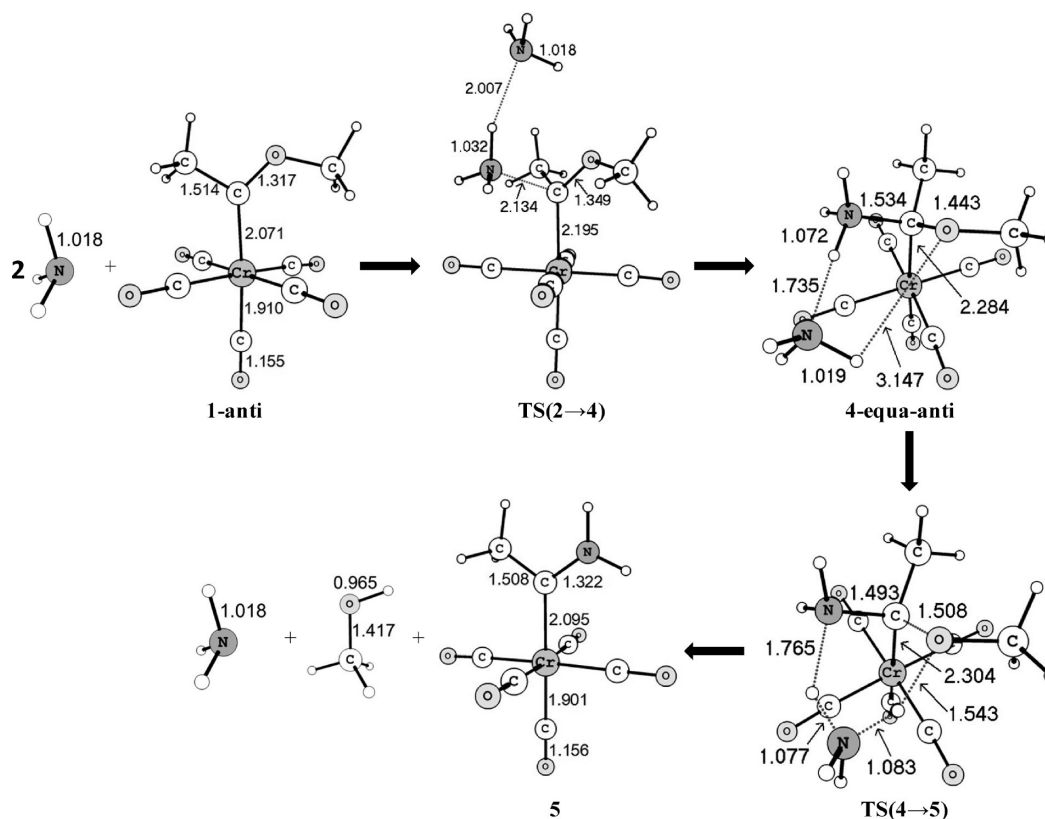


FIGURE 6. B3LYP/Wachters&6-31G(d,p)-optimized structures along the stepwise pathway (route C of Scheme 2) for the catalyzed aminolysis of [methoxy(methyl)carbenepentacarbonyl]chromium(0). Values of bond distances are in angstroms.

conditions, the second transition state, **TS(4→5)**, is the rate-determining step for this mechanism with Gibbs free energy barriers between 30.16 and 32.39 kcal mol⁻¹. In this case, **TS(4→5)** is predicted to have a higher Gibbs free activation energy than the first step (from 6.33 to 9.11 kcal mol⁻¹). However, in a high-pressure regime where molecular collisions are efficient enough to cool the otherwise rovibrationally hot reactant complex **4**, causing it to be in thermal equilibrium with the environment, then the Gibbs free energy barrier for the nucleophilic attack (energy difference between **TS(2→4)** and **1**, step **1→4**) is higher than for the second step corresponding to the breaking of the C_{carb}-X bond and simultaneous restoration of the Cr=C_{carb} bond (energy difference between **TS(4→5)** and **4**, step **4→5** + NH₃ + MeXH) and the nucleophilic attack becomes rate-determining. In this latter case, since differences in energy barriers between the two steps are not very large, the possibility that stronger nucleophilic amines lead to a change in the rate-determining step cannot be ruled out.

When comparing the uncatalyzed and the catalyzed version of the aminolysis (for instance, compare Figures 4 and 8), we find that in the first TS corresponding to the nucleophilic attack, the relative Gibbs free energy as compared to separated reactants is slightly higher (by ca. 2 kcal mol⁻¹) for the catalyzed mechanism (**TS(2→4)**) than for the uncatalyzed one (**TS(1→3)**), but in terms of enthalpy **TS(2→4)** is favored by 6–8 kcal mol⁻¹ with respect to **TS(1→3)**. Moreover, when the ammonia molecule is included, the second TS involving a proton transfer, **TS(4→5)**, becomes significantly lower in energy than **TS(3→5)** of the uncatalyzed mechanism by

9.33 to 10.56 kcal mol⁻¹ in alkoxy-carbenes and by 11.04 to 10.95 kcal mol⁻¹ in thiocarbenes. In fact, the role of the catalyst in the process is to facilitate the proton transfer through a less strained six-membered ring in the TS. The second step is predicted to be the rate-determining step in low-pressure gas-phase regime but the difference becomes smaller. However, at high pressure the predicted rate-determining step is the nucleophilic attack.

It is interesting to note how different the reactivity of esters is with respect to Fischer carbene complexes. All computational studies^{36–40,42,44,45,47,48,65} mentioned in the Introduction have found that the most probable pathway for aminolysis of esters and thioesters is the concerted pathway via a neutral intermediate (paths A and B in Schemes 1 and 2) for both uncatalyzed and catalyzed mechanisms. On the other hand, aminolysis in Fischer carbene complexes proceed through zwitterionic intermediates both for uncatalyzed and catalyzed mechanisms. This seems to be due to the great stability of the zwitterionic intermediate in Fischer carbenes given by the delocalization of the negative charge into Cr(CO)₅ moiety (this charge is stabilized by π -acids such as CO), as compared to the esters and thioesters chemistry. Our results are in agreement with a reaction mechanism through a zwitterionic intermediate; however, we failed in finding a conversion by means of an anionic intermediate

(65) (a) Marlier, J. F.; Haptonsall, B. A.; Johnson, A. J.; Sacksteder, K. A. *J. Am. Chem. Soc.* **1997**, *119*, 8838. (b) Adalstensson, H.; Bruce, T. C. *J. Am. Chem. Soc.* **1998**, *120*, 3440. (c) O'Hair, R. A. J.; Androutsopoulos, N. K. *Org. Lett.* **2000**, *2*, 2567. (d) Kim, C. K.; Li, H. G.; Lee, H. W.; Sohn, C. K.; Chin, Y. I.; Lee, I. J. *Phys. Chem. A* **2000**, *104*, 104.

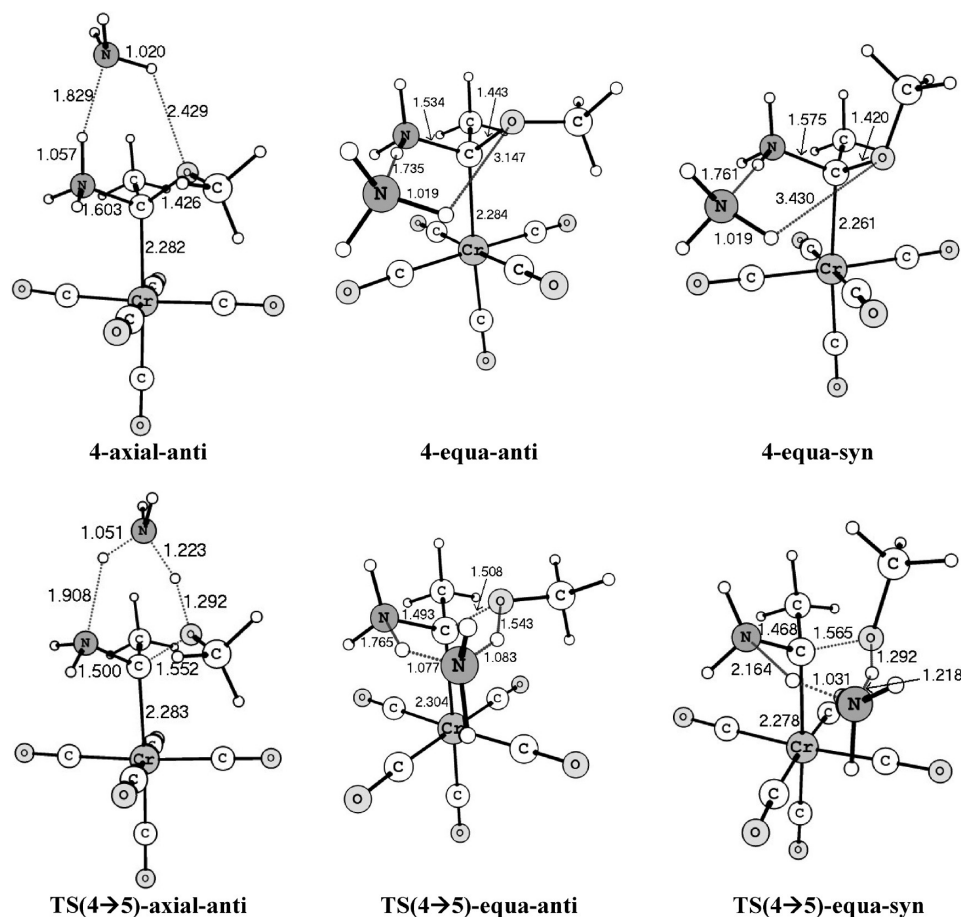


FIGURE 7. Different conformations adopted by the amino-catalyzed amino(methoxy)methylene chromium(0) complex **4** (up) and the associated transition states (down) involved in the general base catalysis reaction mechanism calculated at B3LYP/Wachters&6-31G(d,p) level of theory. Values of bond distances are in angstroms.

Cr-XMe-R-anion (process **4**→**11**) and therefore a general base catalysis mechanism proposed by Bernasconi.¹⁶

B. Solvent Effects. Experimentally, the aminolysis reaction is often accomplished in solution, so it is of great interest to study the influence of the solvent effects on the energy barriers and how this affects the reaction mechanism. A 50% acetonitrile–50% water mixture, which is the most often used in kinetic experiments, was chosen as the solvent.⁴ Table 2 collects the relative Gibbs free energies and enthalpies of the uncatalyzed and catalyzed mechanisms in solution. In addition, the potential energy profiles are also represented in Figures 4 and 5 for the uncatalyzed mechanism and Figures 8 and 9 for the catalyzed mechanism. It is worth mentioning here that the entropic contributions *in solution* may be somewhat overestimated since we have calculated them in the gas phase.⁶⁶ This may artificially slightly favor dissociative processes in solution.

Regarding the uncatalyzed reaction mechanism (zwitterionic species, route C in Scheme 1), the results reveal different behaviors for methoxy- and thiomethylcarbene complexes. As expected, the presence of the polarizable dielectric simulating the solvent substantially decreases the relative Gibbs

free energy of the zwitterionic intermediate **3** for both carbenes. Relative Gibbs free energy of **TS**(**1**→**3**) with respect to separated reactants decreases by 3.85 and 1.47 kcal mol^{−1} when R = Me and Ph in methoxycarbenes in that order and by 0.24 and 0.10 kcal mol^{−1} in thiocarbenes in that order of substituents too. In addition, Gibbs free reaction energies for **1** + NH₃ → **3** process become less endergonic, decreasing by 5.13 and 4.35 kcal mol^{−1} in methoxycarbenes and by 5.08 and 5.59 kcal mol^{−1} in thiomethylcarbenes for R = Me and Ph, respectively. Both reductions of Gibbs free energy barriers and decrease of the endothermicity for the **1** + NH₃ → **3** conversions due to the presence of the solvent are expected because of the build-up of charge separation along the process. Interestingly, the reduction of the barrier for the ammonia insertion into the carbene carbon is larger for the methoxy- than for the thiocarbenes as a result of the TS in methoxycarbenes being structurally late and, therefore, the charge separation more advanced. On the other hand, differences in the relative Gibbs free energies of **TS**(**3**→**5**) are minor. The rate-determining step for the uncatalyzed mechanism corresponds to the proton transfer and simultaneous expulsion of the MeXH group.

In the mechanism catalyzed by ammonia (Figures 8 and 9 and Figures S5 and S6, Supporting Information), solvent effects lead to different results when compared with those of the uncatalyzed mechanism. Thus, for the first step (**1** + 2NH₃ → **4**), the

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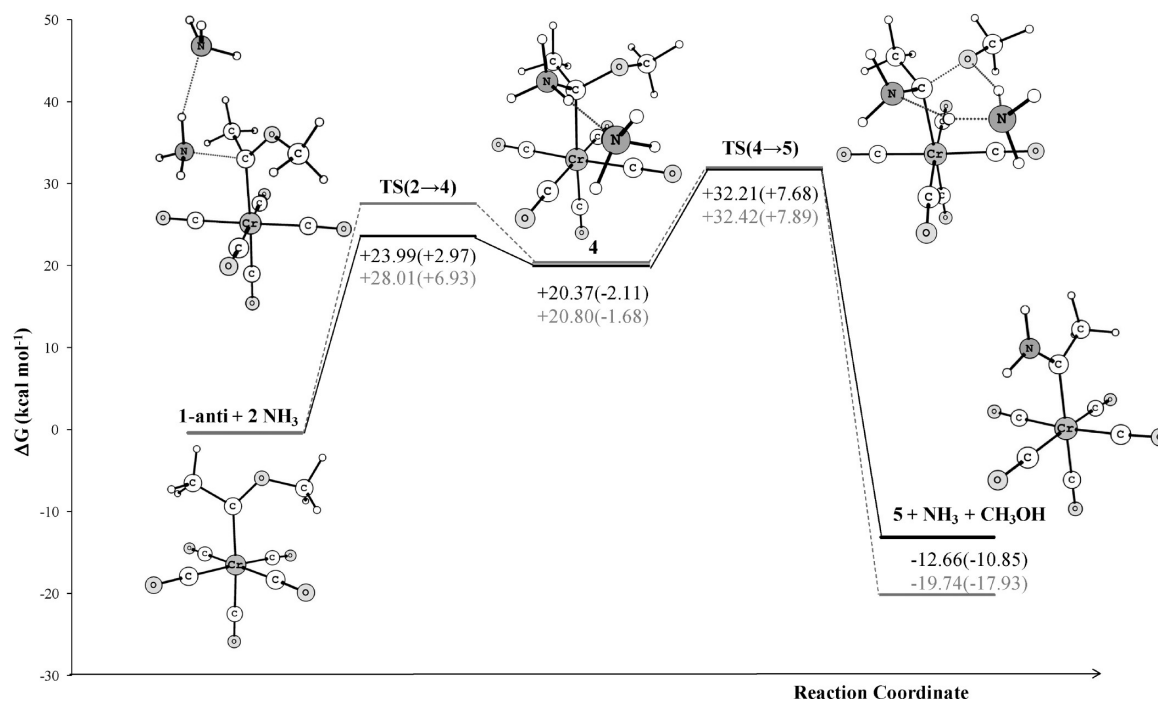


FIGURE 8. Energy profiles for the catalyzed aminolysis reaction of [methoxy(methyl)carbenepentacarbonyl]chromium(0), where the energy of the more favorable conformation of complex 4 and its associated TS is displayed. Black numbers and solid lines point out to the gas-phase calculations. Gray numbers and dotted lines show those ones with the solvent correction. Values are Gibbs free energies (and enthalpies in parentheses) given in kcal mol⁻¹.

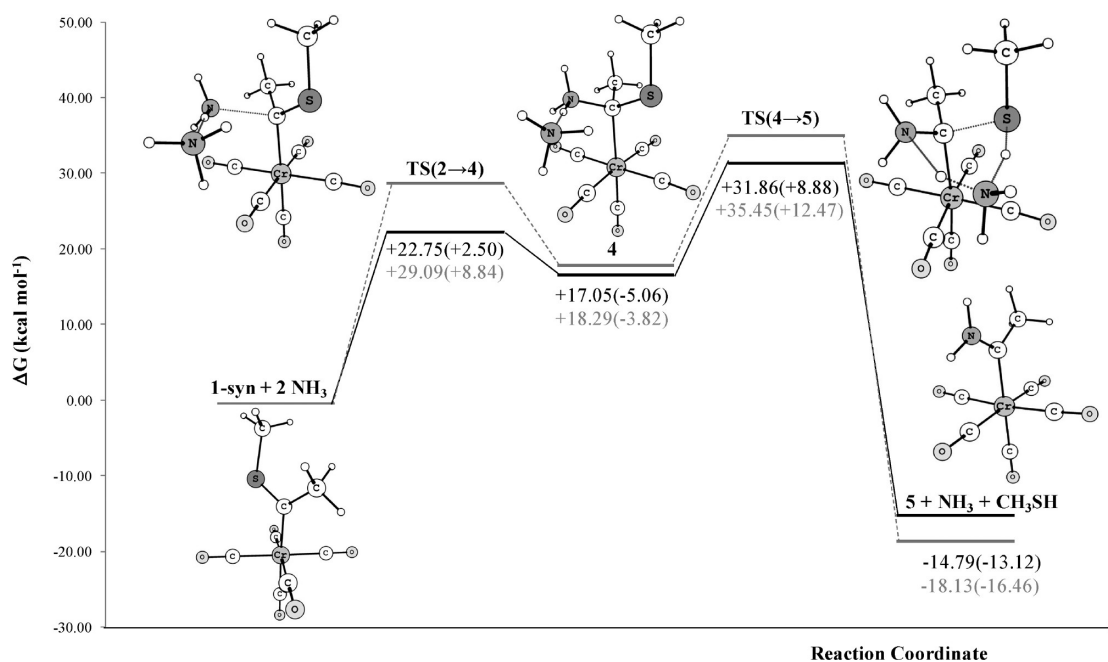


FIGURE 9. Energy profiles for the catalyzed aminolysis reaction of [thiomethoxy(methyl)carbenepentacarbonyl]chromium(0), where the energy of the more favorable conformation of complex 4 and its associated TS is displayed. Black numbers and solid lines point out to the gas-phase calculations. Gray numbers and dotted lines show those ones with the solvent correction. Values are Gibbs free energies (and enthalpies in parentheses) given in kcal mol⁻¹.

results show that relative Gibbs free energies of **TS(2→4)** increase by 4.02 and 6.61 kcal mol⁻¹ for alkoxycarbene with R = Me and Ph (in this order) and by 6.34 and 6.28 kcal mol⁻¹ for thiocarbene, in the same order of R groups. This effect is a consequence of placing the second ammonia molecule to

assist the nucleophilic insertion of the first one that leads to a less advanced TS and therefore to less charge separation in this TS. It is important to note that the solvent Gibbs free energy correction favors **TS(1→3)** and disfavors **TS(2→4)**. Thus, in solution and at variance with the gas phase, the

catalyzed nucleophilic attack has higher energy requirements than the corresponding uncatalyzed pathway. On the other hand, the solvent slightly destabilizes zwitterionic complex **4** from 0.43 to 1.24 kcal mol⁻¹, making it more endergonic than the **1** + 2NH₃ → **4** process. With respect to the relative Gibbs free energy of **TS(4→5)**, solvent effects slightly increase its value by 0.21 and 0.29 kcal mol⁻¹ (R = Me and Ph, respectively) for alkoxycarbenes, whereas the values are clearly decreased by 3.59 and 2.98 kcal mol⁻¹ for thiocarbenes. Thiocarbenes present more destabilization than alkoxycarbenes due to the sluggish character of the leaving group leading to a less charge separation in the zwitterionic-like structure.

Thermodynamics of the whole **1** + NH₃ → **5** + MeXH conversion is favored by 7.08 and 6.38 kcal mol⁻¹ for methoxycarbenes and 3.34 and 3.59 kcal mol⁻¹ for thiomethylcarbenes (R = Me and Ph, in that order of carbenes) when solvents are taken into account. To determine the rate-determining step in solution, we have to compare the Gibbs free energy differences of the **1** + NH₃ → **TS(1→3)** and **4** → **TS(4→5)** steps because intermediate **4** is stable enough in solution to be in thermal equilibrium with the environment. Therefore, in solution the nucleophilic attack becomes the rate-determining step at high amine concentration for the aminolysis reaction. These results are in agreement with the general kinetics observation of a change in rate-limiting step from amine and OH⁻ catalyzed leaving group departure at low amine and OH⁻ concentrations to the nucleophilic attack at high amine and/or OH⁻ concentrations.^{16,17,22} Moreover, predicted energy barriers are consistent with the kinetic parameter for the zwitterionic intermediate collapse (i.e., k_{-1} and k_3^A from eq 1).^{18,20,57}

However, our result implies the operation of two steps and the presence of one intermediate; this result clearly disagrees with the nature of base catalysis proposed by Bernasconi et al.¹⁶ Although attempts have been made, no other possible TS or intermediate on the potential energy surface has been located. Thus, we have analyzed the possible specific-base general-acid catalyzed mechanism suggested as a rapid acid–base equilibrium between zwitterionic intermediate and its conjugated anion (process **4** → **11**, Scheme 2). In solution, Gibbs free energies for the **4** → **11** transformation (Scheme 2) computed with the gas-phase optimized geometries are exergonic by -12.29 and -7.29 kcal mol⁻¹ for alkoxy carbenes with R = Me and Ph (in this order) and -11.23 and -10.94 kcal mol⁻¹ for thiocarbenes with R = Me and Ph. Thus, Fischer carbene complexes could undergo specific-base general-acid catalysis, although our gas-phase optimizations do not allow finding this pathway. Therefore, we carried out a full optimization for this step in solution. Unfortunately, we were unable to find intermediate **11** and the connecting transition states **TS(4→11)** and **TS(11→5)** in solution. All attempts to optimize these structures led to intermediate **4** or product **5**. Because of the inability to find a specific-base general-acid catalysis mechanism, we estimated the energy of the proton transfer NH₃ + **3** → NH₄⁺ + **Cr-XMe-R-anion**. With the optimized structures in solution, the computed Gibbs free energies at PCM[B3LYP/Wachters&6-31G(d,p)] level reveal that the NH₃ + **3** → NH₄⁺ + **Cr-XMe-R-anion** process is disfavored thermodynamically. The values obtained are 12.70 and 9.71 kcal mol⁻¹ for alkoxy carbenes with R = Me and Ph (in this order) and 12.73 and 11.72 kcal

mol⁻¹ for thiocarbenes with R = Me and Ph. It is important to remark that this latter result does not match with the experimental suggestion where for Fischer carbene complexes the pK_a of zwitterionic intermediate is likely to be somewhat lower than the pK_a of the respective NH₄⁺, which would make the proton transfer from **3** to NH₃ thermodynamically favorable.¹⁶ This is probably a consequence of the simplicity of the solvation model used.

These results seem to indicate that there is no specific-base general-acid catalysis in solution and that the concerted base catalysis is the operative mechanism of the aminolysis of Fischer carbenes in the gas phase and in solution. A possible explanation for this disagreement might be that our model reaction with NH₃ is not extensible to the process involving primary, secondary, or tertiary amines. The fact that tertiary amines, which have no transferable proton, are even more active than NH₃ as general base catalysts serves to rule out a cyclic transition state, such as **TS(4→5)**,²⁸ at least for the aminolysis of tertiary amines.

Conclusions

We have investigated the aminolysis reaction on penta-carbonylchromium methoxy- and thiomethylcarbenes in order to better understand the chemistry between these two different kinds of metal carbenes and the effect of two different R substituents. We found that for both gas phase and solvent calculations, the reaction mechanisms support the plausibility of a stepwise reaction where zwitterionic species are involved.

Between the two explored reaction pathways, namely the uncatalyzed and the ammonia-assisted routes, we found that in solution the last one is favored by 7.65 and 9.59 kcal mol⁻¹ (alkoxycarbenes methyl and phenyl group, respectively) and by 6.55 and 5.48 kcal mol⁻¹ (thiocarbenes methyl and phenyl group, respectively). The reason is the six-membered rings formed in the TS structures for the catalyzed process that are less strained and more stable than four-membered rings present in the case of uncatalyzed aminolysis.

Our results indicate that at lower pressure gas-phase conditions the rate-determining step is the concerted proton transfer and MeXH elimination. Thiocarbene complexes show a higher energy barrier for this rate-determining step due to lower basicity of the MeS⁻ substituent. At higher pressure or in solution, however, the rate-determining step corresponds to the initial nucleophilic attack. For this attack, the transition state is more advanced and has a higher barrier for alkoxycarbene than thiocarbene complexes due to the stronger π -donor character of the alkoxy group that reduces the electrophilicity of the attacked carbene atom making the nucleophilic attack more difficult. Finally, it has been found that in solution the uncatalyzed nucleophilic attack has somewhat lower energy requirements than the catalyzed one.

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Supporting Information Available: B3LYP/Wachters&6-31G(d,p)-optimized structures along the stepwise pathway with the zwitterionic intermediate for the uncatalyzed aminolysis of [methoxy(phenyl)carbenepentacarbonyl]chromium(0) and [thiomethoxy(phenyl)carbenepentacarbonyl]chromium(0), energy profiles for the uncatalyzed and catalyzed aminolysis reaction of [methoxy(phenyl)carbenepentacarbonyl]chromium(0) and [thiomethoxy(phenyl)carbenepentacarbonyl]-

chromium(0), a table containing relative energy barriers for the uncatalyzed zwitterionic mechanism of the aminolysis of [methoxy(methyl)carbenepentacarbonyl]chromium(0) and the corresponding thiocarbene complexes in the gas phase computed with the BP86 and PBE functionals and the MP2 method, complete reference 49, and Cartesian coordinates (in Å) and total B3LYP/Wachters&6-31+G(d,p)//B3LYP/Wachters&6-31G(d,p) and PCM[B3LYP/Wachter&6-31G(d,p)] energies (in au, noncorrected zero-point vibrational energies included) of all the stationary points discussed in the text. This material is available free of charge via the Internet at <http://pubs.acs.org>.