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Article

Synthesis of 1,5-Functionalized 1,2,3-Triazoles Using Ionic Liquid/Iron(III) Chloride as Efficient and Reusable Homogeneous Catalyst

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Abstract: An efficient, eco-compatible and very cheap method for the construction of triazoles *via* eliminative azide–olefin cycloaddition (EAOC) reaction has been developed by a catalytic system IL/$FeCl_3$, offering an highly regioselective approach to structurally diverse 1,5-disubstituted 1,2,3-triazoles in up to 95% yield. This strategy features the reuse of catalytic system through simple operations. Mechanistic studies indicated that an asynchronous concerted dipolar cycloaddition-elimination process might be involved.

Keywords: azides, [3+2] cycloaddition, EAOC reaction, electron-deficient olefins, 1,2,3-triazoles

1. Introduction

Triazoles are five member *N*-heterocyclic compounds bearing three nitrogen atoms in the ring. They exist in two isomeric forms namely 1,2,3-triazoles and 1,2,4-triazoles and are important nucleus for the development of drugs, mainly because they are resistant to oxidation, reduction and hydrolysis in both acidic ad basic conditions because of their aromatic nature [1]. Their active participation in hydrogen bond formation, dipole-dipole and π stacking interactions can mimic peptide bonds enhancing their binding ability with different biological targets [2]. Therefore, triazoles represent a significant class of nitrogen compounds with important biological properties, such as antibacterial, anticancer, antivirus, antimalarial, anti-inflammatory and antituberculosis [3-4]. In particular, 1,2,3-triazoles have found a broad spectrum of biological applications such as β-lactum antibiotic tazobactum, cefatrizine and anticancer compound carboxyamidotriazole (CAI) that are some drugs available in the market [5].

Many approaches for the synthesis of 1,2,3-triazoles have been developed so far. The conventional synthetic method of 1,2,3-triazoles is 1,3-dipolar cycloaddition of Huisgen between alkynes and organic azides [6], which generally provides a mixtures of 1,4- and 1,5-regioisomers. The most important developments were achieved in this area by the copper catalyzed azide-alkino cycloaddition (CuAAC) to obtain the 1,5-disubstituted isomer and the ruthenium azide-alkino cycloaddition (RuAAC) to achieve the 1,4-disubstituted isomer [7-11]. However, the (CuAAC)-catalyzed process only works with terminal alkynes whereas the (RuAAC)-catalyzed reaction requires the use of very expensive ruthenium salt as catalyst.

As an alternative approach to azide–alkyne cycloaddition, electron deficient olefins were proposed to replace alkynes because of their easy availability and low cost preparation [12-13]. The azide–olefin cycloaddition furnishes triazoline, an unstable compound that readily decompose but that may be transformed into the stable triazole by eliminative azide olefin cycloaddition (EAOC). In

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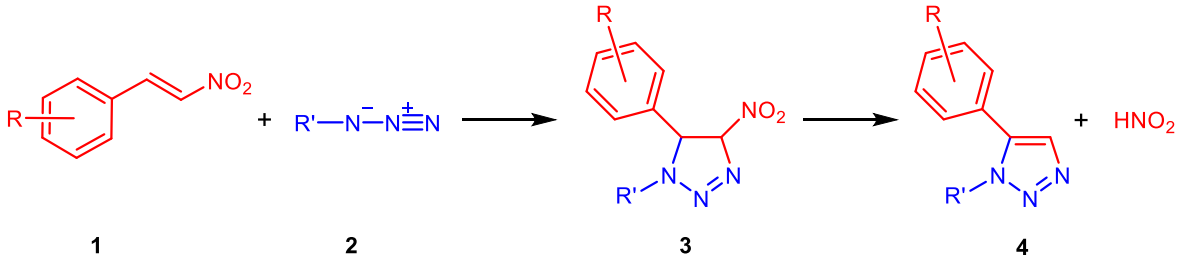
this process, the olefin carrying a leaving group reacts with the azide to form the intermediate triazoline that gives the corresponding triazole by elimination reaction [14].
Nitroolefins, as versatile starting materials, are excellent dipolarophiles to synthesize triazoles by EAOC cycloaddition. In fact, the presence of electron withdrawing nitro group both improves the 1,3-dipolar cycloaddition process and favors the formation of required 1,2,3-triazoles due to the fast nitrous acid loss through elimination step (Scheme 1).



Scheme 1. EAOC cycloaddition to synthesize 1,5-disubstituted 1,2,3-triazoles

Over the past decade, many researchers have shown substantial interest in the EAOC process of nitroolefins. In particular, EAOC of nitroolefins to provide 1,2,3-triazoles was realized in presence of various catalysts such as TBAF [15], *p*-toluene sulfonic acid [16], cerium triflate [17] and Bi_2WO_6 nanoparticles [18]. An alternative route of EAOC was realized generating the nitroolefin in situ [19-20]. Earlier these years, EAOC reaction of nitroolefins in the absence of catalysis, required prolonged times for completion, low regioselectivity and poor efficiency [21].

Considering the importance of 1,2,3-triazoles and in continuation with our experience in catalysis [22-25] herein we report the application of $FeCl_3$ in ionic liquid (ILs) as reusable homogeneous catalyst system. To the best of our knowledge, there is been no report available on the synthesis of EAOC of nitroolefins using iron catalyst in ionic liquid in the open literature so far.

Ionic liquids (ILs) have received in last years a good deal of attention since classical organic reactions, including cycloadditions reactions, can be performed in these media with great advantages (yield and selectivity) as compared to conventional conditions [26-30]. Ionic liquids are distinguished by the advantages pertaining to these solvents such as no measurable vapor pressure, easy solvent recover/recycle and high solubility of the Lewis acids in these solvents [31-33].

Recently, among the plethora of Lewis acids reported in the literature, iron catalysts have been identified as important and effective catalysts in various organic reactions because of their low price, easy availability, sustainability, non-toxicity and environmentally friendly characteristics [34-40].

In this paper, we investigated a number of catalyzed-EAOC reactions of nitroolefins in different ionic liquids and Lewis acids. Finally, we selected the [mpy]OTf/$FeCl_3$ system considering both the strong coordination of NO_2 group to the Fe-catalyst and the use of 1-methyl pyridinium trifluoromethanesulfonate ([mpy]OTf) as ideal reaction medium due the strong stabilization of reaction intermediates. Major advantages in the utilization of this ionic liquid are the low toxicity, the cost and the easy one-step preparation through halide-free direct synthesis, by adding directly methyl trifluoromethane sulfonate to dry pyridine.

2. Results

To begin, we chose the cycloaddition reaction between (*E*)-nitrostyrene **1a** and benzylazide **2a** in the presence of both imidazolium based and pyridinium based ionic liquids and some Lewis acid catalysts as the model system to optimize the reaction conditions to obtain the product **3a** (Table 1).

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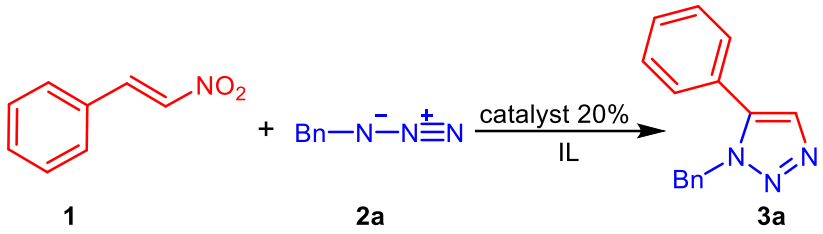
Table 1 Optimization of reaction conditions[1]



1 **2a** **3a**

Entry	Catalyst	IL	Time (h)	T (° C)	Yield (%)
1	$FeCl_3$	[mpy]OTf	48	60	24
2	$FeCl_3$	[mpy]OTf	48	60	40
3	$FeCl_3$	[mpy]OTf	2	100	95
4[2]	$FeCl_3$	[mpy]OTf	2	100	59
5	$CeCl_3$	[mpy]OTf	48	60	30
6	$CeCl_3$	[mpy]OTf	5	100	82
7	$ZnCl_2$	[mpy]OTf	48	60	37
8	$ZnCl_2$	[mpy]OTf	4	100	85
9	none	[mpy]OTf	72	100	28
10	$FeCl_3$	[bmim]OTf	2	100	75
11	$FeCl_3$	[bmim]Cl	2	100	60
12	$FeCl_3$	[bmim]BF_4	2	100	75

[1.] Reaction conditions: 2.0 eq. of **2** were used unless the reaction in entry 1, in which 1.0 eq. of **2** was employed. [2.] 10 mol % $FeCl_3$

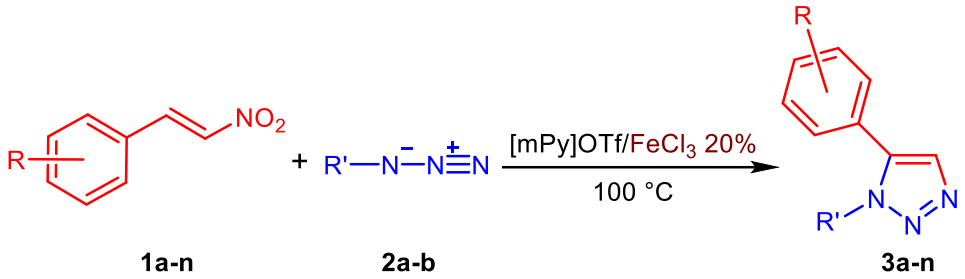
In an initial experiment, the reaction was performed in 1-methyl pyridinium trifluoromethanesulfonate ([mpy]OTf) at 60 °C catalyzed by 20 mol % $FeCl_3$ in a 1:1 ratio of reagents, isolating 1,5-disubstituted triazole **3a** in 24% yield after 48 h reaction due to degradation of benzylazide **2a** (Table1, entry 1). The use of 1.2 eq. or 1.5 eq. of azide did not lead to satisfactory results. A doubling of azide concentration revealed an increase of yield to 40% (Table 1, entry 2). Subsequently, when the reaction temperature was raised to 100 °C, the yield of product improved significantly, also reducing the reaction time (Table 1, entry 3). Any attempt to reduce the amount of catalyst did not provide improvements of the product yield (Table 1, entry 4).

Further screening of Lewis acids (Table 1, entry 5-8) revealed that the optimal results were obtained in the presence of $FeCl_3$ as catalyst (Table 1, entry 3). Moreover, without any catalyst, the reagents **1a** and **2a** in same reaction conditions gave the 1,5-disubstituted triazole **3a** in very low yield after a long reaction time (Table1, entry 9). This last result highlights that the catalyst accelerates the reaction by increasing the electrophilicity of the nitroolefin through coordination but it is not involved in the elimination step.

Changing from 1-methyl pyridinium trifluoromethane sulfonate [mpy]OTf to 1-butyl-3-methylimidazolium triflate [bmim]OTf, 1-butyl-3-methylimidazolium chloride [bmim]Cl or 1-butyl-3-methylimidazolium tetrafluoroborate [bmim]BF_4 as solvent (Table 1, entries 10-12) did not have a significant influence on the outcome, and only minor differences in product yield were observed.

With the optimized reaction conditions in our hand, we extended the investigation to various arylnitroolefins **1a-n** and benzylazide **2a** or phenylazide **2b** (Table 2).

Table 2 Synthesis of 1,5-disubstituted 1,2,3-triazoles **3a-n**



1a-n **2a-b** **3a-n**

Entry	R	R[1]	Product	Yield (%)
1	H	Bn	**3a**	95
2	2-Cl	Bn	**3b**	85
3	3-Cl	Bn	**3c**	84
4	4-Cl	Bn	**3d**	86
5	4-Me	Bn	**3e**	92
6	4-MeO	Bn	**3f**	93
7	2-NO_2	Bn	**3g**	81
8	H	Ph	**3h**	91
9	2-Cl	Ph	**3i**	87
10	3-Cl	Ph	**3j**	93
11	4-Cl	Ph	**3k**	92
12	4-Me	Ph	**3l**	96
13	4-MeO	Ph	**3m**	92
14	2-NO_2	Ph	**3n**	95

Notably, several sensitive functionalities, such as chloro (**3b-d**; **3j-k**), methyl (**3e**; **3l**), methoxy (**3f**; **3m**), and nitro (**3g**; **3n**), were unaffected under the present reaction conditions, and the reaction also tolerated *ortho*-substitution in the aromatic ring.

3. Discussion

In order to confirm the eliminative azide-olefin cycloaddition (EAOC) mechanism we investigated the possible reaction pathway.

To gain deeper insight into the mechanism, the reaction was studied at B3LYP-D3BJ/Def2SVP level of theory to calculate geometries and then single point calculations at B3LYP-D3BJ/Def2TZVP level of theory were performed (for details see SI). We studied as a model the reaction between phenyl azide **PA** and (*E*)-nitrostyrene **NS** to give compound **3h**. Initially, we calculated the direct cycloaddition between **PA** and **NS** without any catalyst to give the two intermediate cycloadducts. We considered two channels corresponding to the obtention of 1,4- (channel 1) and 1,5-adducts (channel 2). Two different relative orientations between the nitroolefin and the azide (*endo*/*exo*) were taken into account thus having a total of four initial approaches (Scheme 2). The different approaches for each regioisomer actually lead to different isomers connected by a pyramidal inversion at the azide nitrogen. Even though such a difference should be taken into consideration when considering the different transition structures, they lead to the same final product.

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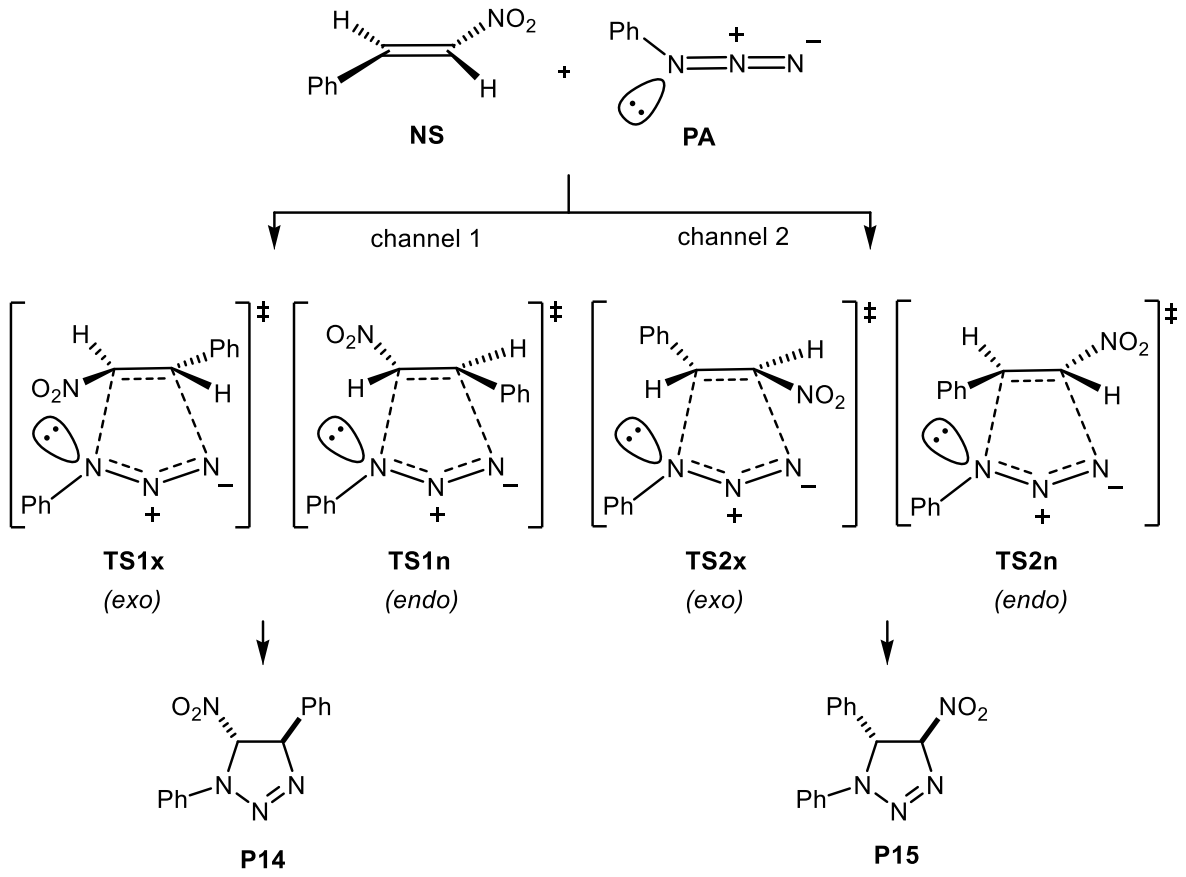

Scheme 2. Approaches for the cycloaddition between **NS** and **PA**

The analysis of the optimized transition structures and the corresponding IRCs revealed concerted processes in all cases. The preferred one, **TS2x**, was that corresponding to channel 2/exo (energy barrier of 29.3 kcal/mol), with differences of 0.2, 2.1 and 2.3 kcal/mol with respect to channel 2/endo (**TS2n**), channel 1/endo (**TS1n**) and channel 1/exo (**TS1x**), respectively (Scheme 2). Next, we evaluated the same reaction catalyzed by iron(III) chloride, which is coordinated at the nitro group. The same trend was observed for the catalyzed reaction; thus, the transition structure **TS2x-Fe** corresponding to channel 2/exo and leading to cycloadduct **P15-Fe** was also the preferred one. In the presence of iron(III) chloride the barrier was reduced to 23.6 kcal/mol (Figure 1). In agreement with an increasing of the polarity for the reaction, a more asynchronous reaction was found.

Denitration reaction is a well-known process that takes place through the thermal elimination of nitrous acid. The electronic nature of the reaction resembles a typical Cope elimination. Accordingly, the coordination of iron(III) chloride to the nitro group clearly disfavors the process and a previous decoordination is required to form **P15**. In fact, any attempt of locating a transition structure corresponding to the denitration in the presence of iron(III) chloride failed. On the contrary, **TS3** corresponding to the elimination of nitrous acid from **P15** was located. A barrier of 22.5 kcal/mol was found, the formation of the final product **3h** being thermodynamically favored by 25 kcal/mol (Figure 1). Consequently, for the iron-catalyzed process the cycloaddition step is the rate-limiting one and it should be expected that the observed product of the reaction is **3h** in agreement with experimental observations.

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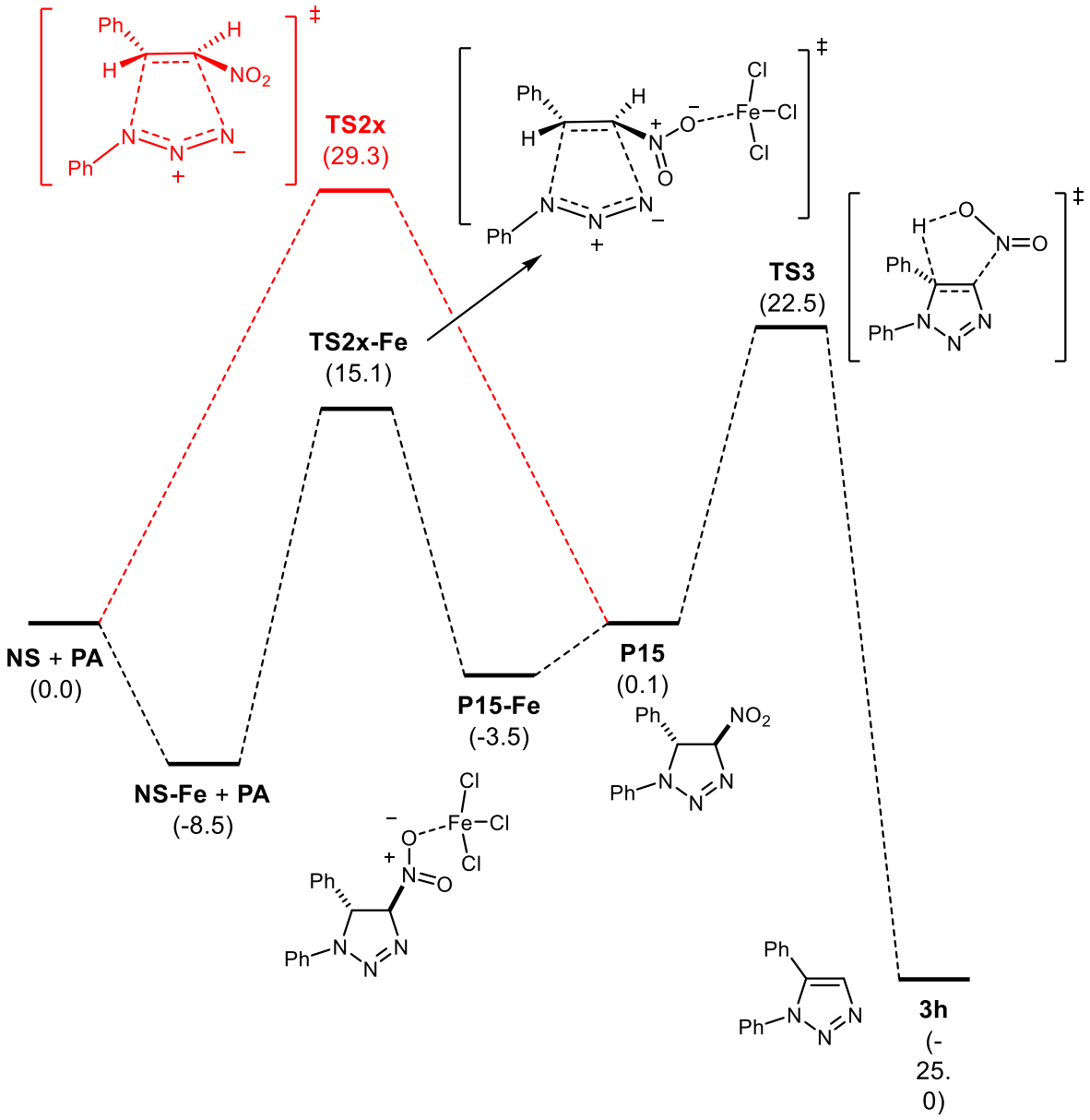

Figure 1. Reaction coordinate for the formation of **3h** from (E)-nitrostyrene and phenyl azide. Both catalyzed (iron(III) chloride) and uncatalyzed (in red) cycloaddition reactions are included for the purpose of comparison. (For detailed data see SI)

The geometries of **TS2x-Fe** and **TS3** are shown in Figure 2. The geometry of the former reflects the higher asynchronicity of the catalyzed cycloaddition in which the N1-C5 bond of the triazoline is formed earlier that the N3-C4 bond.

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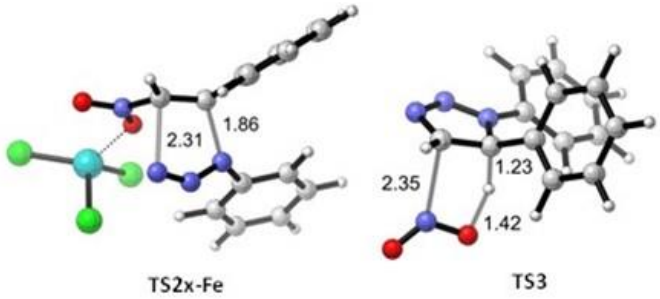
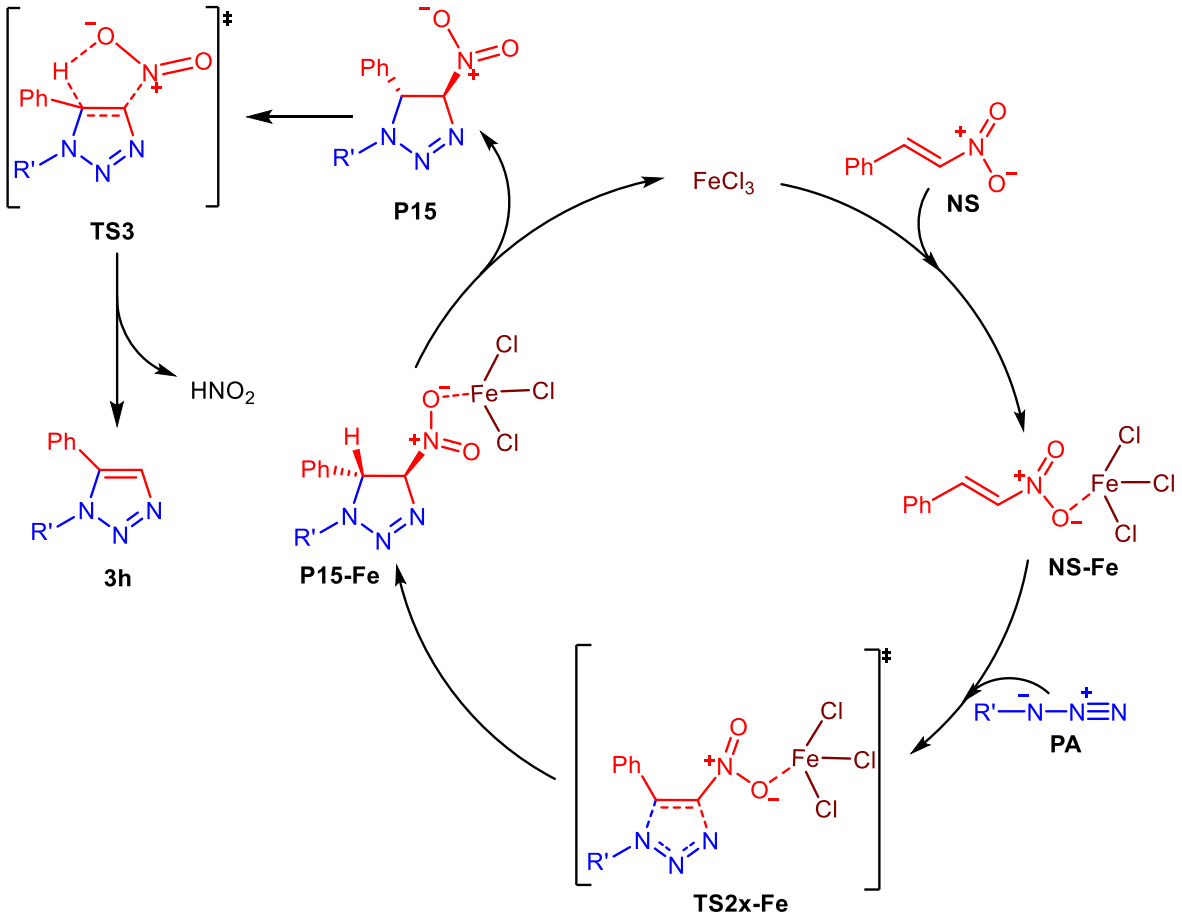


Figure 2. Optimized geometries (B3LYP-D3BJ/Def2SVP) of **TS2x-Fe** and **TS3**.

According to these findings, it is possible to propose the catalytic cycle illustrated in Scheme 3, to hypothesize for the first time, the best of our knowledge, that the nitrous acid elimination step in not supported by coordination of the metal.



Scheme 3. Proposed mechanism of eliminative azide–olefin cycloaddition (EAOC) reaction

The first step of the reaction is the coordination of iron(III) chloride to nitroolefin compound **NS** to form an activated intermediate **NS-Fe** that reacts with the azide derivative **PA** to produce a triazoline intermediate **P15-Fe** through a transition state **TS2n-Fe**. The final step consists of the production of $FeCl_3$ in its original quantity and elimination of HNO_2 to afford 1,5-disubstituted 1,2,3-triazoles **3h** *via* a transition state **TS3**.

Moreover, considering that the used ionic liquid ([mpy]OTf) was a type of excellent reaction medium, we suppose that the IL may stabilize the coordinated intermediates by general electrostatic interactions[41-44], favoring both the cycloaddition reaction with azide compound and the transformation of triazoline derivative in triazole substrate. In fact, a weak interaction between IL cation and anion favors the possibility for the cation (or anion) to solvate the transition state (ionic coordinated intermediate) [45-46].

The catalytic system IL/$FeCl_3$ has been analyzed also with respect to recovery and reuse in the reaction between (*E*)-nitrostyrene **1a** and benzylazide **2a** and the results are shown in Figure 3.

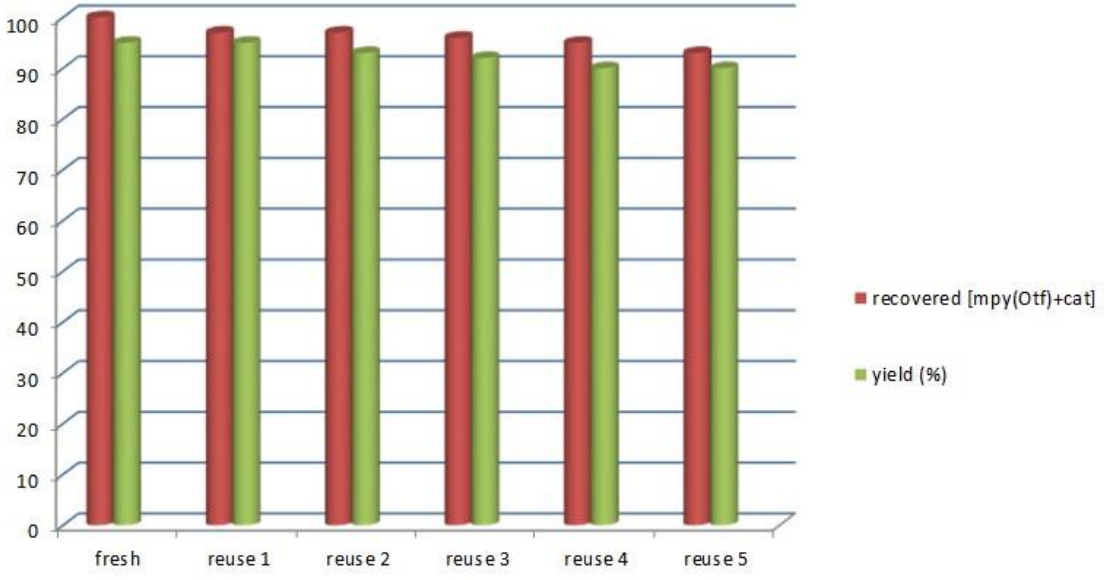


Figure 3. Recovery and re-use of catalytic IL/$FeCl_3$ system until six cycles

As shown in Figure 3 similar conversion were obtained, showing that the ionic liquid/$FeCl_3$ system remains active until six cycles, demonstrating that it could be recovered efficiently in this way.

4. Materials and Methods

All reagents were purchased from Sigma-Aldrich or Alfa Aesar and used without purification. Reactions were monitored by TLC using silica plates 60-F264, commercially available from Merk. ^{1}H and ^{13}C NMR spectra were recorded at 300 MHz and 75 MHz, respectively, in $CDCl_3$ using tetramethylsilane (TMS) as internal standard (Bruker ACP 300 MHz). Chemical shifts are given in parts per million and coupling constants in Hertz. LC-MS analysis were carried using an Agilent 6540 UHD Accurate - Mass Q-TOF LC-MS (Agilent, Santa Clara, CA) fitted with a electrospray ionization source (Dual AJS ESI) operating in positive ion mode. Chromatographic separation was achieved using a C18 RP analytical column (Poroshell 120, SB-C18, 50 x 2.1 mm, 2.7 mm) at 30 °C with a elution gradient from 5% to 95% of B over 13 min., a being H_2O (0.1% FA) and B CH_3CN (0.1% FA). Flow rate was 0.4 mL min^{-1}.

4.1 Synthesis of Ionic Liquids

1-methyl pyridinium trifluoromethanesulfonate ([mpy]OTf) was prepared by halide-free direct synthesis as reported in literature [47-48].

*4.2 General procedure for synthesis of 1,5-disubstituted-1,2,3-triazoles **3a-n***

In a two-necked round bottom flask, equipped with bubble condenser and magnetic stir bar, ionic liquid (5ml), $FeCl_3$ (20 mol%), (*E*)-nitrostyrene 1a-n (1 eq) and azide 2a-b (2 eq) were placed. The reaction was conducted at 100°C for the appropriate time. The crude was extracted with dichloromethane (3x5ml) and the combined organic layer was evaporated under vacuum. The crude product was purified on flash silica gel column by using hexane/ethyl acetate (9:1 v/v) to obtain the desired product (3a-n).

4.3 Procedure of recycling of the catalytic system IL/$FeCl_3$

After the polar phase was extracted three times by dichloromethane, the ionic liquid/$FeCl_3$ mixture was washed with hexane and dried at 65 °C under vacuum condition. Successive runs were performed in the recycled ionic liquid/$FeCl_3$ by reacting fresh reagents at the usual conditions.

5. Conclusions

In conclusion, we have reported an efficient approach to prepare 1,5-disubstitued-1,2,3-triazoles derivatives via a $FeCl_3$ mediated eliminative azide–olefin cycloadditions (EAOC) in ionic liquid as solvent. The principle features of this synthetic method are high atom economy, simple operation, high yields and the reuse of catalytic system IL/$FeCl_3$ until six cycles. The nature of the Lewis acid and ionic liquid appears to have a large impact to the regiocontrol of the reaction, where the ionic liquid anion might stabilize the cationic transition state allowing formation of the triazoline intermediate. Theoretical calculations indicate that an asynchronous concerted dipolar cycloaddition-elimination process might be involved in the formation of 1,5-functionalized triazoles and support the hypothesis that the subsequent elimination step to carry out triazoles proceeds without iron coordination.

Supplementary Materials: The following are available online at www.mdpi.com/xxx/s1, Figure S1: title, Table S1: title, Video S1: title.

Author Contributions: Conceptualization, A. De Nino and L. Maiuolo; Methodology, B. Russo, V. Algieri and M. Tallarida; Software, P. Merino; Validation, A. De Nino, L. Maiuolo and P. Merino; Formal Analysis, M. Nardi and M.L. Di Gioia ; Investigation, P. Merino; Data Curation, L. Maiuolo, V. Algieri; Writing-Original Draft Preparation, A. De Nino and L. Maiuolo; Supervision, P. Merino and A. De Nino.

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Conflicts of Interest: The authors declare no conflict of interest

Appendix A

Data for the products

1-benzyl-5-phenyl-1,2,3-triazole (3a)
^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) 5.55 (s, 2H, CH_2), 7.05-7.12 (m, 2H, Ar), 7.22-7.33 (m, 5H, Ar), 7.38-7.48 (m, 3H, Ar), 7.75 (s, 1H, CH). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) 51.83, 126.97, 127.17, 128.16, 128.82, 128.92, 128.95, 129.50, 133.30, 135.53, 138.15. ESI(+)-MS: *m*/*z* [M+H] calcd for $C_{15}H_{14}N_3$ 236.1182, found: 236.0952

1-benzyl-5-(2-chlorophenyl)-1,2,3-triazole (3b)
^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) 5.45 (s, 2H, CH_2), 6.90-6.99 (m, 2H, Ar), 7.01 (d, 1H, J=7.60 Hz, 1.70 Hz, Ar), 7.15-7.30 (m, 4H, Ar), 7.40 (td, 1H, J=7.70Hz, 1.70Hz, Ar), 7.47-7.52 (m, 1H, Ar), 7.72 (s, 1H, CH). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) 52.50, 126.44, 126.90, 127.72, 128.21, 128.62, 129.97, 131.18, 132.01, 134.32, 134.43, 134.78, 134.83. ESI(+)-MS: *m*/*z* [M+H] calcd for $C_{15}H_{13}ClN_3$ 270.0793, found: 270.1254

1-benzyl-5-(3-chlorophenyl)-1,2,3-triazole (3c)
^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) 5.55 (s, 2H, CH_2), 7.05-7.16 (m, 3H, Ar), 7.23 (m, 1H, Ar), 7.26-7.34 (m, 3H, Ar), 7.36 (d, 1H, J=7.55Hz, Ar), 7.39-7.45 (m, 1H, Ar), 7.75 (s, 1H, CH); ^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) 52.11, 127.03, 127.21, 128.37, 128.64, 128.94, 129.01, 129.66, 130.22, 133.52, 134.92, 135.18, 136.80. ESI(+)-MS: *m*/*z* [M+H] calcd for $C_{15}H_{13}ClN_3$ 270.0793, found: 270.1256

1-benzyl-5-(4-chlorophenyl)-1,2,3-triazole (3d)
^{1}H NMR ($CDCl_3$, 300 MHz): δ (ppm) 5.54 (s, 2H, CH_2), 7.03-7.10 (m, 2H, Ar), 7.14-7.21 (m, 2H, Ar), 7.25-7.33 (m, 3H, Ar), 7.36-7.43 (m, 2H, Ar), 7.74 (s, 1H, CH); ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 51.95, 125.37, 127.07, 128.31, 128.94, 129.26, 130.19, 133.46, 135.30, 135.85, 137.04. ESI(+)-MS: *m*/*z* [M+H] calcd for $C_{15}H_{13}ClN_3$ 270.0793, found: 270.1252

1-benzyl-5-(4-methylphenyl)-1,2,3-triazole (3e)
^{1}H NMR ($CDCl_3$, 300 MHz): δ (ppm) 2.43 (s, 3H, CH_3), 5.57 (s, 2H, CH_2), 7.09-7.22 (m, 4H, Ar), 7.22-7.29 (m, 2H, Ar), 7.29-7.37 (m, 3H, Ar), 7.75 (s, 1H, CH); ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 21.31, 51.71, 123.94, 128.10, 128.76, 128.81, 129.64, 133.16, 135.67, 139.63. ESI(+)-MS: *m*/*z* [M+H] calcd for $C_{16}H_{16}N_3$ 250.1339, found: 250.1241

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1-benzyl-5-(4-methoxyphenyl)-1,2,3-triazole (3f)
^{1}H NMR ($CDCl_3$, 300 MHz): δ (ppm) 3.87 (s, 3H, CH_3), 5.56 (s, 2H, CH_2), 6.92-6.99 (m, 2H, Ar), 7.08-7.16 (m, 2H, Ar), 7.17-7.24 (m, 2H, Ar), 7.28-7.37 (m, 3H, Ar), 7.73 (s, 1H, CH); ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 51.67, 55.39, 114.42, 119.01, 127.12, 128.12, 128.84, 130.25, 133.09, 135.69, 137.99, 160.52. ESI(+)-MS: *m*/*z* [M+H] calcd for $C_{16}H_{16}N_3O$ 266.1288, found: 266.1609

1-benzyl-5-(2-nitrophenyl)-1,2,3-triazole (3g)
^{1}H NMR ($CDCl_3$, 300 MHz): δ (ppm) 5.42 (s, 2H, CH_2), 6.90-6.97 (m, 2H, Ar), 7.00 (dd, 1H, J=7.50Hz, 1.53Hz, Ar), 7.15-7.25 (m, 3H, Ar), 7.55 (td, 1H, J=7.54Hz, 1.56Hz, Ar), 7.62 (dd, 1H, J= 7.95 Hz, 1.56Hz, Ar), 7.66 (s, 1H, CH),8.12 (dd, 1H, J=8.21Hz, 1.43Hz, Ar);^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 52.85, 122.27, 124.92, 127.77, 128.42, 128.72, 131.01, 133.04, 133.11, 133.23, 133.94, 134.40. ESI(+)-MS: *m*/*z* [M+H] calcd for $C_{15}H_{13}N_4O_2$ 281.1033, found: 281.1016

1,5-diphenyl-1,2,3-triazole (3h)
^{1}H NMR ($CDCl_3$, 300 MHz): δ (ppm) 7.22-7.31 (m, 2H, Ar), 7.36-7.44 (m, 5H, Ar), 7.44-7.50 (m, 3H, Ar),7.90 (s, 1H, CH); ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 125.23, 126.79, 128.61, 128.87, 129.24, 129.37, 133.41, 136.64, 137.75. ESI(+)-MS: *m*/*z* [M+H] calcd for $C_{14}H_{12}N_3$ 222.1026, found: 222.0591

5-(2-chlorophenyl)-1-phenyl-1,2,3-triazole (3i)
^{1}H NMR ($CDCl_3$, 300 MHz): δ (ppm) 7.22-7.32 (m, 2H, Ar), 7.32-7.43 (m, 6H, Ar), 7.43-7.50 (m, 1H, Ar),7.90 (s, 1H, CH); ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 124.16, 126.60, 127.02, 129.02, 129.26, 130.22, 131.07, 131.95, 134.13, 134.75, 134.90, 136.62. ESI(+)-MS: *m*/*z* [M+H] calcd for $C_{14}H_{11}ClN_3$ 256.0636, found: 256.0782

5-(3-chlorophenyl)-1-phenyl-1,2,3-triazole (3j)
^{1}H NMR ($CDCl_3$, 300 MHz): δ (ppm) 7.06-7.13 (m, 1H, Ar), 7.26-7.35 (m, 2H, Ar), 7.35-7.44 (m, 3H, Ar), 7.45-7.55 (m, 3H, Ar), 7.92 (s, 1H, CH); ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 125.21, 126.73, 128.57, 129.39, 129.53, 129.55, 130.14, 133.64, 134.89, 136.28, 136.42. ESI(+)-MS: *m*/*z* [M+H] calcd for $C_{14}H_{11}ClN_3$ 256.0636, found: 256.0781

5-(4-chlorophenyl)-1-phenyl-1,2,3-triazole (3k)
^{1}H NMR ($CDCl_3$, 300 MHz): δ (ppm) 7.13-7.20 (m, 2H, Ar), 7.30-7.39 (m, 4H, Ar), 7.43-7.50 (m, 3H, Ar),7.87 (s, 1H, CH); ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 125.23, 129.23, 129.47, 129.52, 129.83, 133.45, 135.51, 136.38, 136.68. ESI(+)-MS: *m*/*z* [M+H] calcd for $C_{14}H_{11}ClN_3$ 256.0636, found: 256.0781

5-(4-methylphenyl)-1-phenyl-1,2,3-triazole (3l)
^{1}H NMR ($CDCl_3$, 300 MHz): δ (ppm) 2.36 (s, 3H, CH_3), 7.08-7.18 (m, 4H, Ar), 7.33-7.41 (m, 2H, Ar), 7.41-7.48 (m, 3H, Ar),7.84 (s, 1H, CH); ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 21.30, 116.82, 123.74, 125.25, 128.47, 129.21, 129.58, 133.14, 137.89, 139.42. ESI(+)-MS: *m*/*z* [M+H] calcd for $C_{15}H_{14}N_3$ 236.1182, found: 236.0834

5-(4-methoxyphenyl)-1-phenyl-1,2,3-triazole (3m)
^{1}H NMR ($CDCl_3$, 300 MHz): δ (ppm) 3.81 (s, 3H, CH_3), 6.83-6.90 (m, 2H, Ar), 7.10-7.18 (m, 2H, Ar), 7.34-7.41 (m, 2H, Ar),7.41-7.48 (m, 3H, Ar), 7.81 (s, 1H, CH); ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 55.32, 114.35, 118.95, 125.24, 129.14, 129.35, 129.96, 132.96, 136.76, 137.60, 160.28. ESI(+)-MS: *m*/*z* [M+H] calcd for $C_{15}H_{14}N_3O$ 252.1131, found: 252.1197

5-(2-nitrophenyl)-1-phenyl-1,2,3-triazole (3n)
^{1}H NMR ($CDCl_3$, 300 MHz): δ (ppm) 7.28-7.31 (m, 1H, Ar), 7.33-7.42 (m, 3H, Ar), 7.46 (dd, 1H, J=7.42 Hz, 1.70 Hz, Ar), 7.60-7.75 (m, 3H, Ar), 7.84 (s, 1H, CH), 8.04 (dd, 1H, J=7.90 Hz, 1.60 Hz, Ar); ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 122.56, 124.53, 125.17, 129.38, 129.46, 130.92, 132.78, 133.45, 133.75, 135.94, 148.34. ESI(+)-MS: *m*/*z* [M+H] calcd for $C_{14}H_{11}N_4O_2$ 267.0877, found: 267.1267

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