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Deciphering the Differences in Ambident Reactivity between the Cyanate, Thiocyanate Ions, and their P- and As-Containing Analogues

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Abstract: Although the cyanate and thiocyanate anions belong to the most known textbook examples of ambident nucleophiles, the electronic factors that determine their markedly differing reactivities are still unclear. The recently discovered P- and As-containing [PCX][−] and [AsCX][−] analogues (X: O, S, Se), whose ambident nature is practically unexplored, may serve as ideal basis for comparison to clarify these differences. This study presents comprehensive theoretical investigations on the nucleophilic behaviours of the whole set of so far known [ECX][−] (E: N, P, As, X: O, S, Se) anions, aiming for a systematic understanding of the reactivity patterns and identifying the factors that govern the nucleophilic substitutions. The results indicate that the S_N2 reactions of the O-containing [ECO][−] ions are thermodynamically

preferred at the pnictogen centres E, while the kinetic contributions are only substantial for the N-containing [NCX][−] anions. The ambident reactivities of the congeners that contain N or O significantly differ from those with P, As, S, or Se heteroatoms, in line with the inert s-orbital effect, characteristic for the heavier elements. By analysing the electronic structures and bonding patterns of the anions and relevant transition state structures, clear explanations are offered for the differing reactivities of the whole set of [ECX][−] anions. To serve for synthetic investigations, possible outcomes of nucleophilic substitutions are predicted, and the target molecules are expected to be versatile and useful synthons.

Introduction

Ambident nucleophiles, species that can undergo the same type of chemical transformations at two (or more) reacting sites with the same electrophile, have an unquestionably important role in several aspects of organic synthesis.^[1–5] Investigations aiming for a deeper understanding of ambident reactivity are crucial for developing and controlling new regioselective or even regiospecific reactions.^[6–14]

Unquestionably, the cyanate [NCO][−] and thiocyanate [NCS][−] anions are among the most known textbook examples of ambident nucleophiles,^[15–17] and their ambident behaviours can be well represented by two leading resonance structures (Figure 1A). Their Se-containing analogue, the selenocyanate, [NCSe][−] anion, is also known but lesser explored.^[17] Organic (thio)cyanates and iso(thio)cyanates [R–X–C≡N, and R–N=C=X,

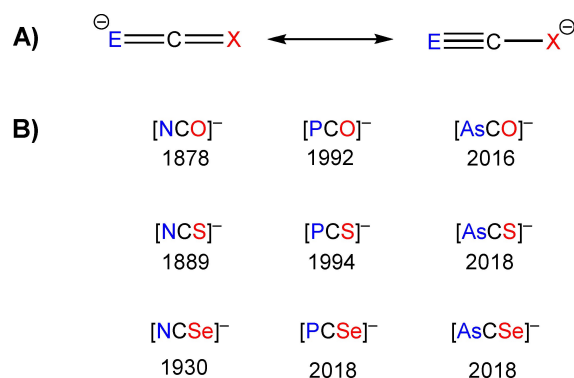


Figure 1. (A) The leading resonance structures contributing to the electronic structures of the [ECX][−] anions and (B) the investigated anions with the years of their first experimental documentations.

respectively; X: O, S] accessed using the ambident character of the [NCO][−] and [NCS][−] anions have important roles in industry and medicinal chemistry.^[18–22] While the cyanate ion typically leads to the formation of the isocyanate isomer (R–N=C=O) due to its higher thermodynamic stability; from the [NCS][−] ion, thiocyanate isomers (R–S–C≡N) can be accessed under kinetic control. Although the versatile reactivity patterns of the [NCO][−] and [NCS][−] anions have thoroughly been investigated both experimentally and theoretically, these two anions are still in the focus of ongoing research, and the origin of the reactivity differences is not fully understood yet.^[23–25]

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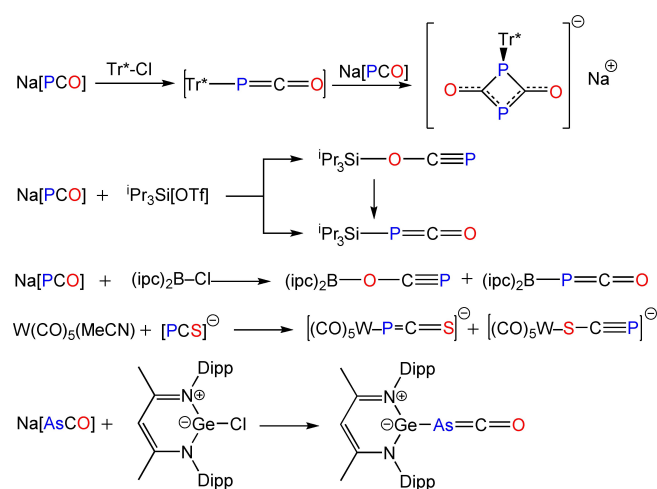
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During the past decade, the P-containing analogue of cyanate anion, the phosphaeethynolate, $[\text{PCO}]^-$ anion, first reported by Becker et al.^[26] (Figure 1B), has also attracted significant interest,^[27–44] accelerated by the recent development of straightforward synthetic methods leading to the sodium salt of this anion.^[45] Indeed, the chemical reactivity of the $[\text{PCO}]^-$ anion has been explored extensively: In general, the $[\text{PCO}]^-$ anion can participate in various reactions, including cycloadditions, P⁺-transfer reactions, and nucleophilic substitutions (S_N).^[46–48]

To our knowledge, only one study deals delicately with nucleophilic substitutions toward C-centred electrophiles (Scheme 1): The $[\text{PCO}]^-$ anion has been shown to react exclusively on its P centre with simple organic electrophiles, such as $^i\text{Pr}-\text{I}$ or Tr^*-Cl ($\text{Tr}^* = 4,4',4''\text{-trimethoxytriphenylmethyl}$); however, the initially formed phosphaketenes undergo subsequent cycloaddition reactions.^[49] Later, the ambident character of the $[\text{PCO}]^-$ ion was proven by its reaction with $^i\text{Pr}_3\text{Si}-\text{OTf}$: At room temperature, this reaction leads predominantly to the O-silylated kinetic product, $^i\text{Pr}_3\text{Si}-\text{O}-\text{C}\equiv\text{P}$, which then isomerises to the thermodynamically favoured P-silylated product ($^i\text{Pr}_3\text{Si}-\text{P}=\text{C}=\text{O}$).^[50] A further example for the parallel detection of both possible isomers was achieved using a boryl chloride [$(\text{ipc})_2\text{B}-\text{Cl}$, $\text{ipc} = \text{diisopinocampheyl}$].^[51] Although in most cases, the phosphaketene ($\text{R}-\text{P}=\text{C}=\text{O}$) isomers are observed exclusively, oxyphosphaealkynes ($\text{R}-\text{O}-\text{C}\equiv\text{P}$) have also been accessed, especially with rather oxophilic electrophiles (e.g. in actinide and lanthanide complexes or with boryl electrophiles).^[52–55] The S_N reactions involving the $[\text{PCO}]^-$ ion in the initial steps of synthetic processes enabled straightforward access toward a plethora of interesting species representing unique bonding features or electronic structures: the first room-temperature-stable singlet phosphinidene,^[56] cyaphido-,^[57] and Grignard-type complexes,^[31] as well as a variety of P-containing heterocycles,^[42,49,51,58,59] radicals^[43] and biradicaloids.^[60]

In stark contrast to the $[\text{PCO}]^-$ anion, the chemical properties of further $[\text{ECX}]^-$ analogues with E: P, As and X: S, Se are lesser known. Plausibly, the main reason for this fact is that most of these anions have only been accessed in the past few years (Figure 1B),^[61–63] typically using procedures, similar to those reported for the $[\text{PCO}]^-$ anion: The $[\text{PCS}]^-$ anion was discovered shortly after the $[\text{PCO}]^-$ congener already three decades ago,^[61] but recently a more convenient route to the $\text{K}[\text{PCS}]$ salt was developed by the Goicoechea group.^[64] The synthesis of the even heavier Se- and As-containing analogues have only been described recently.^[62,63,65] Among these anions, to the best of our knowledge, exclusively the $[\text{PCS}]^-$ and $[\text{AsCO}]^-$ anions were subjects of reactivity studies.^[64] The coordination of the $[\text{PCS}]^-$ anion toward tungsten pentacarbonyl resulted in the formation of both possible isomers, the P- and the S-coordinated species, in a nearly equimolar ratio. Interestingly, the $[\text{PCS}]^-$ anion can even coordinate in an η^3 fashion involving all three centres, as recently demonstrated for a lanthanum(III)-complex.^[66] The $[\text{AsCO}]^-$ anion paved the way to several metal-complexes ($[\text{M}]-\text{As}=\text{C}=\text{O}$) via salt metathesis reactions,^[67,68] and this anion also reacts at its As centre both with a stannylene and a germylene.^[65,69] Apart from the $[\text{PCO}]^-$, $[\text{PCS}]^-$ and $[\text{AsCO}]^-$ ions, the reactivity patterns (including nucleophilic substitutions) of the remaining analogues, namely the $[\text{PCSe}]^-$, $[\text{AsCS}]^-$ and $[\text{AsCSe}]^-$ ions are practically unexplored using synthetic techniques; only theoretical or spectroscopic studies on their electronic structures are available.^[70–72] Nevertheless, all of the “exotic” anions denoted with the general formula $[\text{ECX}]^-$ (where E: P, As and X: O, S, Se) can be envisioned as useful synthetic synthons.

Knowing the well-documented ambident characters of the $[\text{NCO}]^-$ or $[\text{NCS}]^-$ ions and the promising results obtained previously with the $[\text{PCO}]^-$ anion, it is reasonable to hypothesise that the heavier congeners can also serve as potential ambident nucleophiles. The recent developments in this field prompted us to systematically explore the possible ambident characters of all the P- and As-containing analogues accessed successfully so far (Scheme 1). One of the main goals of this study is to compare the $[\text{ECX}]^-$ anions by understanding the factors that affect the outcomes of their $\text{S}_\text{N}2$ reactions through the activation barriers. In addition, although the $[\text{NCO}]^-$ and $[\text{NCS}]^-$ anions were extensively studied in the past, the fundamental differences between them are yet to be fully understood. Thus, expanding the scope of ambident reactivity toward the heavier analogues may lead to a two-dimensional comparison of the E and X centres and shed light on the relationship between these $[\text{ECX}]^-$ anions. Not only will our results enable us to predict the outcomes of these nucleophilic substitutions, but the differences in the electronic properties of the investigated anions can also be reconned.



Scheme 1. Selected examples for previously reported nucleophilic reactivities of the $[\text{PCO}]^-$, $[\text{PCS}]^-$ and $[\text{OCAs}]^-$ anions.^[49–51,64,65] ($\text{Tr}^* = 4,4',4''\text{-trimethoxytriphenylmethyl}$, $\text{ipc} = \text{diisopinocampheyl}$, $\text{Dipp} = 2,6\text{-diisopropylphenyl}$)

Results and Discussion

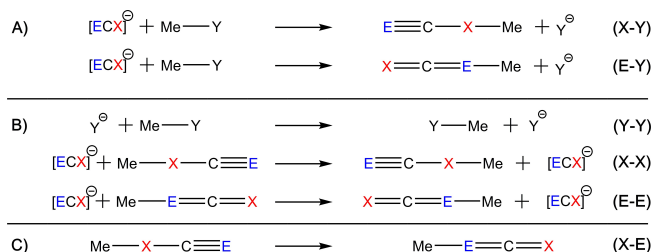
1. Methodology

Although the HSAB (Hard and Soft Acids and Bases) concept proposed by Pearson,^[73–75] targeting explanations and predictions for ambient nucleophilicity, is widely employed due to its simplicity and easy applicability in many cases, several criticisms have been formulated over the years.^[76–82] Indeed, this simple concept fails to describe correctly the outcome of a substantial portion of reactions involving ambident nucleophiles.^[23,24,83–89] Kinetic studies have also outlined that the rate constants of nucleophilic substitutions follow the same trend regardless of the HSAB type (“hard” or “soft”) of the electrophiles.^[89] As a further important drawback, the HSAB approach cannot account separately for the kinetic and thermodynamic aspects of a given reaction.^[77] To solve the problems related to the erroneous predictions derived from the HSAB theory, a partitioning scheme based on Marcus theory adjusted for group transfer reactions has been developed by Mayr et al.^[1,4] In the following, we will briefly introduce the cornerstones of this procedure.

The fundament of this concept is to separate the kinetic and the thermodynamic contributions to the activation barrier of a reaction, generalised in the Marcus equation^[90,91] [Equation (1)], which approximates the *total* Gibbs free energy barrier ($\Delta G^\ddagger$) as a combination of the *intrinsic* Gibbs free energy barrier ($\Delta G_0^\ddagger$) and the *reaction* Gibbs free energy (ΔG_r).

$$\Delta G^\ddagger = \Delta G_0^\ddagger + \Delta G^0/2 + [\Delta G^0]^2/[16 \cdot \Delta G_0^\ddagger] \quad (1)$$

To compare the nucleophilic reactivities of the two reacting sites, which in our case are the E and X centres of the $[\text{ECX}]^-$ anions, the Marcus concept is represented for two model reactions of a general electrophile $\text{Me}-\text{Y}$ with the two sites of the $[\text{ECX}]^-$ anion, shown by Equations (X–Y) and (E–Y) in Scheme 2A. The goal is to quantify the difference of the overall activation barriers for the attack of the two nucleophilic centres E and X, defined as $\Delta\Delta G^\ddagger = \Delta G^\ddagger(\text{E}-\text{Y}) - \Delta G^\ddagger(\text{X}-\text{Y})$. By neglecting the last, quadratic term in the Marcus equation [Equation (1)], which is typically insignificant for nucleophilic substitutions,^[1,4] $\Delta\Delta G^\ddagger$ can be decomposed into two meaningful terms as shown in Equation (2):



Scheme 2. A) Prototype reactions of the $[\text{ECX}]^-$ anions with a nucleophile, $\text{Me}-\text{Y}$ [Equations (X–Y) and (E–Y)], B) the corresponding identity reactions [Equations (Y–Y), (X–X) and (E–E)] and C) the isomerisation reaction in our formalism [Equation (X–E)].

$$\Delta\Delta G^\ddagger \approx \Delta\Delta G_0^\ddagger + \Delta\Delta G^0/2 \quad (2)$$

The intrinsic term $\Delta\Delta G_0^\ddagger = \Delta G_0^\ddagger(\text{E}-\text{Y}) - \Delta G_0^\ddagger(\text{X}-\text{Y})$ can be determined by employing identity reactions (Scheme 2B). In an *identity* reaction [Equations (Y–Y), (X–X), and (E–E)], the starting materials and the products are identical, and thus the thermodynamic factor is eliminated ($\Delta G^0=0$). Importantly, previous studies demonstrated that the intrinsic barrier ($\Delta G_0^\ddagger$) of a given *non-identity* reaction, such as those shown in Equations (X–Y) and (E–Y), can be accurately estimated as the average of the barriers of the two corresponding identity reactions [Equation (3)].^[92,93]

$$\Delta G_0^\ddagger(\text{X}-\text{Y}) \approx [\Delta G^\ddagger(\text{X}-\text{X}) + \Delta G^\ddagger(\text{Y}-\text{Y})]/2, \text{ and} \quad (3)$$

$$\Delta G_0^\ddagger(\text{E}-\text{Y}) \approx [\Delta G^\ddagger(\text{E}-\text{E}) + \Delta G^\ddagger(\text{Y}-\text{Y})]/2$$

Thus, the *difference* between the intrinsic barriers of the two non-identity reactions in question [Equations (X–Y) and (E–Y)] can be obtained by using Equation (4):

$$\Delta\Delta G_0^\ddagger \approx [\Delta G_0^\ddagger(\text{E}-\text{E}) - \Delta G_0^\ddagger(\text{X}-\text{X})]/2 \quad (4)$$

Regarding the thermodynamic component, the $\Delta\Delta G^0$ term in Equation (2) is the difference of the reaction Gibbs free energies (ΔG^0) corresponding to reactions (X–Y) and (E–Y), and thus it can be obtained as the reaction Gibbs free energy of the isomerisation reaction presented by Equation (X–E) (Scheme 2C). Notably, the $\Delta\Delta G_0^\ddagger$ and $\Delta\Delta G^0$ components are independent of the leaving group Y^- , thus, on the basis of their relative weights, the outcome of a reaction can be proposed straightforwardly. Finally, the difference of the total barriers $\Delta\Delta G^\ddagger$ can be obtained by Equation (5):

$$\Delta\Delta G^\ddagger = [\Delta G^\ddagger(\text{E}-\text{E}) + \Delta G^\ddagger(\text{X}-\text{X})]/2 + \Delta\Delta G^0/2 \quad (5)$$

As both contributions in this equation are divided by 2, for simplicity, these divisions are typically omitted in the literature,^[1,4] and we also follow this rationale.

We have obtained the isomerisation Gibbs free energies ($\Delta\Delta G^0$) and the intrinsic Gibbs free energy barriers ($\Delta G_0^\ddagger$) for all of the $[\text{ECX}]^-$ anions with E: N, P, As and X: O, S, Se at the CCSD(T)/aug-cc-pVQZ//MP2/6-311+G(2d,p) level with entropy corrections at the MP2/6-311+G(2d,p) level of theory. For computational details and data at the MP2/6-311+G(2d,p) level, see Computational Section and the Supporting Information (SI, Tables S2–S4 and S1–S8), respectively.

2. Thermodynamic factor (isomerisation reactions)

First, we discuss the relative thermodynamic stabilities of the two possible isomers represented by the isomerisation Gibbs free energies (Scheme 2C and Table 1) and the trends thereof. Note that, in our formalism, **negative** $\Delta\Delta G^0$ is consistent with the thermodynamic preference of the **$\text{Me}-\text{E}=\text{C}=\text{X}$ isomer**.

Table 1. Isomerisation Gibbs free energies ($\Delta\Delta G^\circ$, kcal·mol^{−1}, Scheme 2C) for the [ECX][−] anions, Equation (X–E), at the CCSD(T)/aug-cc-pVQZ//MP2/6-311+G(2d,p) level of theory.

[ECX] [−]	$\Delta\Delta G^\circ$	[ECX] [−]	$\Delta\Delta G^\circ$	[ECX] [−]	$\Delta\Delta G^\circ$
[NCO] [−]	−27.6 ^[a]	[PCO] [−]	−28.3	[AsCO] [−]	−32.1
[NCS] [−]	−2.6 ^[a]	[PCS] [−]	−1.6	[AsCS] [−]	−4.3
[NCSe] [−]	−0.1	[PCSe] [−]	−3.3	[AsCSe] [−]	0.7

[a] Literature values: −27.7 and −3.7 kcal·mol^{−1} for [NCO][−] and [NCS][−], respectively, see Ref. [4].

In general, on the basis of the E and X heteroatoms, two different trends can be observed: The $\Delta\Delta G^\circ$ values indicate minor variation on the nature of the pnictogen centre E (for a given chalcogen X, horizontal trend in Table 1), but the differences are more substantial when changing the chalcogen centres (for a given pnictogen E, vertical trends in Table 1). Indeed, the $\Delta\Delta G^\circ$ values increase monotonously in the order X: O < S < Se.

In the case of the oxygen-containing [ECO][−] anions, the $\Delta\Delta G^\circ$ values are dominantly negative, pointing out the clear thermodynamic preference of the heterocumulene-type, Me–E=C=O (E: N, P, As) isomers. In stark contrast, the isomerisation Gibbs free energies are much less significant for the [ECS][−] and [ECSe][−] anions, indicating that the two possible isomers have similar relative stabilities. Among these, the largest (but still rather small) differences are found for the [NCS][−], [AsCS][−] and [PCSe][−] anions: The Me–E=C=S (E: N, P, As) isomers are slightly more stable than the corresponding Me–S–C≡E isomers. In contrast, for the [PCSe][−] anion, the formation of the pnictaalkyne-type Me–Se–C≡P isomer is slightly favoured thermodynamically. For the remaining two anions, [NCSe][−] and [PCS][−], the $\Delta\Delta G^\circ$ values show practically no difference between the thermodynamic stabilities two isomers.

To gain a deeper understanding of the trends observed for the $\Delta\Delta G^\circ$ terms, we analysed the bonding energy contributions in the two possible reaction products Me–E=C=X and Me–X–C≡E (Figure 2; for details, see the Computational Section and Tables S5–S6 in Supporting Information). By inspecting the bonding patterns (Figure 2A), the major differences between these isomers are the σ (E–C^{Me}) and σ (X–C^{Me}) bonds as well as the π (C=X) and the “second” π_2 (C≡E) bonds.^[50] The contributions of the C–E and C–X σ -bonds were obtained as homolytic bond dissociation energies (E_σ). The E_π energies of the E=C and C=X π -bonds and those of the π_2 -bonds in the E≡C moieties were calculated with appropriate isodesmic reactions (see Supporting Information). In addition to these, the extent of delocalisation within the “ECX” π -systems of the two isomers may differ considerably; hence the delocalisation energies (E_d) were also estimated by suitable isodesmic reactions (for details see Supporting Information). The sum of these three increments results in the total stabilisation energy ($E_{\text{tot}} = E_\sigma + E_\pi + E_d$).

The suitability of our decomposition scheme is convincingly demonstrated by the excellent agreement of the relative product stabilities estimated by the three increments above [$\Delta E_{\text{tot}} = E_{\text{tot}}(\text{Me–ECX}) - E_{\text{tot}}(\text{Me–XCE})$] and the explicitly calculated relative electronic energies (ΔE_{rel}) of the two isomers. (The largest absolute discrepancies of only 4.3 and 5.2 kcal·mol^{−1} can be found for the [NCS][−] and [NCSe][−] anions, respectively.)

By analysing the relative weights of the three increments, crucial differences can be observed: (1) both the σ (N–C) and the π_2 (N≡C) bonds have remarkably large bonding energies; however, the corresponding values for the bonds with the P or As elements are significantly smaller (by 40–50%). (2) The σ (C–O) bonding energy is exceptionally large, and the energy contribution of the π (C=O) bond is also much larger than the analogous values of the π (C=S) and π (C=Se) bonds. (3) The E_d delocalisation energies are substantial for all the heterocumulene (Me–E=C=X) species but are rather small for the

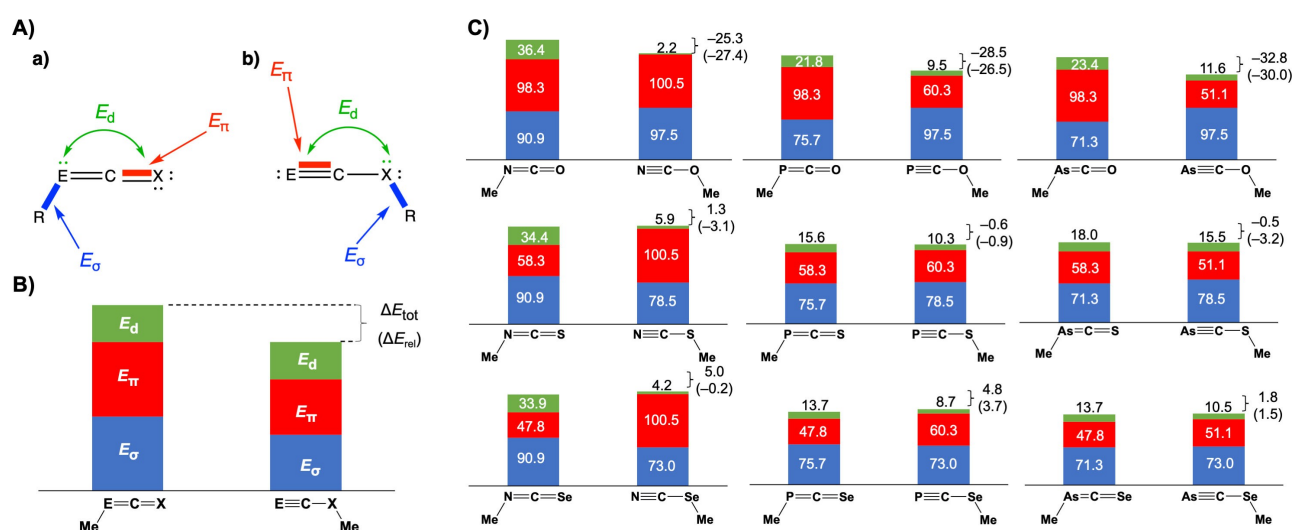


Figure 2. A) Visual representation of the differences in the bonding patterns of the pnictaketene (a) and the pnictaalkyne (b) isomers, B) notations for the contributions, the blue, red, and green colours represent E_σ , E_π and E_d , respectively, C) the Bonding Energy Fragmentation Analysis (BEFA) on the pnictaketene (R–E=C=X) and the pnictaalkyne (R–X–C≡E) products at the CCSD(T)/aug-cc-pVTZ//MP2/6-311+G(2d,p) level of theory (energy values in kcal·mol^{−1}).

Me–X–C≡E analogues, indicating negligible interactions between the lone pairs of the X centres and the $\pi^*(\text{C}\equiv\text{E})$ orbitals.

In the cases of X: O, as shown above, all the Me–E–C=O isomers are more stable than the corresponding Me–O–C≡E species, but the source of the higher stability is different for the lighter N- and the heavier P/As-analogues. For the former (E: N), the effect of delocalisation is deterministic since the bonding energies of the $\sigma(\text{C}=\text{O})/\sigma(\text{C}=\text{N})$ -bonds and the $\pi_2(\text{C}=\text{O})/\pi_2(\text{C}=\text{N})$ -bonds are similar. For the latter case (E: P, As), the higher stability of the pnictaketene isomer arises mainly from the remarkable bonding energy of the $\pi(\text{C}=\text{O})$ -bond compared with that of the $\pi_2(\text{C}\equiv\text{P})$ -bond. Importantly, the $\sigma(\text{C}^{\text{Me}}-\text{O})$ -bond is significantly stronger than the $\sigma(\text{C}^{\text{Me}}-\text{P})$ - or $\sigma(\text{C}^{\text{Me}}-\text{As})$ -bonds, underlining the importance of the σ -contributions. Finally, the differences in E_{O} and E_{d} cancel out each other.

For all the S-containing congeners, the two possible isomers have similar stabilities. However, for the NCS-analogues, we found significant differences between the corresponding bonding components (up to 40 kcal·mol^{−1} for the E_{π} term), and the differences between the E_{π} and E_{d} values altogether lead to very similar total stabilisation (and consequently to similar stability). For the P- and As-analogues, all the contributions are rather similar (with differences below 10 kcal·mol^{−1}), but none of the three increments has a decisive role, and the total stabilisation arises from the overall contribution of all increments.

For X: S, Se, the situation of the N-containing selenocyanate isomers (Me–N–C=Se and Me–Se–C≡N) is similar to the thiocyanate analogues (see above). In the case of the [PCSe][−] and [AsCSe][−] anions, the pnictaalkyne isomers (Me–Se–C≡E) are more stable than the pnictaketenes (Me–E–C=Se). This is primarily due to the differing E_{π} contributions: The $\pi_2(\text{P}\equiv\text{C})$ and $\pi_2(\text{As}\equiv\text{C})$ -bonds have larger bonding energies than the $\pi(\text{C}=\text{Se})$ bonds.

3. Kinetic factor (identity reactions)

According to Equation (2), besides the thermodynamic factors, the kinetic components represented by intrinsic barriers $\Delta G_0^{\ddagger}$ also have a crucial role in determining the activation barrier and, thus the outcome of a reaction. The intrinsic barriers

calculated for E and X attacks of the [ECX][−] anions (Table 2) encompass a wide interval between 5.1 and 22.5 kcal·mol^{−1}.

First, we compare the trends of the $\Delta G_0^{\ddagger}$ intrinsic barriers corresponding to the pnictogen (E: N, P, As) attacks of the [ECX][−] anions. These $\Delta G_0^{\ddagger}$ values show only minor variations (within 2 kcal·mol^{−1}) upon changing the chalcogen centres, but they depend on the nature of the pnictogen encompassing a range between 13.7 and 22.0 kcal·mol^{−1}. Additionally, the $\Delta G_0^{\ddagger}$ values decrease in the order E: N > P > As for a given X centre. Second, the picture of the chalcogen (X: O, S, Se) attacks is more puzzling, and here the intrinsic barriers significantly depend on both heteroatoms, in an even wider range of 5.1 to 17.0 kcal·mol^{−1}. In general, the barriers change non-monotonously with descending among the chalcogen elements. Indeed, compared to the Se-attacks, the O- and S-attacks have lower and higher barriers, respectively. As for the dependency on the pnictogen centres, the attacks by the chalcogen centres X of the [NCX][−] anions possess 1.6 to 6.9 kcal·mol^{−1} lower intrinsic barriers compared to the corresponding P- and As-analogues.

Importantly, on the basis of the $\Delta G_0^{\ddagger}$ values, the kinetically preferred sites can be determined. Uniformly, for the five anions that contain either N or O centres (that are [NCO][−], [NCS][−], [NCSe][−], [PCO][−] and [AsCO][−]), the intrinsic barriers for the chalcogen X attacks are significantly lower than those for the pnictogens E, indicating the kinetic preferences of the chalcogen attacks. In marked contrast to these, for the [PCS][−], [PCSe][−], [AsCS][−] and [AsCSe][−] anions, the intrinsic barriers corresponding to the X and E sites are rather similar, and the largest difference is only 4.5 kcal·mol^{−1} (for the [PCSe][−] anion). In most of these cases (except for the [AsCO][−] ion), the attacks by the chalcogen centres are favoured but only marginally.

To further bolster the results obtained for the [ECX][−] anions, we calculated the intrinsic barriers for the simple monodentate nucleophilic anions [XH][−] (X: O, S, Se) and [EH₂][−] (E: N, P, As), serving as references (Table 2). These values agree well with those of previous studies.^[94,95] In their pioneering work, Hoz et al. analysed the intrinsic activation barriers of identity reactions involving anionic nucleophiles containing group 14 to 17 elements (e.g. halides, chalcogenides [MeX][−], pnictides [MeEH][−]) and identified simple rules now known as Hoz's rules.^[96] According to their observations, if the attacking centres are from the same main group of the periodic table, the

Table 2. Intrinsic Gibbs free energy barriers ($\Delta G_0^{\ddagger}$, kcal·mol^{−1}) determined using identity reactions in Scheme 2B at the CCSD(T)/aug-cc-pVQZ//MP2/6-311 + G(2d,p) level of theory and the local charge transfer (Δq , in e) values in TSs for the attacking E or X centre at the B3LYP/aug-cc-pVTZ level of theory.

Anion	Attack	$\Delta G_0^{\ddagger}$	Δq	Anion	Attack	$\Delta G_0^{\ddagger}$	Δq	Anion	Attack	$\Delta G_0^{\ddagger}$	Δq
[NCO] [−]	N	21.1 ^[a]	0.11	[PCO] [−]	P	19.3	0.34	[AsCO] [−]	As	15.8	0.37
	O	5.1 ^[a]	0.11		O	12.0	0.04		O	11.7	0.03
[NCS] [−]	N	22.0 ^[a]	0.04	[PCS] [−]	P	19.1	0.27	[AsCS] [−]	As	13.7	0.31
	S	13.6 ^[a]	0.35		S	17.0	0.27		S	15.2	0.25
[NCSe] [−]	N	20.6	0.04	[PCSe] [−]	P	18.3	0.26	[AsCSe] [−]	As	14.5	0.30
	Se	9.2	0.39		Se	13.8	0.32		Se	13.4	0.30
[NH ₂] [−]	N	36.2	0.41	[PH ₂] [−]	P	32.8	0.54	[AsH ₂] [−]	As	27.1	0.55
[OH] [−]	O	21.2	0.33	[SH] [−]	S	21.0	0.45	[SeH] [−]	Se	16.9	0.51

[a] Literature values for the pnictogen and chalcogen attacks, respectively: 18.7 and 5.2 kcal·mol^{−1} for [NCO][−], 22.4 and 12.5 kcal·mol^{−1} for [NCS][−], respectively, see Ref. [4].

intrinsic barriers are very similar independently of the period. However, from left to right among the main groups, the $\Delta G_0^\ddagger$ values drop gradually, approx. by $10 \text{ kcal}\cdot\text{mol}^{-1}$. Indeed, as Table 2 shows, the intrinsic barriers are remarkably higher for pnictogen attacks of $[\text{EH}_2]^-$ than for chalcogen attacks of $[\text{XH}]^-$ (also see Figure S1).

It is now instructive to evaluate to what extent the $\Delta G_0^\ddagger$ barriers of the delocalised $[\text{ECX}]^-$ anions obey Hoz's rules, originally established only for monodentate ions. For the three $[\text{NCX}]^-$ anions, the $\Delta G_0^\ddagger$ values are clearly in line with Hoz's rules: The chalcogen attacks have lower barriers than the pnictogen attacks, and the differences between the intrinsic barriers of the two sites ($\Delta\Delta G_0^\ddagger$) are around $10 \text{ kcal}\cdot\text{mol}^{-1}$ (for $[\text{NCO}]^-$ even larger). In stark contrast to the $[\text{NCX}]^-$ ions, for all of the P- and As-containing anions, the differences between the $\Delta G_0^\ddagger(\text{E})$ and $\Delta G_0^\ddagger(\text{X})$ values for a given anion are significantly smaller, typically well below $10 \text{ kcal}\cdot\text{mol}^{-1}$. This is especially remarkable for the "heaviest" $[\text{PCS}]^-$, $[\text{PCSe}]^-$, $[\text{AsCS}]^-$ and $[\text{AsCSe}]^-$ ions, all of which exhibit rather similar $\Delta G_0^\ddagger$ values at the two reacting centres E and X ($\Delta\Delta G_0^\ddagger < 4.5 \text{ kcal}\cdot\text{mol}^{-1}$). Specifically, in the case of the $[\text{AsCS}]^-$ ion, the pnictogen (As) attack has an even lower intrinsic barrier than the chalcogen attack by $2.1 \text{ kcal}\cdot\text{mol}^{-1}$. Notably, these results clearly contradict the predictions that could be outlined based on Hoz's rules: Indeed, the attacks by the heavier pnictogen centres do not have significantly higher barriers than those by the chalcogens. Although the ambident reactivities of the $[\text{NCO}]^-$ and $[\text{NCS}]^-$ anions were explained successfully by applying Hoz's rules,^[4,96] we emphasise that the application of this rule of thumb may have limitations for the ambident reactivities of heavier elements. Therefore, explicit $\Delta G_0^\ddagger$ values need to be obtained for each of the reacting sites. Furthermore, we may conclude that the additional atoms in the $[\text{ECX}]^-$ anions must have a substantial modulating effect on the intrinsic barriers compared with monodentate nucleophiles (e.g. $[\text{EH}_2]^-$ and $[\text{XH}]^-$ anions). In the following, to understand why the $\Delta G_0^\ddagger$ values of the delocalised $[\text{ECX}]^-$ anions are significantly smaller than those of monodentate ions $[\text{EH}_2]^-$ and $[\text{XH}]^-$, we will scrutinise the electronic and structural properties of the transition states corresponding to these identity reactions.

3.1. Interactions in the activated complexes

In his seminal work,^[94] Uggerud thoroughly analysed the molecular properties that possibly influence the barriers of identity reactions of simple monodentate nucleophiles by considering several variables of the attacking centres, including electronegativity, ionisation energy, basicity of the attacking centre, and electron density in the TS. While most of these parameters show no correlation with the intrinsic barriers, the ionisation energy (IE) of the anions was found to qualitatively describe the trends of the intrinsic barriers. Indeed, the ionisation energy accounts for the ability of the given nucleophile to transfer an electron to the electrophile. Consequently, the covalent or electrostatic nature of the interaction in the TS can be outlined as a decisive factor: higher electro-

static (and thus lower covalent) character leads to lower activation Gibbs free energy. This means that, due to the increased electrostatic character of the interaction arising between the nucleophile and the electrophile, less hindrance arises for the incoming negatively charged second nucleophile, which results in lower $\Delta G_0^\ddagger$.^[94]

In the case of the ambident $[\text{ECX}]^-$ anions, however, the IE cannot differentiate between the E and X centres, as all of the HOMOs represent delocalised π -systems involving the p orbitals of all the E, C, and X atoms, and thus the IE would be the same for both attacks. To solve this problem, here we recommend the use of *local charge transfer* (Δq , local CT) as a more applicable alternative for quantifying the covalent character of the interaction in the transition state.^[97] The Δq value accounts for the transferred electron density from the nucleophile toward the electrophile and is obtained as the difference between the NPA (natural population analysis) partial charges of a given attacking centre in the TS and that in the free anion: $\Delta q = q(\text{TS}) - q(\text{anion})$. Note that the larger Δq value indicates a higher covalent character for the interaction in the transition state (TS).

Based on the Δq values of the attacking E and X centres in the $[\text{ECX}]^-$ anions (Table 2), the attacks by the "lighter" (N, O) and the "heavier" (P, As, S and Se) centres differ remarkably: In the case of the N and O attacks of the $[\text{ECX}]^-$ anions, the Δq values are similarly low (maximum 0.11e) indicating low covalent (and high electrostatic) characters in the TSs. In stark contrast, for all the remaining attacks (P, As, S or Se), the Δq values are significantly higher, again encompassing a narrow range between 0.26 and 0.39e. Compared to the delocalised, ambident $[\text{ECX}]^-$ anions, the Δq values for all the corresponding $[\text{EH}_2]^-$ and $[\text{XH}]^-$ anions are substantially larger (0.33–0.53e). Again, the Δq values of the lighter $[\text{NH}_2]^-$ and $[\text{OH}]^-$ ions are significantly smaller (0.41 and 0.33e, respectively) than those of the heavier analogues.

According to Figure 3, the decrease in the intrinsic barriers corresponding to the attacks of the delocalised $[\text{ECX}]^-$ anions compared to the relevant monodentate ions $[\text{EH}_2]^-$ or $[\text{XH}]^-$ (marked with dotted boxes) can be explained by the lower covalent (and higher electrostatic) character of the interaction in the TS, reflected in the significantly lower Δq values. Importantly, these observations are in line with Uggerud's concept on ionisation energies.^[94] Furthermore, the similar $\Delta G_0^\ddagger$ values of the attacks by the two reacting sites of the heaviest $[\text{PCS}]^-$, $[\text{PCSe}]^-$, $[\text{AsCS}]^-$ and $[\text{AsCSe}]^-$ anions (see above) can also be explained on the basis of Figure 3: As the relative changes are different for the pnictogen and chalcogen attacks, the intrinsic barriers of the E attacks of the $[\text{ECX}]^-$ ions approach the range of the X attacks.

The substantially lower Δq values of the ambident anions compared to the monodentate counterparts can be traced back to the deterministic role of the HOMOs of the nucleophiles, from which the newly forming bonds are established. The HOMOs of the $[\text{EH}_2]^-$ and $[\text{XH}]^-$ anions are practically p_z -type lone pairs located on the E and X centres, respectively. In contrast, in the $[\text{ECX}]^-$ anions, the corresponding p_z orbitals are parts of delocalised π -systems. Consequently, due to π -delocalization, the contributions of the E and X centres to the

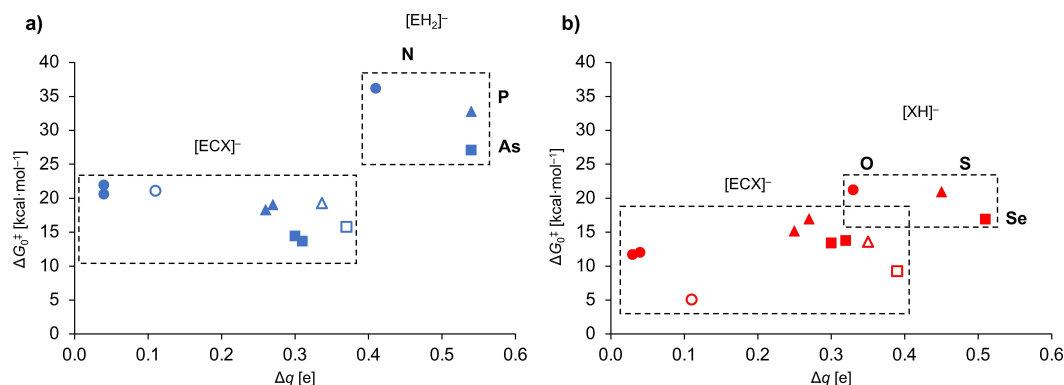


Figure 3. The Δq values vs the $\Delta G_0^\ddagger$ [kcal·mol⁻¹] activation barriers of the [ECX]⁻ and the monodentate anions: a) for the pnictogen attacks and b) for the chalcogen attacks. The unfilled markers represent the [ECO]⁻ and [NCX]⁻ anions in parts a) and b), respectively.

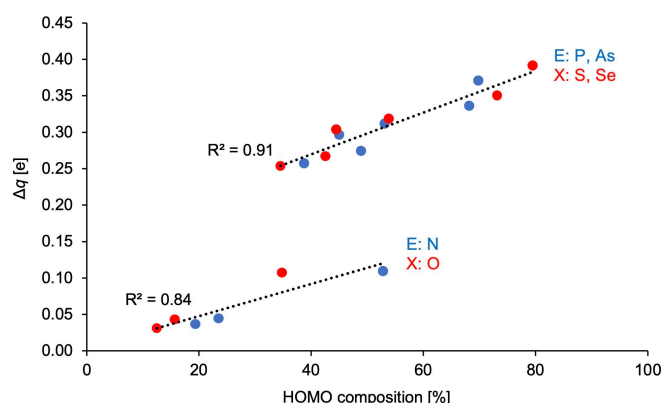


Figure 4. The Δq values vs the HOMO contributions of the E or X sites of the [ECX]⁻ anions based on the Mulliken partition scheme.^[98] The red and blue colours stand for the attacks by the chalcogen and the pnictogen centres, respectively.

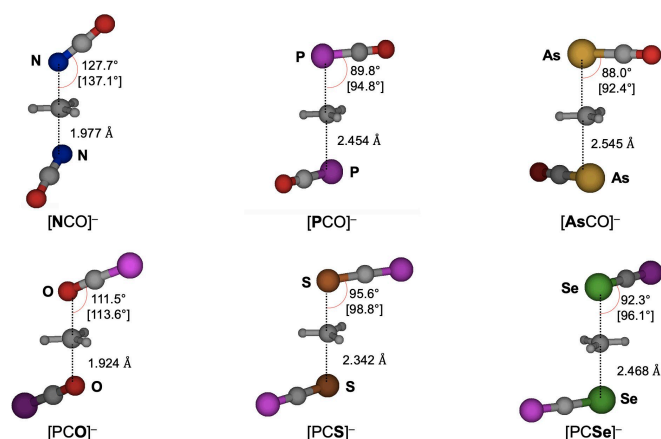


Figure 5. Selected examples for transition state geometries: the attacking angles (α , in degrees) and the distances (in angstroms) between the C...E or C...X atoms. In square brackets, the relevant bond angles in the products are indicated. [C: grey, N: blue, P: magenta, As: yellow, O: red, S: orange, Se: green] (for the remaining anions, see Table S13).

HOMOs are necessarily lower in the [ECX]⁻ ions compared to the [EH₂]⁻ and [XH]⁻ anions. Indeed, the contributions of the E or X attacking centres to HOMOs based on the Mulliken partition scheme (for numerical values, see Table S15) nicely correlate with the Δq values (Figure 4), demonstrating a direct relationship between the covalent character of the interaction and the atomic distributions of the HOMOs. Furthermore, the separation between the “lighter” and the “heavier” elements is again well represented.

3.2. Structural analysis of the transition states

To gain insight into the crucial differences between the lighter (N or O) and heavier (P, As, S or Se) attacking centres in terms of the Δq and $\Delta G_0^\ddagger$ values, we analysed the structural characteristics of TS structures of the identity reactions with the [ECX]⁻ ions (Figure 5). While, for all attacks by the lighter N or O, the “attacking” α angles are larger than 110°; for all the remaining attacks, they are around 90°. Importantly, these angles are in good agreement with the analogous angles in the corresponding products (e.g. Me–E=C=X or Me–X–C=E), showing that the interactions in the transition states are similar to those in the methylated products (see Figure S2). These results led us to conclude that the inert s orbital effect,^[99,100] being characteristic for the heavier P, As, S, and Se elements, is a determining factor: The valence shell s orbitals of these heavier elements are not prone to hybridisation; thus, the newly forming C...E or C...X bonds are established mainly from the p orbitals of the E or X atoms, respectively, without significant contributions of the s orbitals. Hence, the attacking angles are around 90° (like the angle between two p orbitals). To support this, the s characters of the lone pairs at the E and X centres were determined by NBO (natural bond orbitals) calculations performed on the products (Table S16). Indeed, the lone pairs at the heavier P, As, S, and Se centres have much higher s characters (66.3–80.1%) than those at the N or O centres (13.3–45.7%). Note that, previously, the angular dependencies of the attacks by the [NCO]⁻ and [NCS]⁻ ions were described as important factors.^[25]

4. Total barriers (selectivities) and experimental considerations

Finally, using the Equation (5), we calculated the total barrier differences (selectivities, $\Delta\Delta G^\ddagger$, see Figure 6 and Figure S7) corresponding to the pnictogen and chalcogen attacks. For clarity, the 1/2-times factors were omitted, as generally employed in the literature.^[1,4] Again, in our formalism, the negative and positive values refer to the favoured attack by the pnictogen E and chalcogen X centres, respectively.

The N- or O-containing anions separate from those containing the heavier P, As, S, or Se elements, and based on the magnitude of the $\Delta\Delta G_0^\ddagger$ and $\Delta\Delta G^0$ terms, the anions can be sorted into four groups: (a) $[\text{NCO}]^-$ (b) $[\text{PCO}]^-$ and $[\text{AsCO}]^-$ (c) $[\text{NCS}]^-$ and $[\text{NCSe}]^-$ (d) $[\text{PCS}]^-$, $[\text{PCSe}]^-$, $[\text{AsCS}]^-$ and $[\text{AsCSe}]^-$ ions. This separation is the result of two governing trends (Figure 6): (1) The kinetic component ($\Delta\Delta G_0^\ddagger$) is dominant for all the $[\text{ECO}]^-$ anions but is negligible for the ions containing the heavier chalcogens (S or Se). (2) The thermodynamic component is only substantial for the $[\text{NCX}]^-$ anions and is marginal for the $[\text{PCX}]^-$ and $[\text{AsCX}]^-$ analogues.

- (a) The situation of the $[\text{NCO}]^-$ ion is unique since it is located at the crossing point of these two directions, and both $\Delta\Delta G_0^\ddagger$ and $\Delta\Delta G^0$ contributions are non-negligible: As the $\Delta\Delta G^0$ term is more substantial, the resulting selectivity ($\Delta\Delta G^\ddagger = -11.6 \text{ kcal}\cdot\text{mol}^{-1}$) predicts the formation of isocyanates ($\text{R}-\text{NCO}$). According to the literature, the reactions of $[\text{NCO}]^-$ against a series of carbon-electrophiles result in the exclusive formation of isocyanates.^[23] Although the $\text{R}-\text{OCN}$ isomers can also be synthesised using indirect pathways, these species easily isomerise to the thermodynamically more stable $\text{R}-\text{NCO}$ isomers.^[101]
- (b) In the cases of the $[\text{PCO}]^-$ and $[\text{AsCO}]^-$ anions, the pnictaketene-type ($\text{Me}-\text{P}=\text{C}=\text{O}$ and $\text{Me}-\text{As}=\text{C}=\text{O}$) isomers can be expected to form. Among these, experimental validation with carbon-electrophiles is only available for the

$[\text{PCO}]^-$ ion: its reaction with $^i\text{Pr}-\text{I}$ or Tr^+-Cl indicates the primary formation of the elusive phosphaketene ($\text{R}-\text{P}=\text{C}=\text{O}$) isomer (see Introduction).^[49] Our computational results agree nicely with these observations. Similar reactivity can be proposed for the $[\text{AsCO}]^-$ anion as well: organyl arsenaketenes are expected to form in S_N reactions.

- (c) For the $[\text{NCS}]^-$ and $[\text{NCSe}]^-$ ions, the positive $\Delta\Delta G^\ddagger$ values indicate the formation of the thio/selenocyanate isomers ($\text{R}-\text{XCN}$, X: S, Se). According to experiments using the $[\text{SCN}]^-$ anion, both isomers have been accessed with carbon-electrophiles, but the thiocyanate ($\text{R}-\text{SCN}$) isomer is typically favoured kinetically, as implied by the positive $\Delta\Delta G^\ddagger$ values.^[24,102–104] Furthermore, the reaction of $[\text{NCSe}]^-$ ion with $^i\text{Pr}-\text{Br}$ results exclusively in the selenocyanate ($\text{Me}-\text{SeCN}$) isomer,^[105] in line with the calculated positive $\Delta\Delta G^\ddagger$ selectivity value.
- (d) For the remaining $[\text{PCS}]^-$, $[\text{PCSe}]^-$, $[\text{AsCS}]^-$ and $[\text{AsCSe}]^-$ anions, neither the kinetic nor the thermodynamic component is significant. Due to the different signs of these increments, however, minor differences among these four anions can be found. In the cases of the $[\text{PCSe}]^-$ and $[\text{AsCS}]^-$ ions, the two small contributions ($\Delta\Delta G^0$ and $\Delta\Delta G_0^\ddagger$) have the same signs; therefore, they additively give a non-negligible selectivity favouring the $\text{Me}-\text{Se}-\text{C}\equiv\text{P}$ and $\text{Me}-\text{As}-\text{C}\equiv\text{S}$ isomers, respectively. In contrast, the $\Delta\Delta G^\ddagger$ selectivities for $[\text{PCS}]^-$ and $[\text{AsCSe}]^-$ are around zero, predicting ideal ambident characters. Unfortunately, the nucleophilic reactivities of these anions are yet to be studied. The only exception is limited to the $[\text{PCS}]^-$ anion whose ideal ambident character was proven using tungsten pentacarbonyl (see above).^[64]

5. Further, non-carbon electrophiles

To expand the findings obtained with the model carbon-centred methyl electrophile, we investigated further electrophiles at the DF-CCSD(T)/aug-cc-pVQZ//MP2/6-311+G(2d,p) level of theory (for method testing see Supporting Information). Based on previously reported experimental studies involving the $[\text{PCO}]^-$ anion, we selected methyl-substituted boryl (BMe_2), alumanyl (Me_2Al), silyl (Me_3Si), germlyl (Me_3Ge), and phosphinyl (Me_2P) model substituents (Me_nZ) as well as the tert-butyl group (Me_3C). In the following, we will focus on the relative thermodynamic stabilities of the two possible products ($\text{R}-\text{E}=\text{C}=\text{X}$ and $\text{R}-\text{X}-\text{C}\equiv\text{E}$, where R: Me_nZ and Z: B, Al, Si, Ge, P) because, in most cases, the intrinsic barriers were found to be less important (see above), and reactions with such electrophiles usually do not follow classical $\text{S}_\text{N}2$ type pathways.^[106–111] The $\Delta\Delta G^0$ values (Figure 7, see also Tables S17–S18) were calculated as shown in Equation (X–E) in Scheme 2C.

5.1. Trends in the isomerisation Gibbs free energies

Although exchanging the electrophilic carbon centre with another main group element has a remarkable effect on the

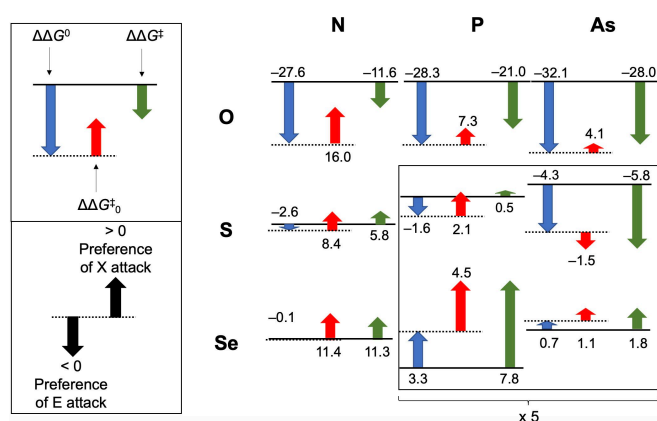


Figure 6. Visual representation of the composition of the total barrier differences ($\Delta\Delta G^\ddagger$) corresponding to the two sides of the $[\text{ECX}]^-$ anions based on the kinetic and thermodynamic increments [based on Equation (3), without the division by 2] at the CCSD(T)/aug-cc-pVQZ//MP2/6-311+G(2d,p) level of theory. The lengths of the arrows are proportional to the values, and the blue inset shows a five times magnification due to the small values.

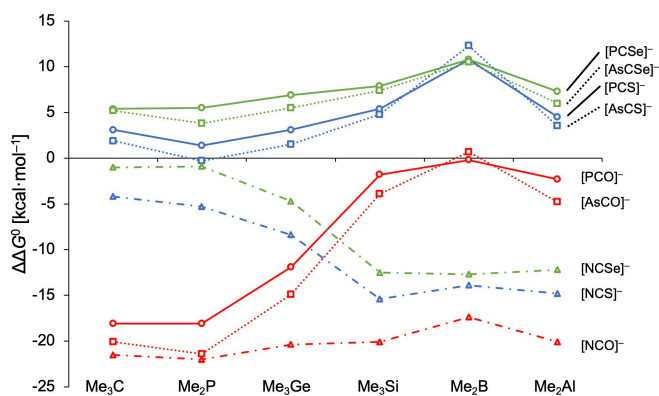


Figure 7. Gibbs free energies for the isomerisation reactions ($R-X-C\equiv E \rightarrow R-E-C\equiv X$) for R groups indicated by the $[ECX]^-$ anions. The negative and positive values correspond to the preference of the pnictaketene, and the pnictaalkyne isomer, respectively. (See also Figure S8.)

$\Delta\Delta G^0$ values, the trends described above for the methyl group remain similar (see Section 2). Again, differences between the $[ECX]^-$ ions can be observed: On one hand, the N-containing species separate from those containing the P or As heteroelements. On the other hand, the congeners with lighter O atom differ from the group of those with heavier chalcogens (S or Se). Further similarities can be found based on the nature of the electrophilic centres. For example, the $\Delta\Delta G^0$ relative stabilities are similar for the “diagonal neighbours” P and C. Also, the Al- and Si-containing analogues exhibit rather similar $\Delta\Delta G^0$ values.

Based on the bond fragmentation analysis in Section 2., it is reasonable to assume that the relative strength of the Z–E and Z–X bonds may influence the relative stabilities of the two possible isomers ($Me_nZ-E-C\equiv X$ and $Me_nZ-X-C\equiv E$). Therefore, we have obtained the homolytic bond dissociation energies (E_b) in the corresponding Me_nZ-EH_2 and Me_nZ-XH species denoted as $E_b(Z-E)$ and $E_b(Z-X)$, respectively at the DF-CCSD(T)/aug-cc-pVTZ//MP2/6-311+G(2d,p) level of theory (see Tables S21–S22 for numerical values). Figure 8 shows the $\Delta\Delta G^0$ relative stabilities as a function of the relative σ -bond energies $\Delta E_b =$

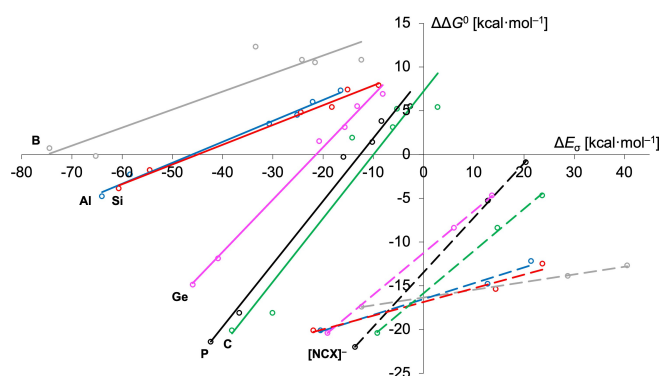


Figure 8. The $\Delta\Delta G^0$ isomerisation Gibbs free energies for elements $Z = B, Al, P, Si, Ge, C$ plotted as function of the relative σ -bond energies $\Delta E_b = E_b(Z-E) - E_b(Z-X)$. The filled and dashed lines represent the P/As- and the N-analogues, respectively.

$E_b(Z-E) - E_b(Z-X)$ (for separated graphs see Figure S9–S14). In the case of all elements Z, the data points follow similar trends, however, those corresponding to the $[NCX]^-$ anions clearly separate from those of the heavier analogues $[PCX]^-$ and $[AsCX]^-$. Indeed, for a given element Z the points of the $[NCX]^-$ anions are significantly shifted toward negative values along $\Delta\Delta G^0$ axis (but the slopes remain similar), outlining the increased thermodynamic preference of the $Me_nZ-N-C\equiv X$ isomer. A possible explanation for this difference between E: N and E: P, As can be found in their markedly differing π -bond energies (see Figure 2) albeit the differing delocalisation effects may also have an impact. Altogether, the similar appearance of these trends indicates that the ΔE_b relative σ -bond energies have an impact on the relative thermodynamic stability of the two possible isomers in question. Again, for the electrophiles with Z: P and C, the trendlines are almost identical and similar behaviour can also be observed for Z: Al and Si. Moreover, in the case of E: P/As the thermodynamic preference of $Me_nZ-E-C\equiv X$ isomer increases in the $B < Al \approx Si < Ge < P \approx C$ order, which is in line with the general trend in the E_b σ -bond energies involving the elements Z (see Tables S19–S20).^[112]

5.2. N-containing anions

For all the $[NCX]^-$ ions, the $\Delta\Delta G^0$ values are generally negative; therefore, in most cases, the $R-N-C\equiv X$ isomers are clearly preferred thermodynamically. However, the trends for the $[NCO]^-$ ion separate from those of the $[NCS]^-$ and $[NCSe]^-$ anions. Not only are the $\Delta\Delta G^0$ values for the $[NCO]^-$ ion lower than those for the other two anions, but they also show negligible variation upon the quality of the electrophilic centre. In general, the $[NCS]^-$ and $[NCSe]^-$ ions follow the same trends; however, the $\Delta\Delta G^0$ values decrease in the R: $Me_3C > Me_2P > Me_3Ge > Me_3Si$ order. Although the $[NCX]^-$ anions are well known, to the best of our knowledge, the reactivities of these ions with the electrophiles shown in Figure 7 are still unexplored, especially for the S- and Se-analogues. Nevertheless, the available experimental results indicate that the thermodynamic factor governs the formation of the products with these electrophiles. Indeed, the formation of the thermodynamically favoured $R-NCX$ isomers was observed in the following reactions: the $[NCO]^-$ ion with P-^[113] or B-electrophiles,^[114] $[NCO]^-$ and $[NCS]^-$ ions with Ge-centred electrophiles,^[115] and silylation of all the $[NCX]^-$ anions.^[116–119]

5.3. P- and As-containing anions

Although the As-analogues show somewhat lower $\Delta\Delta G^0$ values, the $[PCX]^-$ and $[AsCX]^-$ anions follow the same trends (Figure 7); therefore, we discuss them jointly. Importantly, the O-containing anions separate from those with X: S, Se. In the case of the $[PCO]^-$ and $[AsCO]^-$ anions, the $\Delta\Delta G^0$ values with most of the electrophiles are negative, indicating that the pnictaketene isomers ($R-P-C\equiv O$ or $R-As-C\equiv O$) are clearly preferred. However, with R: BMe_2 , $AlMe_2$, and $SiMe_3$ substituents, the two

possible isomers have quite similar stabilities ($|\Delta\Delta G^0| < 5 \text{ kcal}\cdot\text{mol}^{-1}$). Previous reports on the $[\text{PCO}]^-$ anion also support these observations. Indeed, the P- and Ge-centred electrophiles led to the clean formation of the phosphaketene isomers $\text{R}-\text{P}=\text{C}=\text{O}$ (similar to the C-electrophiles, see above).^[56,120–122] As for R: Me_2Al , the phosphalkyne ($\text{R}-\text{O}-\text{C}\equiv\text{P}$) isomer was accessed using diisobutylaluminum chloride,^[123] and our calculations predict only negligible difference between the stabilities of the two isomers. The $\Delta\Delta G^0$ values for R: Me_3Si or Me_2B groups are also close to zero, indicating very similar stabilities of the two possible isomers. In previous experimental studies, both the $\text{R}-\text{P}=\text{C}=\text{O}$ and $\text{R}-\text{O}-\text{C}\equiv\text{P}$ isomers were accessed using boryl and silyl electrophiles.^[50,54,124,125] For the $[\text{ECS}]^-$ and $[\text{ECSe}]^-$ (E: P, As) ions, the isomerisation Gibbs free energies are generally higher than for the O-containing ones, and in most cases, they are positive, indicating that the $\text{R}-\text{X}-\text{C}\equiv\text{E}$ isomers are favoured thermodynamically.

In the absence of experimental data, in the case of the $[\text{PCS}]^-$, $[\text{PCSe}]^-$, $[\text{AsCO}]^-$, $[\text{AsCS}]^-$ and $[\text{AsCSe}]^-$ anions, predictions can only be targeted. Due to the analogies in the electronic structures of the $[\text{AsCO}]^-$ and $[\text{PCO}]^-$ ions, we propose that the nucleophilic behaviour of the $[\text{AsCO}]^-$ ion is similar to that of $[\text{PCO}]^-$. Importantly, based on our results, using $[\text{ECX}]^-$ ions that contain S or Se, the pnictaalkyne-type $\text{R}-\text{X}-\text{C}\equiv\text{E}$ isomers seem to be accessible, especially with germyl, silyl, and boryl electrophiles. The resulting pnictaalkynes, which are so far unprecedented, can be useful synthons containing $\text{C}\equiv\text{P}$ and $\text{C}\equiv\text{As}$ bonds for cycloaddition reactions (e.g. as dienophiles in Diels–Alder reactions).

Conclusion

In this comprehensive study we have applied Marcus theory treatment to compare the nucleophilic substitution reactions involving all of the so far known $[\text{ECX}]^-$ anions (where E: N, P, As; X: O, S, Se) leading to either $\text{Me}-\text{E}=\text{C}=\text{X}$ or $\text{Me}-\text{X}-\text{C}\equiv\text{E}$. This methodology enabled us to separately explore the kinetic and thermodynamic factors contributing to the activation Gibbs free energy barriers in terms of the intrinsic barriers and isomerisation Gibbs free energies, respectively. In general, the comparison of these components reveals remarkable differences between the anions depending on the nature of heteroatoms: the congeners with the “lighter” N or O elements markedly separate from those containing the “heavier” P, As, S, or Se centres.

The thermodynamic factor epitomised by the isomerisation Gibbs free energies is of importance in the case of the O-containing anions (ranging between $\Delta\Delta G^0 = -27.6$ and $-32.1 \text{ kcal}\cdot\text{mol}^{-1}$), favouring the $\text{Me}-\text{E}=\text{C}=\text{X}$ isomers. In contrast, these energies are negligible for the S- and Se-containing anions.

The intrinsic Gibbs free energy barriers representing the kinetic factors to the total barriers only play a crucial role for the $[\text{NCX}]^-$ anions, favouring the attacks by chalcogen X centres. In contrast, these terms are of much less significance for the remaining cases (all of the $[\text{PCX}]^-$ and $[\text{AsCX}]^-$ ions).

These findings can be further bolstered by structural and electronic characteristics of the related transition states, revealing remarkable differences between the “lighter” and “heavier” centres. As a simple concept, these features can be rationalised using the inert s pair effect, characteristic for the elements below the second period. Importantly, the nucleophilic attacks by the E and X centres embedded in the delocalised systems of the $[\text{ECX}]^-$ anions are accompanied by significantly lower intrinsic barriers than the corresponding monodentate $[\text{EH}_2]^-$ and $[\text{XH}]^-$ nucleophiles. This barrier-lowering effect can be traced back to the decreased covalent character of the interactions in the TS structures of the $[\text{ECX}]^-$ anions compared to the monodentate analogues. Furthermore, in the case of the $[\text{ECX}]^-$ anions, the lower covalent character of the interaction (expressed as local charge transfer) correlates with the HOMO contributions of the attacking centres. Consequently, the π -delocalization is responsible for the lower intrinsic barriers of the $[\text{ECX}]^-$ type ions.

Our results also highlight that the similarities and differences among the nine studied $[\text{ECX}]^-$ anions lead to a two-dimensional understanding of the nucleophilic properties. Moreover, we have expanded the knowledge on the $[\text{NCX}]^-$ ions, commonly regarded as prototypes of ambident nucleophiles, toward heavier congeners. Indeed, the $[\text{NCO}]^-$ ion shows relationships with the $[\text{NCX}]^-$ (X: S, Se) as well as with the $[\text{ECO}]^-$ (E: P, As) ions, however, in different aspects: While for the former congeners, the kinetic, for the latter group, the thermodynamic components are deterministic. In contrast to the N- or O-containing ions, the “heaviest” $[\text{PCS}]^-$, $[\text{PCSe}]^-$, $[\text{AsCS}]^-$ and $[\text{AsCSe}]^-$ ions cluster as a distinct group, posing high similarity to each other.

Beyond understanding the electronic effects of the $[\text{ECX}]^-$ anions, we target to predict the reactivities of the so far unexplored ions: Using the S-containing $[\text{PCS}]^-$ and $[\text{AsCS}]^-$ anions as nucleophiles, both the pnictaketene and the pnictaalkyne isomers can be expected in comparable quantities. Starting from the $[\text{AsCO}]^-$ anion, arsaaketenes ($\text{R}-\text{As}=\text{C}=\text{O}$) seem to be accessible in a straightforward manner, offering applications as synthons similar to phosphaketenes in various chemical modifications. Additionally, the previously unexplored $[\text{PCSe}]^-$ and $[\text{AsCSe}]^-$ ions are proposed to lead to phospho- and arsaalkynes with selenoxy functions ($\text{R}-\text{Se}-\text{C}\equiv\text{P}$ and $\text{R}-\text{Se}-\text{C}\equiv\text{As}$). These unprecedented compounds may be regarded as sterically uncrowded alternatives of kinetically stabilised phosphalkynes that bear sterically encumbered substituents, such as $^t\text{BuCP}$, being well known for its rich and versatile chemistry (e.g. in cycloadditions).^[126–128] Importantly, since the chemistry of species containing $\text{C}\equiv\text{As}$ bond is less explored than those with $\text{C}\equiv\text{P}$ bond,^[129,130] the $\text{R}-\text{Se}-\text{C}\equiv\text{As}$ arsaalkyne derivatives may open a route to unprecedented low-coordinate arsenic compounds.

Computational Section

The MP2, CCSD(T) and DFT calculations were carried out using the Gaussian09 Rev. E01. suite of programs, and the MRCC

(2020) quantum chemistry program package was used for the DF-CCSD(T) calculations.^[131–133]

In order to compare our results with those of previous studies, first, we employed the MP2/6-311+G(2d,p) level of theory. The accuracy of the calculations was tested at the CCSD(T)/aug-cc-pVQZ level of theory (single point calculations). In certain cases, these results deviate substantially (the mean of the differences is 1.64 kcal·mol^{−1} with a maximum difference of 5.0 kcal·mol^{−1}) compared to the MP2/6-311+G(2d,p) level. Therefore, we only focus on the higher-level Coupled Cluster results. In the case of the methyl-substituted non-carbon electrophiles, we applied the density-fitted DF-CCSD(T)/aug-cc-pVQZ level of theory to reduce the computational cost.

All the geometries were optimized in vacuum at the MP2/6-311+G(2d,p) level of theory, which is identical to that of a previous study on similar nucleophiles.^[4] The optimization of the transition states was carried out using the force constants from a previous vibrational analysis, and intrinsic reaction coordinate (IRC) calculations were performed both forward and backward along the reaction coordinate to locate the two corresponding minima. The harmonic vibrational analyses were also carried out at the MP2/6-311+G(2d,p) level of theory to check the nature of the stationary points and to calculate the Gibbs free energy correction values. For local minima, all force constants were positive, while for TSs one imaginary frequency was found. In all the cases the relative energies refer to the separated reagents instead of reactant complexes as suggested in the literature previously.^[4]

The Natural Bond Orbital (NBO) calculations for NPA charges were performed at the B3LYP/aug-cc-pVTZ//MP2/6-311+G(2d,p) level of theory using the NBO 7.0 package.^[134] The charge transfer (CT) values were calculated based on the NPA charges in the transition state structures as the sum of the differences in the partial charges of the atoms summarized in the 'ECX' moiety.

To determine the contributions of the atomic orbitals to the HOMOs, the Mulliken partition scheme was employed as implemented in the multiwfn wavefunction analysis program package.^[98]

Supporting Information

Energies and Gibbs free energies for the intrinsic barriers and the isomerisation reactions, the optimised geometries in xyz format and the corresponding electronic energies. Additional references cited within the Supporting Information.^[135]

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Conflict of Interests

The authors declare no conflict of interest.

Data Availability Statement

The data that support the findings of this study are available in the supplementary material of this article.

Keywords: chalcogen · charge transfer · electrostatic interactions · nucleophilic substitution · pnictogen · transition state

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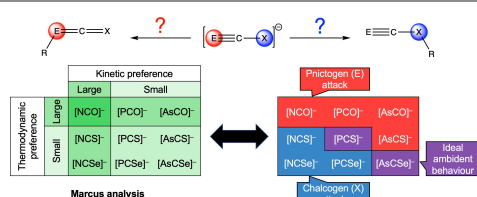
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While the ambident nature of the [NCX]⁻ (X: O, S, Se) anions is well known, the analogous heavier P- or As-containing species are lesser explored. This computational study explores the ambident S_N2 reactivities of all existing [ECX]⁻ (E: N, P, As; X: O,

S, Se) anions. The results conceptualise reactivity patterns and offer explanations on the trends so that the accessibility of unprecedented low-coordinate organopnictogen species can be proposed.

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Deciphering the Differences in Ambident Reactivity between the Cyanate, Thiocyanate Ions, and their P- and As-Containing Analogues

