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ARTICLE TYPE

Experimental and Theoretical Studies on Polar Diels-Alder Reactions of 1-Nitronaphthalene developed in Ionic Liquids

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The reactions between 1-nitronaphthalene **1** and two nucleophilic dienes, Danishefsky's diene **2** and 1-trimethylsilyloxy-1,3-butadiene **3**,
10 to yield phenanthrenols **7** and **8** developed in protic and aprotic ionic liquids (ILs) with an imidazolium cation base permit to conclude
that the reactions occur in better experimental conditions than in molecular solvents. The yields obtained with protic ILs are better than
those observed with aprotic ILs. In this sense, the higher yields obtained with aprotic ILs, (working at 60°C, 48 h) are comparable with
the lower yields observed in protic ILs (60 °C, 24 h). DFT calculations for the reaction of 1-nitronaphthalene **1** with diene **3**, in the
15 absence and in the presence of tetrafluoroborate of 1-metilimidazolium [HMIM] [BF₄] as protic ILs, indicate that this reaction is a
domino process that comprises two consecutive processes: i) a polar Diels-Alder (P-DA) reaction between **1** and **3**, and ii) an elimination
of nitroso acid **5** to yield dihydrophenanthrene **11**. Thermodynamic calculations indicate that while the first reaction is the rate-
determining step of this domino process, the nitroso acid elimination is the driving force responsible for the formation of
dihydrophenanthrene **11**. Implicit and explicit solvent effects indicate that while the hydrogen bond formation between HMIM and one
20 oxygen atom of the nitro groups favour the two reactions, implicit solvent effects modelled by PCM decelerate the P-DA reaction by a
large solvation of reagents. Finally, DFT analysis of reagents offers an explanation of the catalytic role of protic ILs in these P-DA
reactions.

Introduction

The Diels-Alder (DA) reaction is one of the most significant and
25 useful tools available in synthetic chemistry. This reaction
provides the chemist with one of the best methods for the
preparation of cyclic and heterocyclic aromatic compounds. It is
an elegant and fundamental process since it allows the formation
of a six-membered ring, generates stereocentres and introduces
30 functional groups, all in a single step, often by observing the
exclusive formation or preponderant isomer among several
possible ones. This reaction supports a wide range of functional
groups, thus leading to multiple products. Its potential in natural
product synthesis is very well known.¹ In a first approach, we can
35 consider that this reaction takes place in one-step inter- or
intramolecular from a diene and dienophile bearing an almost
unlimited number of variants. It is worth noting that these
variants exist not only in the substitution of the reaction
component but also in the electronic nature of these dienes and
40 dienophiles.²

In the 1980s, studies on cycloaddition reactions of carbonyl or
carboxyl substituted aromatic heterocycles such as indoles,
benzofurans, pyrroles, furans, and thiophenes demonstrated the
viability of these aromatic systems as dienophiles.³ Further
45 studies focused on the dienophilic character of indoles since their
adducts seemed to be appealing for the total synthesis of
carbazole and *Aspidosperma* alkaloids.⁴

Moreover, attention has been turned to the investigation of the
dienophilicity of substituted naphthalenes. While the use of these
50 substrates as dienes in thermal and high-pressure DA reactions

has been widely studied,^{5,6} the use of such compounds as
dienophiles has received relatively little attention in the literature.

In previous articles, we have reported that naphthalenes properly
substituted with an electron withdrawing (EW) group act as
55 dienophiles in DA reactions. These electrophilic dienophiles were
exposed to different dienes, strongly, moderately and poorly
nucleophilic activated, under thermal conditions using molecular
solvents as reaction media to achieve the corresponding
hydroxyphenanthrene.⁷

60 According to the nature of the substituent groups, this
cycloaddition is considered a polar process. Thus, there are some
interesting aspects related to the solvent dependence. Taking into
account the aromaticity of this dienophile, classical
methodologies -employing molecular solvents + media- require
65 elevated temperatures and long reaction times, which may lead,
in certain situations, to undesirable side reactions. It is therefore
useful to explore other working conditions. Based on this
possibility and knowing that the use of solvents in most cases is
an essential part of the polar chemical process, for their influence
70 on the development of the reaction and its impact on the
environment, we decided to study this type of reaction in the
presence of an ionic liquid (IL). An IL is a salt, substance
composed exclusively of cations and anions, and this fact
differentiates them from simple ionic solutions, in which ions are
75 dissolved in a molecular medium. ILs are called "designer"
solvents since various thermophysical properties and functions can
be created by the choice of cation and anion. Some of the recent
reviews presenting an overview of the potential of ILs as solvents
for synthesis and catalysis are available.⁸

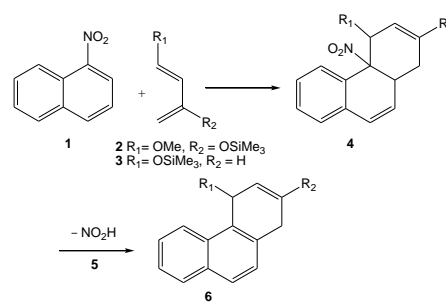
The interest of this class of molecules arises in part from their use as liquid media for a variety of chemical transformations as a substitute for molecular solvents. The design and discovery of ILs displaying a melting point below 100 °C, in particular room temperature ionic liquids (RTILs), have been the subject of considerable efforts over the past decade. In particular, RTILs attract considerable attention as they are expected to be ideal solvents that provide a novel reaction field in sustainable chemistry.⁹ RTILs exhibit a variety of desirable properties, such as negligible vapour pressure, which makes them interesting for various applications. In particular, the option of fine-tuning chemical and physical properties by an appropriate choice of cations and anions has stimulated much of the current excitement with respect to these compounds. ILs have a high solvation capacity for a wide variety of polar, non-polar, organic and inorganic molecules as well as organometallic compounds. These salts can be classified as moderately polar solvents (ϵ ca. 13). However, these behaviours indicated markedly lower polarities than those found by spectroscopy with polarity sensitive solvatochromic dyes [e.g. for 1-*n*-butyl-3-methylimidazolium tetrafluoroborate $E_T(33)$ is 61.60]. The normalised value E_T^N is 0.7, while the value corresponding to water is 1.00. On the other hand, the π^* for the IL is 1.1.¹⁰

Also, their properties can be changed allowing the selective solvation of solutes and the control of the mutual miscibility of particular organic compounds such as, for instance, alcohols and water. As a consequence, the characterization of the properties of different classes of ILs used as solvents for specific applications and for chemical reactions and catalysis have been intensively investigated.¹¹ Due to their ionic nature, the structure of ILs is able to incorporate different levels of complexity. First, and in order to maintain local electro-neutrality, the high-charge density parts of cations and anions must create a three-dimensional network where the nearest neighbours of a given ion are of the opposite sign. Second, the low-charge density residues that are often present in ions (generally as alkyl side chains) are segregated from the polar network, forming non-polar domains. This nano-segregation/structuration between polar and non-polar regions, first predicted by molecular dynamics simulation studies and later corroborated by diffraction techniques, implies the existence of differentiated and complex interactions not only in pure ILs but also in their mixtures with molecular solutes or even other ILs.

It has been demonstrated that aqueous solutions remarkably increase the reactivity and selectivity in DA reactions. The remarkable increase in reactivity and selectivity observed in aqueous solutions was discussed in the pioneering work of Breslow *et al*¹² in terms of hydrophobic effects.¹³ The possibility of using ILs as a substitute for water, which has become an alternative solvent to carry out DA reactions, has been explored. The first study was centred on the reaction of cyclopentadiene with methyl acrylate and methyl vinyl ketone in ethyl ammonium nitrate [EtNH₃][NO₃].¹⁴ This reaction led to a mixture of *exo* and *endo* products, and the solvent influences on the *endo/exo* selectivity of the reaction are well understood. Changes in selectivity can be attributed to solvophobic interactions that generate an “internal pressure” and promote the association of the reagents in a “solvent cavity” during the activation process. These reactions have shown a strong preference for the *endo* product and an acceleration of the reaction in comparison to non-polar organic solvents. Although the increased rate and selectivities were not as great as those seen in water, ILs have the advantage that moisture-sensitive reagents may be used. A “hydrophobic effect”, originating from the IL-organic interface can be considered. Consequently, the reaction rate is increased, due to

the proximity of reactants in the corresponding transition state structure (TS). These effects as well as the hydrogen bridges between ILs and organic molecules play an important role in the reaction rate. Protic ionic liquids (PILs) with similar properties to water, i.e. being a highly ordered medium and a good hydrogen bonding donor, have also been shown to have potential influence on the outcome of DA reactions. The response of DA reactions to their solvent environment is complex, and different dependencies are found when measuring selectivity or kinetics and when different dienophiles are used. Solvent effects that are seen in these DA reactions are a function of both the solvent and the solute. For a solvent effect to be seen, the solute must have a complimentary character. In this sense, a different behaviour of DA reactions of nitropyrrroles and nitroindoles, both acting as dienophiles with some dienes in the presence of ILs, is observed.¹⁵ Recently we have developed DA reactions using nitrofurans, nitro-*N*-tosylpyrroles, and *N*-tosyl-3-nitroindole as dienophiles in the presence of PILs with better results than when a molecular solvent was used.¹⁶

The reactivity and regioselectivity of cycloaddition reactions can be easily explained through the density functional theory (DFT), being applied in this context along the last years.¹⁷ Current studies, based on the conceptual DFT¹⁸ applied to DA reactions, have shown that the classification of the diene/dienophile pair within a unique scale of electrophilicity is a powerful tool to predict the feasibility of the process and the type of reaction mechanism involved.^{17a} In this sense, the reaction of 1-nitronaphthalene **1** with Danishefsky's diene **2** developed in benzene as solvent has been theoretically studied using DFT methods (see Scheme 1).¹⁹ The reaction is a domino process that is initialized by a polar Diels-Alder (P-DA) reaction²⁰ between electrophilic **1**, acting as the dienophile component, and nucleophilic **2**, acting as the diene one, to give formally [2 + 4] cycloadduct (CA) **4**. The subsequent elimination of nitrous acid **5** yields hydrophenanthrene derivative **6**. Analysis of the global electrophilicity indices as well as the thermodynamic data for this domino process indicate that while the strong electrophilic character of **1** and the strong nucleophilic character of diene **2** are responsible for the participation of these reagents in a P-DA reaction, the irreversible extrusion of nitrous acid **5** from CA **4** is responsible for the feasibility of the overall process.¹⁹



Scheme 1

Herein, we explore the behaviour of 1-nitronaphthalene **1** as the dienophile component in P-DA reactions using two dienes of varying nucleophilicity, developed in presence of protic and aprotic ILs. In this sense, we try to compare these results with those obtained in thermal DA reactions using molecular solvents and thus analyzing the influence of the solvent nature. The second aim concerns theoretical studies using DFT methods, trying to obtain a valuable model of the dienophile-PIL aggregate, to obtain some information about the factors affecting reactivity, selectivity and reaction mechanism. Moreover, we

have discussed the dynamic of the reaction in the presence of an IL using this theory.

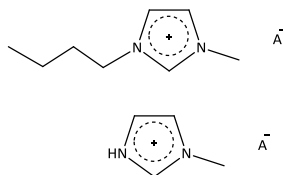
2. Result and discussion

5 a) Experimental results.

To explore the electrophilic behaviours of 1-nitronaphthalene **1** in P-DA reactions in the presence of ILs we selected 1-methoxy-3-trimethylsilyloxy-1,3-butadiene (Danishefsky's diene) **2**, and 1-trimethylsilyloxy-1,3-butadiene **3** as nucleophilic dienes (see

10 Scheme 1). The choice of these dienes depended on the type of substitution present in their structures and the relative nucleophilicity. In order to study the solvent dependence of P-DA reactions of 1-nitronaphthalene **1**, 1-methylimidazolium tetrafluoroborate ([HMIM][BF₄]), 1-methylimidazolium hexafluorophosphate ([HMIM][PF₆]), 1-butyl-3-methylimidazolium tetrafluoroborate ([BMIM][BF₄]), 1-butyl-3-methylimidazolium hexafluorophosphate ([BMIM][PF₆]) were chosen as representative protic and aprotic ILs. This selection allowed us

20 to compare the influence of ILs vs molecular solvents on the reactivity and the regioselectivity when participating in P-DA reactions.



25 **Figure 1** – Ionic Liquids (A: BF₄⁻/PF₆⁻)

When **1** reacted with diene **2** in a sealed ampoule at 60°C for 24 h using [HMIM][BF₄] as solvent the reactions proceeded to produce phenanthren-2-ol (**7**)⁶ in reasonable yield (51%). If the reaction time increased to 48 h, we also observed the formation of **7** although a yield of 60%. Using [HMIM][PF₆] under the same conditions we also observed the cycloadduct **7** formation although the yield was higher (62%, 24 h, 60°C; 70%, 48 h, 60°C)

35 (Table 1, Scheme 2). Similar results were observed when the reaction was developed in [BMIM][BF₄] and [BMIM][PF₆] although the yields were lower (35% and 49%, 24 h 60 °C, respectively) (Table 1, Scheme 2).

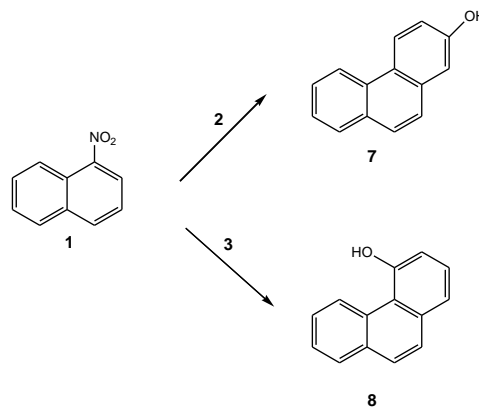
Entry	Diene	Conditions ^a	Product	Yield ^b
1	2 , 2 equiv	HMIM BF ₄ , 24 h	7	51
2		HMIM BF ₄ , 48 h	7	60
3		HMIM PF ₆ , 24 h	7	62
4		HMIM PF ₆ , 48 h	7	70
5		BMIM BF ₄ , 24 h	7	35
6		BMIM BF ₄ , 48 h	7	41
7		BMIM PF ₆ , 24 h	7	49
8		BMIM PF ₆ , 48 h	7	55
9	3 , 2 equiv	HMIM BF ₄ , 24 h	8	48
10		HMIM BF ₄ , 48 h	8	55
11		HMIM PF ₆ , 24 h	8	61
12		HMIM PF ₆ , 48 h	8	65
13		BMIM BF ₄ , 24 h	8	32
14		BMIM BF ₄ , 48 h	8	37
15		BMIM PF ₆ , 24 h	8	43
16		BMIM PF ₆ , 48 h	8	48

40 ^a Reaction temperature 60 °C.

^b Based on consumed dienophile.

Table 1

The reactions of **1** with diene **3** using [HMIM][BF₄] as solvent in a sealed ampoule at 60°C for 24 and 48 h afforded in all cases phenanthren-4-ol **8**⁶ in 48% and 55% yields, respectively. Using [HMIM][PF₆] as solvent under the same conditions, the product **8** was obtained in 61 and 65% yields. Similarly, reactions in [BMIM][PF₆] and [BMIM][BF₄] offered **8** with lower yields (24 h, 60 °C, 43 and 32 %, respectively). (Table 1, Figure 3). All the reactions were carried out at least three times each.



Scheme 2

55 It can be seen that anion PF₆ produces a better effect on the reactions than BF₄. The effect of the different anions depends on the cation nature.

The hydrogen bond (HB) donor capacity of PILs through the cation, moderated by the HB acceptor's ability of the anion, makes possible the existence of a competitive equilibrium between both of them. Moreover, ILs containing PF₆ are more hydrophobic than those with BF₄ as the anion.

In all cases, the presence of ILs as reaction media, results in a similar or higher yields with respect to the use of a molecular solvent, while the temperature and reaction time decrease significantly, an important reaction factor which can prevent the formation of potential byproducts. The reaction of **1** with diene **2** working for 72 h at 120°C in benzene shows a yield ca 50 % (product **7**). Alternatively, the reaction of **1** with diene **3** indicates a change in the reaction pathway. Under similar conditions than diene **2**, we observed two products being the results of the competition between the expected P-DA yielding [2+4] CA **8** vs the hetero DA process yielding [4+2] CA **9** (see Figure 2), with a global yield of ca 40%. In the latter reaction we noted a difference in the behaviour of the reaction system when working in the presence of an IL.

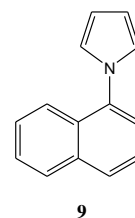


Figure 2

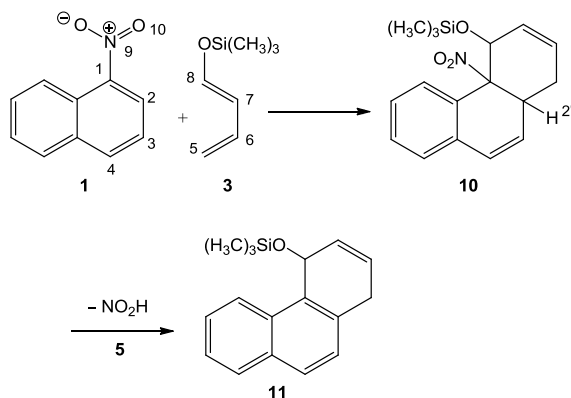
b) Calculations

DFT study of the role of PILs in the reaction between 1-nitronaphthalene **1** and 1-trimethylsilyloxy-1,3-butadiene **3**.

In order to understand the catalytic role of PILs in P-DA reactions, the domino reaction between 1-nitronaphthalene **1** and 1-trimethylsilyloxy-1,3-butadiene **3**, in the absence and in the presence of [HMIM][BF₄] as a model of PILs, was theoretically studied using DFT methods at the MPWB1K/6-31G* and MPWB1K/6-311G** levels.

Study of the domino reaction between 1-nitronaphthalene 1 and 1-trimethylsilyloxy-1,3-butadiene 3.

The reaction between 1-nitronaphthalene **1** and 1-trimethylsilyloxy-1,3-butadiene **3** to yield dihydrophenanthrene **11** is a domino process that comprises two consecutive reactions: i) a P-DA reaction between 1-nitronaphthalene **1**, acting as dienophile, and diene **3** to yield the formal [2+4] CA **10**; and ii) a subsequent elimination of nitroso acid **5** in CA **10** to yield dihydrophenanthrene **11** (see Scheme 3).



Scheme 3

For the initial attack of the C5 carbon of diene **3** on the C2 carbon of 1-nitronaphthalene **1**, two stereoisomeric channels are feasible: the *endo* and the *exo* ones. Since both *endo* and *exo* channels yield the same dihydrophenanthrene **11** after elimination of nitroso acid **5**, only the channel associated with the *endo* approach mode of diene **3**, with respect to the electron-withdrawing nitro group of 1-nitronaphthalene **1**, was considered.

An analysis of the gas-phase potential energy surfaces (PES) associated with this P-DA reaction indicates that the cycloaddition takes place through a one-step mechanism via high asynchronous TS. Therefore, reagents, **1** + **3**, one TS, **TS1**, and [2+4] CA **10**, were located and characterised. The second reaction of this domino process also takes place via a one-step mechanism through high asynchronous TS. Thus, one TS **TS2**, and the corresponding final products, **5** and **11**, were located and characterised (see Scheme 3). The relative gas-phase energies are given in Table 2.

TS1	17.0
10	-16.1
TS2	16.0
11 + 5	-28.0

Table 2. MPWB1K/6-311G** Relative energies, in kcal/mol, of the stationary points involved in the reaction between 1-nitronaphthalene **1** and 1-trimethylsilyloxy-1,3-butadiene **3**.

In the gas phase, the activation energy associated with the nucleophilic attack of the C5 carbon of diene **3** on the C2 carbon

of 1-nitronaphthalene **1** via **TS1** presents a high value, 17.0 kcal/mol; formation of CA **10** is exothermic by -16.1 kcal/mol. The MPWB1K/6-311G** activation energy is closer to that found for the P-DA reaction between 1-nitronaphthalene **1** and Danishefsky's diene **2** at the B3LYP/6-31G* level, 16.5 kcal/mol.¹⁹ However, the B3LYP functional underestimates the exothermic character of the reaction, 0.2 kcal/mol.

CA **10** undergoes an elimination of nitroso acid **5** regenerating the aromatic system present in naphthalene. The activation energy associated with the elimination of nitroso acid **5** via **TS2** is 32.1 kcal/mol; formation of dihydrophenanthrene **11** plus nitroso acid **5** is exothermic by -11.9 kcal/mol. Taking into account the favourable reaction entropies associated with the extrusion processes, we can consider this reaction thermodynamically irreversible (see later).

The MPWB1K/6-31G* gas-phase geometries of the TSs involved in the domino reaction between 1-nitronaphthalene **1** and 1-trimethylsilyloxy-1,3-butadiene **3** are given in Figure 4. The distances between the C2 and C5, and C1 and C8 carbons at **TS1** associated with the P-DA reaction between 1-nitronaphthalene **1** and diene **3** are 1.929 and 2.761 Å, respectively. Recent studies devoted to bonding changes along polar reactions have shown that the C-C bond formation begin in the narrow region of 2.07-1.95 Å. Consequently, the C2-C5 distance at the high asynchronous **TS1**, 1.929 Å, indicates that the C2-C5 bond formation already have started, while the distance between the C1 and C8 atoms, 2.761 Å, shows that they are not bonding. This clearly indicates that this one-step P-DA reaction is non-concerted.²¹

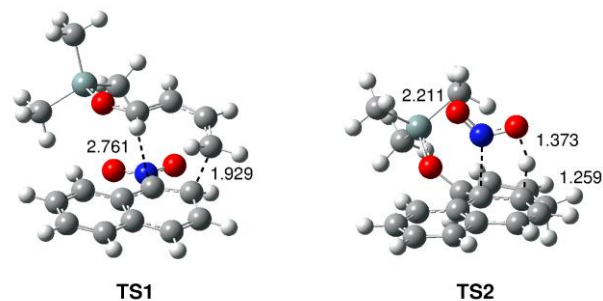


Figure 4. MPWB1K/6-31G* transition structures involved in the reaction between 1-nitronaphthalene **1** and 1-trimethylsilyloxy-1,3-butadiene **3**. The distances are given in Angstroms.

At **TS2** associated with the elimination of nitroso acid **5**, the length of the C1-N9 breaking bond is 2.211 Å, while the lengths of the C2-H2' breaking- and O10-H2' forming-bonds are 1.259 and 1.373 Å, respectively. These values suggest an asynchronous process in which the C1-N9 breaking bond is more advanced than the H2' proton transfer process from C2 to the O10 oxygen.

The polar nature of the DA reaction was evaluated analysing the charge transfer (CT) at **TS1**. The natural charges at this TS were shared between the nitronaphthalene and the butadiene frameworks. At **TS1**, the CT that flows from the diene to the nitronaphthalene framework is 0.32eV. This value points to the strong zwitterionic character of this TS. This value is lower than that obtained at the TS associated with the nucleophilic attack of Danishefsky's diene **2** on nitronaphthalene **1**,¹⁹ 0.39eV, as a consequence of the stronger nucleophilic character of Danishefsky's diene **2** than that of diene **3**.

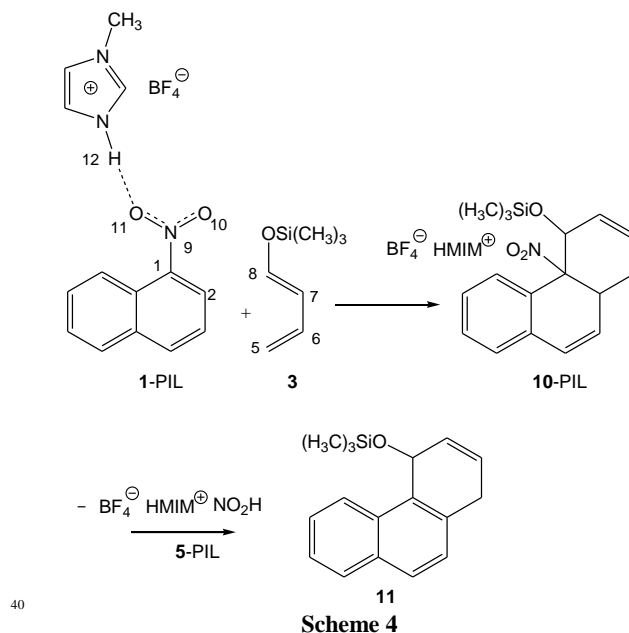
Study of the domino reactions between 1-nitronaphthalene 1 and 1-trimethylsilyloxy-1,3-butadiene 3 in the presence of the [HMIM][BF₄] PIL.

The effects of the [HMIM][BF₄] PIL on the domino reaction between 1-nitronaphthalene **1** and 1-trimethylsilyloxy-1,3-butadiene **3** were evaluated considering two computational models. In *Model I*, implicit effects of the PIL were considered by forming an HB between the acidic H12 hydrogen of HMIM⁺ and the O11 oxygen of the nitro group of 1-nitronaphthalene **1** (see Scheme 4), while in *Model II*, explicit solvent effects of the PIL are completed including electrostatic interactions modelled by the polarisable continuum model (PCM) of Tomasi's group. For PCM calculations, 1-heptanol was considered as solvent since it has a dielectric constant closer to IL ($\epsilon = 11.3$). The energy results are given in Table 3.

	<i>Model I</i>	<i>Model II</i>
TS1-PIL	11.0	14.9
10-PIL	-16.2	-14.3
TS2-PIL	12.9	13.2
11 + 5-PIL	-22.7	-25.0

Table 3. MPWB1K/6-311G** Total (E, in au) and relative (ΔE , in kcal/mol) energies, in gas phase, *Model I*, and in 1-heptanol, *Model II*, of the stationary points involved in the reaction between complex **1-PIL** and 1-trimethylsilyloxy-1,3-butadiene **3**.

In Scheme 4, the stationary points involved in the domino reaction between [HMIM][BF₄]:1-nitronaphthalene complex **1-PIL** and diene **3** are given. In the study of *Models I* and *II*, the BF₄⁻ counter anion was also included to minimise the positive charge present in the HMIM⁺ cation. Implicit solvent effects of PIL do not change the molecular mechanism of this domino reaction. Formation of the HB between HMIM and an oxygen atom of the nitro group decreases the activation energy associated with this P-DA reaction significantly. Now, in gas phase **TS1-PIL** is located 11.1 kcal/mol only above of the separated reagents, **1-PIL** + **3**. In spite of this behaviour, the exothermic character of the P-DA reaction remains unmodified (-11.6 kcal/mol). The large acceleration found in the presence of the PIL can be understood as an increase of the polar character of the reaction as a consequence of the increased electrophilic character of complex **1-PIL**, which favours the CT process (see later).²⁰



The second reaction of this domino process appears also catalysed by the presence of [HMIM][BF₄] PIL, since it remains hydrogen-bonded to the nitro group in intermediate **10-PIL**. Now, the activation energy associated with the extrusion of **5-PIL** is 29.0 kcal/mol. This reaction is exothermic by -6.6 kcal/mol.

Inclusion of the solvent effects by means of PCM single-point energy calculations in *Model II* stabilises all species between 20.0 and 24.0 kcal/mol, as a consequence of the charged [HMIM][BF₄] PIL. In spite of the zwitterionic character of **TS1-PIL**, **1-PIL** is slightly more stabilised than the TS. As a consequence, the activation energy associated with the P-DA reaction increases by 3.9 kcal/mol respect to the gas-phase calculations. In spite of this unfavourable solvation effect, the activation energy associated with **TS1-PIL** in 1-heptanol remains below (2.1 kcal/mol) in the gas phase **TS1**. These energy results suggest that the HB formation at 1-nitronaphthalene **1** is the main factor responsible for the acceleration of this domino reaction in PILs.

The MPWB1K/6-31G* gas-phase geometries of **TS1-PIL** and **TS2-PIL** are given in Figure 5. The distances between the C2 and C5, and C1 and C8 carbons at **TS1-PIL** associated with the P-DA reaction between complex **1-PIL** and diene **3** are 1.950 and 3.088 Å, respectively. These lengths indicate that such as **TS1**, this highly asynchronous **TS1-PIL** corresponds with a no-concerted process. At **TS1-PIL**, the distance between the nitro O11 oxygen and the acidic H12 hydrogen of HMIM, 1.749 Å, suggests a strong BH interaction. Note that at complex **1-PIL**, this distance is 1.898 Å.

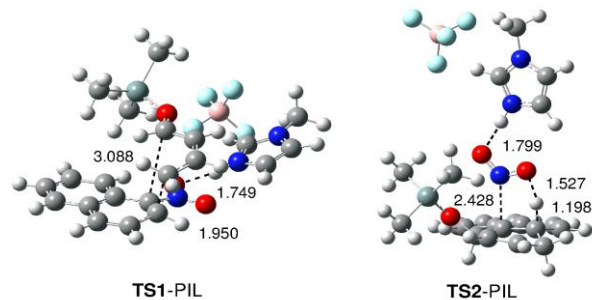


Figure 5. MPWB1K/6-31G* transition structures involved in the reaction between complex **1**-PIL and 1-trimethylsilyloxy-1,3-butadiene **3**. The distances are given in Angstroms.

At **TS2**-PIL associated with the extrusion of **5**-PIL, the length of the C1-N9 breaking bond is 2.428 Å, while the lengths of the C2-H2' breaking- and O10-H2' forming-bonds are 1.527 and 1.198 Å, respectively. These values also suggest a highly asynchronous process in which the C1-N9 breaking bond is very advanced with respect to the H1' proton transfer process.

In the P-DA reaction between complex **1**-PIL and diene **3**, the CT at **TS1**-PIL, which flows from **3** to **1**-PIL, is 0.38e, being indicative of the strong zwitterionic character of the TS. Consequently, the acceleration found in the P-DA between 1-nitronaphthalene **1** and diene **3** in PILs can be understood through an increase of the polar character of the reaction achieved by the HB formation between 1-nitronaphthalene **1** and the PIL.

Finally, as the two reactions involved in this domino reaction have different molecularity, thermodynamic calculations concerning reaction *Model II* were performed in order to establish the rate-determining step (RDS) of this domino process. The relative enthalpies (ΔH , in kcal/mol), entropies (ΔS , in eu) and free energies (ΔG , in kcal/mol) of the stationary points involved in the reaction *Model II* are given in Table 4.

Inclusion of thermal corrections to the electronic energies does not substantially modify the relative enthalpies. Thus, the activation enthalpy associated with the P-DA reaction is 12.7 kcal/mol, formation of **10**-PIL being exothermic by -13.6 kcal/mol. On the other hand, the activation enthalpy associated with the elimination of nitroso acid **5**-PIL is 23.3 kcal/mol, the overall domino process being exothermic by -26.4 kcal/mol.

	ΔH	ΔS	ΔG
TS1 -PIL	12.7	-63.6	33.9
10 -PIL	-13.6	-65.0	8.0
TS2 -PIL	9.7	-64.8	31.3
11 + 5 -PIL	-26.2	-8.4	-23.4

Table 4. Relative enthalpies (ΔH , in kcal/mol), entropies (ΔS , in eu) and free energies (ΔG , in kcal/mol) in 1-heptanol, computed at 60 °C and 1 atm, of the stationary points involved in reaction *Model II*.

Inclusion of entropies to the enthalpies increases the free activation energy associated with the P-DA reaction to 33.9 kcal/mol. In addition, the unfavourable $T\Delta S$ term associated with this bimolecular process turns the P-DA reaction into endergonic by 8.0 kcal/mol. A different result is observed in the step associated with the elimination of nitroso acid, which presents a free activation energy of 23.3 kcal/mol, the overall domino reaction being exergonic by -23.4 kcal/mol. Analysis of the free energy results given in Figure 6 indicates that while the first P-DA reaction is the RDS of the domino process, the subsequent elimination of nitroso acid **5** is the driving force responsible for the formation of dihydrophenanthrene **11**.

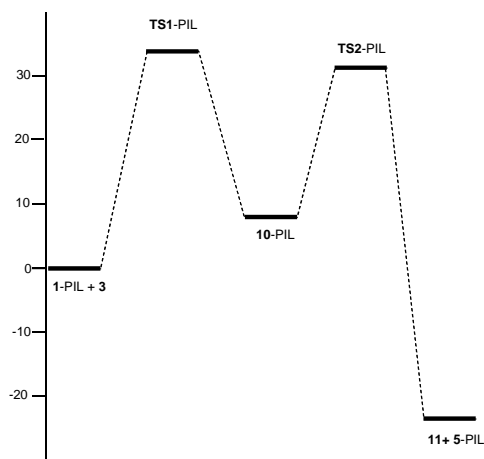


Figure 6. Free energy profile, in kcal/mol, for the reaction between complex **1**-PIL and 1-trimethylsilyloxy-1,3-butadiene **3**.

Analysis based on DFT reactivity indices.

Studies carried out on cycloaddition reactions have shown that the indices defined within the conceptual DFT¹⁸ are powerful tools for analysing the reactivity and the regioselectivity in polar reactions. The B3LYP/6-31G* static global properties, namely electronic chemical potential μ , chemical hardness η , global electrophilicity ω , and global nucleophilicity, N , for 1-nitronaphthalene **1**, complexes **1**-[HMIM][PF₆] and **1**-[HMIM][BF₄], dienes **2** and **3** are displayed in Table 5.

	μ	η	ω	N
1 -[HMIM][PF ₆]	-5.28	3.49	4.00	2.09
1 -[HMIM][BF ₄]	-5.25	3.51	3.93	2.12
1	-4.47	4.00	2.50	2.65
3	-2.84	5.38	0.75	3.59
2	-2.69	5.32	0.68	3.77

Table 5. B3LYP/6-31G* Electronic chemical potential μ , chemical hardness η , global electrophilicity ω , and global nucleophilicity, N , in eV, for 1-nitronaphthalene **1**, complexes **1**-[HMIM][PF₆] and **1**-[HMIM][BF₄], diene **2** and diene **3**.

The electronic chemical potential μ of 1-nitronaphthalene **1**, $\mu = -4.47$ eV, and complexes **1**-[HMIM][PF₆] and **1**-[HMIM][BF₄] $\mu = -5.28$ and -5.25 eV, are below the electronic chemical potential μ of dienes **2** and **3**, $\mu = -2.69$ and -2.84 eV, respectively, thereby indicating that in a polar process, the net CT will take place from dienes **2** and **3** to these nitronaphthalene derivatives, in clear agreement with the CT observed at the TSs.

1-Nitronaphthalene **1** has a high electrophilicity ω index, 2.50 eV, being classified as a strong electrophile within the electrophilicity scale.^{17a} On the other hand, it presents a nucleophilicity N index of 2.65 eV, being classified as a moderate nucleophile.²² Formation of an HB between the acidic H12 hydrogen of HMIM⁺ and the O11 oxygen of the nitro group increases the electrophilicity ω index of complexes **1**-[HMIM][PF₆] and **1**-[HMIM][BF₄] to 4.00 and 3.93 eV and decreases the nucleophilicity N index to 2.09 and 2.12 eV. The slightly higher electrophilic character of **1**-[HMIM][PF₆] than **1**-[HMIM][BF₄] can justify the better results obtained in [HMIM][PF₆] PIL.

Danishefsky's diene **2** and 1-trimethylsilyloxy-1,3-butadiene **3** have electrophilicity ω indices of 0.68 and 0.75 eV, being classified as marginal electrophiles, and nucleophilicity N indices of 3.77 and 3.59 eV, being classified as strong nucleophiles.

Consequently, it is expected that the P-DA reactions of 1-nitronaphthalene **1** with dienes **2** and **3** will have polar character, in clear agreement with $\Delta\omega$ between reagents, *ca.* 1.8 eV, and with the CT found at **TS1**. On the other hand, the high electrophilicity of complex **1-PIL** accounts for the acceleration observed in the P-DA reactions between 1-nitronaphthalene **1** and diene **3** in PILs, as a consequence of the increase of the polar character of the reactions. Note that the increase of the polar character of the reaction in PILs measured by $\Delta\omega$ between complex **1-PIL** and diene **3**, 3.18 eV, is in clear agreement with the high CT found at **TS1-PIL**.

Local electrophilicity, ω_k , and nucleophilicity, N_k , indices can be used to measure the distribution of the global electrophilicity and nucleophilicity at the different atomic sites of a molecule, and thus state the local reactivity. Along a polar reaction involving asymmetric reagents, the most favourable reactive channel is that involving the initial two-centre interaction between the most electrophilic and nucleophilic centre of both reagents.

Analysis of the local electrophilicity ω_k indices of 1-nitronaphthalene **1** indicates that the C4 carbon, $\omega_{C4} = 0.69$ eV, is more electrophilically activated than the C2 carbon, $\omega_{C2} = 0.45$ eV (see Figure 7). Note that they correspond to the *ortho* and *para* positions of the aromatic ring with respect to the nitro group. As we have already demonstrated, the nucleophilic attack on C4 yields a CA, which reverts to reagents **1** + **3** since it can not eliminate nitroso acid **5**.¹⁹

Formation of the HB between the acidic H12 hydrogen of HMIM⁺ and the O11 oxygen of the nitro group does not only increases the electrophilicity index of complex **1-PIL**, but also polarises the nitronaphthalene system. The most electrophilic centres are the C4 carbon, $\omega_{C4} = 1.01$ eV, and the C2 carbon, $\omega_{C2} = 0.84$ eV. These results are similar to those found in nitronaphthalene **1**.

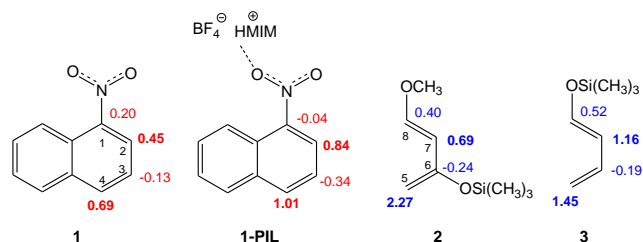


Figure 7. Local electrophilicity indices, ω_k , in 1-nitronaphthalene **1** and complex **1-PIL**, and local nucleophilicity indices, N_k , in butadienes **2** and **3**.

Analysis of the local nucleophilicity N_k indices of dienes **2** and **3** indicates that the non-substituted C5 carbon is the most nucleophilically activated centre of these dienes, $N_{C5} = 2.27$ and 1.45 eV (see Figure 7). Interestingly, the presence of the TBSiO group at C6 in diene **2** not only increases the global nucleophilicity index, but also polarises the local nucleophilicity towards C5.

Conclusions

The reactions between 1-nitronaphthalene **1** and two nucleophilic dienes, **2** and **3**, to yield phenanthrenols **7** and **8** developed in

protic and aprotic ILs with an imidazolium cation base permit to conclude that the reactions occur under better experimental conditions, shorter time and lower temperature than thermal cycloadditions in molecular solvents, proving the influence of ILs in this type of polar processes. The yields obtained with PILs are better than those observed with non-PILs. In this sense, it is convenient to mention that the higher yields obtained with non-PILs (working at 60°C, 48 h) are comparable with the lower values observed in PILs (60 °C, 24 h). When nucleophilic diene **3** is used in ILs, only the formation of CA **8** is observed. In this context, it is necessary to take into account that when molecular solvents were used, together with CA **8**, product **9** was also formed resulting from of a hetero process. ILs can be divided in two groups: water immiscible or hydrophobic ILs (e.g. [BMIM][PF₆]) and water miscible or hydrophilic (e.g. [BMIM][BF₄]). Thus, it is not surprising that the yields obtained with anion PF₆ in all cases and with both types of ILs, are better than those obtained with anion BF₄, possibly due to their major hydrophobicity.

The reaction of 1-nitronaphthalene **1** with diene **3**, in the absence and in the presence of [HMIM][BF₄] as a PIL, has been studied using DFT methods. This reaction is a domino process that comprises two consecutive reactions: i) a P-DA reaction between **1** and **3** yielding [2+4] CA **10**, and ii) an elimination of nitroso acid **5** from **10** to afford dihydrophenanthrene **11**. Solvent effects of [HMIM][BF₄] were considered using two models: while implicit effects of PILs modelled by formation of an HB between the acidic hydrogen of HMIM⁺ and one oxygen atom of the nitro group favours both the P-DA reaction as well as the nitroso acid elimination, explicit solvent effects modelled by PCM decelerate the reaction by a larger solvation of reagents. The net solvent effects indicate that the reaction is favoured by the HB formation. Thermodynamic calculations indicate that while the first reaction is the RDS, the nitroso acid elimination is the driving force responsible for the formation of the tricyclic compound.

DFT analysis of reagents indicates that the strong electrophilic character of 1-nitronaphthalene **1** and the strong nucleophilic character of diene **3** are responsible for the polar character of the DA reaction. HB formation accelerates the reaction by an increase of the electrophilic character of the corresponding HB complex **1-PIL**. This behaviour justifies that the reaction in PILs such as [HMIM][BF₄] takes place under better reaction conditions than in non-PILs such as [BMIM][BF₄].

General Aspects

¹H and ¹³C NMR spectra were recorded with the deuterated solvent as the lock and residual solvent as internal on 300 and 75 MHz FT-spectrometers, respectively; GC-MS analyses were performed in an instrument equipped with a PE-5-type column. IR spectra were recorded from NaCl cells. The silica gel and neutral alumina used for chromatography were 70-230 mesh. 1-Nitronaphthalene and the dienes were obtained from commercial sources.

Preparation of ionic liquids employed in the thermal reactions were done following the published methods²³ and they consisted in the following steps:

1-Methylimidazoliumtetrafluoroborate/1-Methylimidazolium hexafluorophosphate ([HMIM][BF₄]/ [PF₆]):

1-Methylimidazole was placed in a round-bottomed flask equipped with a stirring bar and tetrafluoroboric acid (48% solution in water) or hexafluorophosphoric acid (65% solution in water) was added in portions with stirring. The mixture was stirred at room temperature for 3 h and then concentrated on a

rotary evaporator. The product was washed with ethyl acetate and dried under a vacuum (2-3 Torr) for 10 h at 70 °C (90% yield).

1-Methyl-3--butylimidazolium tetrafluoroborate/1-Methyl-3-butylimidazolium hexafluorophosphate: ([BMIM][BF₄]/PF₆):

1-Methylimidazole, 1-chlorobutane (excess) and dry acetonitrile were placed in a round-bottomed flask (under nitrogen atmosphere) equipped with a stirring bar. The mixture was stirred for 72 h at 80°C and then concentrated under vacuum.

Metathetic exchange of anion: [BMIM][Cl] and sodium tetrafluoroborate or potassium hexafluorophosphate were dissolved in distilled water, the reaction mixture was stirred at room temperature for 3 h. The product was concentrated and then purified by recrystallization in Cl₂CH₂.

Computational details

DFT calculations were carried out using the MPWB1K²⁴ hybrid meta functional, together with the 6-31G* and 6-311G** basis sets.²⁵ Optimizations were carried out using the Berny analytical gradient optimization method.²⁶ Stationary points were characterized by frequency calculations in order to verify that TSs have one and only one imaginary frequency. Intrinsic reaction coordinate (IRC)²⁷ paths were traced in order to check the energy profiles connecting each TS to the two associated minima of the proposed mechanism using the second order González-Schlegel integration method.²⁸ Solvent effects of 1-heptanol ($\epsilon = 11.3$) were taken into account through single-point energy calculations using the polarizable continuum model (PCM) as developed by Tomasi's group²⁹ in the framework of self-consistent reaction field (SCRF).³⁰ Thermodynamic calculations in 1-heptanol were calculated with the standard statistical thermodynamics at 60 °C and 1 atm over the optimized gas phase structures.²⁵ The electronic structures of stationary points were analyzed by the natural bond orbital (NBO) method.³¹ All calculations were carried out with the Gaussian 09 suite of programs.³²

The global electrophilicity index, ω , is given by the following simple expression,³³ $\omega = (\mu^2/2\eta)$, in terms of the electronic chemical potential μ ³⁴ and the chemical hardness η .³⁴ Both quantities may be approached in terms of the one electron energies of the frontier molecular orbital HOMO and LUMO, ϵ_H and ϵ_L , as $\mu \approx (\epsilon_H + \epsilon_L)/2$ and $\eta \approx (\epsilon_L - \epsilon_H)$, respectively.³⁴ Recently, we have introduced an empirical (relative) nucleophilicity index, N , based on the HOMO energies obtained within the Kohn-Sham scheme³⁶ and defined as $N = E_{\text{HOMO(Nu)}} - E_{\text{HOMO(TCE)}}$. Nucleophilicity refers to tetracyanoethylene (TCE), as it presents the lowest HOMO energy in a large series of molecules already investigated in the context of polar cycloadditions. This choice allows us to conveniently handle positive values for a nucleophilicity scale.^{35a}

The electrophilic, P_k^+ , and nucleophilic, P_k^- , Parr functions,³⁷ were obtained through the analysis of the Mulliken atomic spin density (ASD) of the radical anion and the radical cation by single-point energy calculations over the optimized neutral geometries using the unrestricted UB3LYP formalism for radical species. With these values at hand, local electrophilicity indices, ω_k ³⁸, and the local nucleophilicity indices,³⁹ N_k , were evaluated using the following expressions:³⁷ $\omega_k = \omega P_k^+$ and $N_k = N P_k^-$. All reactivity indices were computed at the B3LYP/6-31G* level at the ground state of the reagents.

General Procedure for the thermal reactions of nitronaphthalenes

The temperature, the length of the reaction, and the diene/dienophile ratio were dependent on the starting material

and are indicated in Table 1. An ampule containing a solution of 1.0 mmol of the dienophile and the required amount of diene in 1 ml of dry benzene or ionic liquid was cooled in liquid nitrogen, sealed (under nitrogen atmosphere), and then heated with stir in a bath. After the reaction time was completed, it was cooled once more in liquid nitrogen and opened. The solution was evaporated and the residue purified by column chromatography on silica gel or alumina using hexane/ethyl acetate mixtures as eluent.^{16a}

3.2.1. Phenanthren-2-ol (7). IR [cm⁻¹]: 3397, 3078, 1604, 1630, 1426. ¹H NMR (CDCl₃) δ : 7.80 (m, 2H), 8.13 (d, 1H, $J=8.2$ Hz), 8.16 (d, 1H, $J=8.14$ Hz), 8.25 (t, 1H, $J=2.1$ Hz), 8.28 (d, 1H, $J=8.2$ Hz), 8.40 (d, 1H, $J=8.21$ Hz), 8.44-8.47 (m, 2H), 9.62 (br s, 1H). ¹³C NMR (CDCl₃) δ : 111.2, 121.2, 121.6, 124.5, 126.0, 128.1, 130.5, 133.4, 137.1.⁴⁰

3.2.2. Phenanthren-4-ol (8). IR [cm⁻¹]: 3614, 3054, 1601, 1450, 1093. ¹H NMR (CDCl₃) 7.83 (t, 2H, $J=2.2$ Hz), 8.18 (d, 1H, $J=8.1$ Hz), 8.27 (d, 1H, $J=8.1$ Hz), 8.31 (d, 1H); 8.42 (d, 1H, $J=8.2$ Hz), 8.48 (m, 2H), 8.52 (s, 1H), 9.64 (br s, 1H) ¹³C NMR (CDCl₃) δ : 110.3, 120.5, 121.7, 125.7, 127.8, 128.1, 131.2, 134.4, 136.3.

3.3.3. N-naphthylpyrrole (9). IR [cm⁻¹]: 1596, 1508, 1489, 1398, 1312. ¹H NMR (CDCl₃) δ : 6.45 (t, 2H, $J=2.2$ Hz), 7.03 (t, 2H, $J=2.2$ Hz) 7.43-7.53 (m, 4H), 7.78 (d, 1H, $J=8.4$ Hz), 7.91 (d, 1H, $J=8.0$ Hz), 7.96 (d, 1H, $J=8.2$ Hz). ¹³C NMR (CDCl₃) δ : 109.0, 123.2, 123.3, 125.3, 126.3, 126.9, 127.9, 128.1, 129.9, 134.3, 138.4.

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- ‡ Footnotes should appear here. These might include comments relevant to but not central to the matter under discussion, limited experimental and spectral data, and crystallographic data.
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