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Theoretical Study of the Addition Reaction of Arylazides to 1,3-Dicarbonyl Compounds †

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Abstract: Our research focuses on the synthesis of 1,2,3-triazoles through 1,3-dipolar cycloaddition involving arylazides. The reaction demonstrates high efficiency when conducted in the presence of morpholine, resulting in 100% regioselectivity towards a single isomer. A theoretical study of this reaction can be conducted to gain insights into its mechanism and provide valuable information for its optimization. This study involves the use of computational methods, such as density functional theory (DFT), to calculate the structures, energies, and properties of the reactants, intermediates, transition states, and products involved in the reaction. The calculations were performed using the Gaussian09 program with the B3LYP(GD3BJ)/6-31G(d,p) method.

Keywords: triazoles; 1,3-dipolar cycloaddition; arylazides; active methylene compounds; regioselectivity; conceptual DFT; transition state theory

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1. Introduction

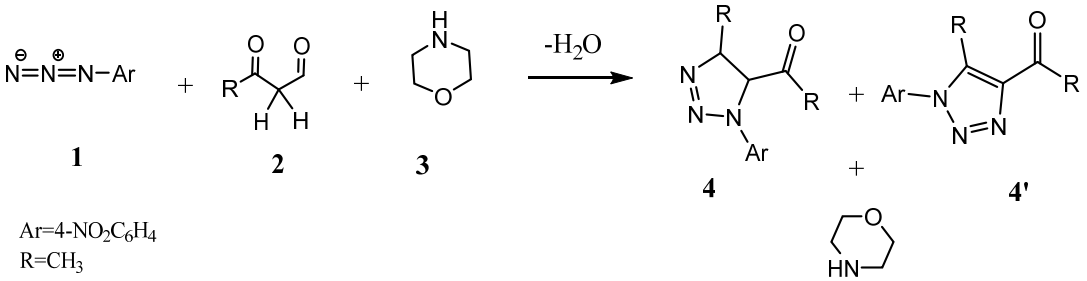
Heterocyclic chemistry constitutes a vast and important field in organic synthesis. Heterocycles exist naturally in essential molecules such as nucleic acids or certain alkaloids. Synthetic heterocycles are widely used for various applications (dyes, herbicides, insecticides, etc.) and particularly in the synthesis of bioactive molecules.

Among heterocyclic compounds, triazolic derivatives hold a significant position. They are applied as pharmaceuticals, cytostatics [1–3], antivirals [4], and antiproliferatives [5], as well as γ-aminobutyric acid antagonists [6]. They are used as intermediates in antibiotic synthesis [7], antihistamine preparations [8], and chemiluminescent compounds [9]. They also exhibit inhibitory activity against tuberculosis mycobacteria [10] and HIV-1 protease [11].

1,2,3-triazole derivatives are also applied as insecticides [12], fungicides [13], plant growth regulators [14], antimicrobials [15] and corrosion inhibitors [16]. Triazoles also possess complexing properties and serve as excellent ligands for transition metals [17]. Consequently, in the last two decades, the chemistry of 1,2,3-triazole derivatives has been intensively developed. Numerous publications are dedicated to the development of new synthesis methods and the improvement of existing ones [18–20]. The use of "one-pot" reactions allows for reduced reaction time and number of steps, decreased pollution, and minimized cost [21–24].

One of the key properties of a molecule is the study of its chemical reactivity. Indeed, predicting reactivity facilitates and guides experimentalists in their syntheses. Therefore, many theoretical methods based on the principles of quantum mechanics are currently employed [25]. In this study, we will attempt to determine the reaction mechanism and regioselectivity of the 1,3-dipolar cycloaddition through DFT theoretical calculations, starting from an active aliphatic and cyclic methylene compound in the presence of morpholine

(Scheme 1). We have chosen the reaction between para-nitrophenyl azide and ethyl acetoacetate.



Scheme 1. Domino reactions of acetylacetone compounds with 4-nitrophenyl azide in the presence of morpholine.

2. Methodology of Calculations

Static ab initio calculations were performed using the Gaussian09 program [26]. The Density Functional Theory (DFT) with the B3LYP(GD3BJ) functional, dispersion forces were taken into account [27,28] for exchange and correlation functions associated to 6-31G(d, p) basis set [29]. Each identified transition state (TS) was confirmed by calculating the intrinsic reaction coordinate (IRC). The solvent effect, diethyl ether identical to the experimental solvent, was implicitly considered in our calculations using the polarizable continuum model of the integral equation formalism (IEFPCM) [30]. The values of enthalpies, entropies, and Gibbs free energies in diethyl ether were calculated using standard statistical thermodynamics at 298 °C and 1 atm [31]. The electronic structures of stationary points were analyzed using the natural bond orbital (NBO) method [32,33]. The analysis of the reactivity of the studied reactants depends on chemical indices calculated from the energies of the frontier molecular orbitals LUMO and HOMO.

3. Results and Discussion

3.1. Prediction of the Relative Reactivity of the Reactants

Due to the existence of enol form in pentane–dicarbonyl (pentane-2,4-dione), as well as the presence of the morpholine base that plays a role in the tautomeric equilibrium, we started by studying the reactivity indices for all reactants with and without morpholine for acetylacetones in keto and enol forms (E or Z configuration) (see Figure 1). In order to highlight the donor (nucleophile) or acceptor (electrophile) character of the reactants, we calculated the HOMO/LUMO energy gaps of the reactants, electronic chemical potentials μ, hardness η, electrophilicity index ω, and nucleophilicity index N (Table 1).

Table 1. HOMO/LUMO energies (a.u.), electronic chemical potentials μ, hardness η, electrophilicity index ω, and nucleophilicity index N for the reactants with and without morpholine for acetylacetones in keto and enol forms (E or Z configuration).

	LUMO	HOMO	HOMO * −LUMO	LUMO * −HOMO	μ (a.u.)	η (eV)	ω (eV)	N (eV)
4-nitrophenyl azide	−0.116	−0.263	0.195	0.107	−0.190	0.147	3.341	2.019
(Z)-4-hydroxy-3-penten-2-one + Morpholine	−0.068	−0.224	0.217	0.122	−0.146	0.156	1.856	3.092
(E)-4-hydroxy-3-penten-2-one + Morpholine	−0.051	−0.241	0.223	0.125	−0.146	0.190	1.523	2.616
(E)-4-hydroxy-3-penten-2-one	−0.054	−0.256	0.202	0.139	−0.155	0.201	1.626	2.220
(Z)-4-hydroxy-3-penten-2-one	−0.061	−0.256	0.199	0.152	−0.158	0.195	1.751	2.216
Acetylacetone	−0.064	−0.268	0.195	0.107	−0.166	0.205	1.832	1.875

* LUMO and HOMO of 4-nitrophenyl azide.

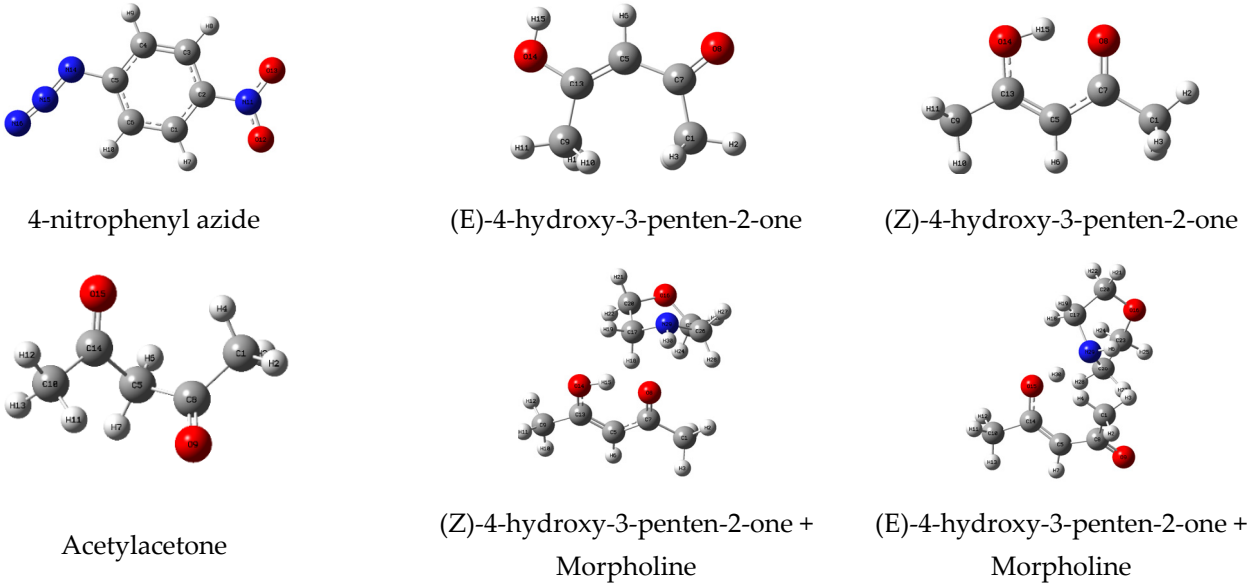


Figure 1. Configurations for all possible reactant combinations with and without morpholine for acetylacetones in the keto and enol forms (E or Z configuration).

The results show that the energy gaps ELUMO(4-nitrophenyl azide) − EHOMO (n = 2–6) are lower than the energy gaps EHOMO(4-nitrophenyl azide) − ELUMO (n = 2–6), indicating that 4-nitrophenyl azide behaves as an electrophile, while the other reactants (n = 2–6) behave as nucleophiles.

According to Table 1, it is also observed that the addition of morpholine reduces the gap for pentane–dicarbonyl, with the Z configuration for pentane–dicarbonyl being more reactive compared to the E isomer. This is further confirmed by the calculation of the overall hardness, which decreases with the addition of the base, making the carbonyl less hard and more reactive.

Indeed, 4-nitrophenyl azide has the highest electrophilicity index (ω = 3.341 eV) and the lowest nucleophilicity index (N = 2.019 eV). Furthermore, the electronic potential of 4-nitrophenyl azide (μ = −0.146 a.u.) is lower than that of the five dicarbonyls, indicating that electron transfer will occur from the carbonyl to 4-nitrophenyl azide.

It is also observed that the electrophilic character is reduced by the presence of the base in the carbonyls and vice versa for the nucleophilic character, which increases with the presence of the base.

In conclusion, 4-nitrophenyl azide acts as an electrophile, while the five carbonyls act as nucleophiles.

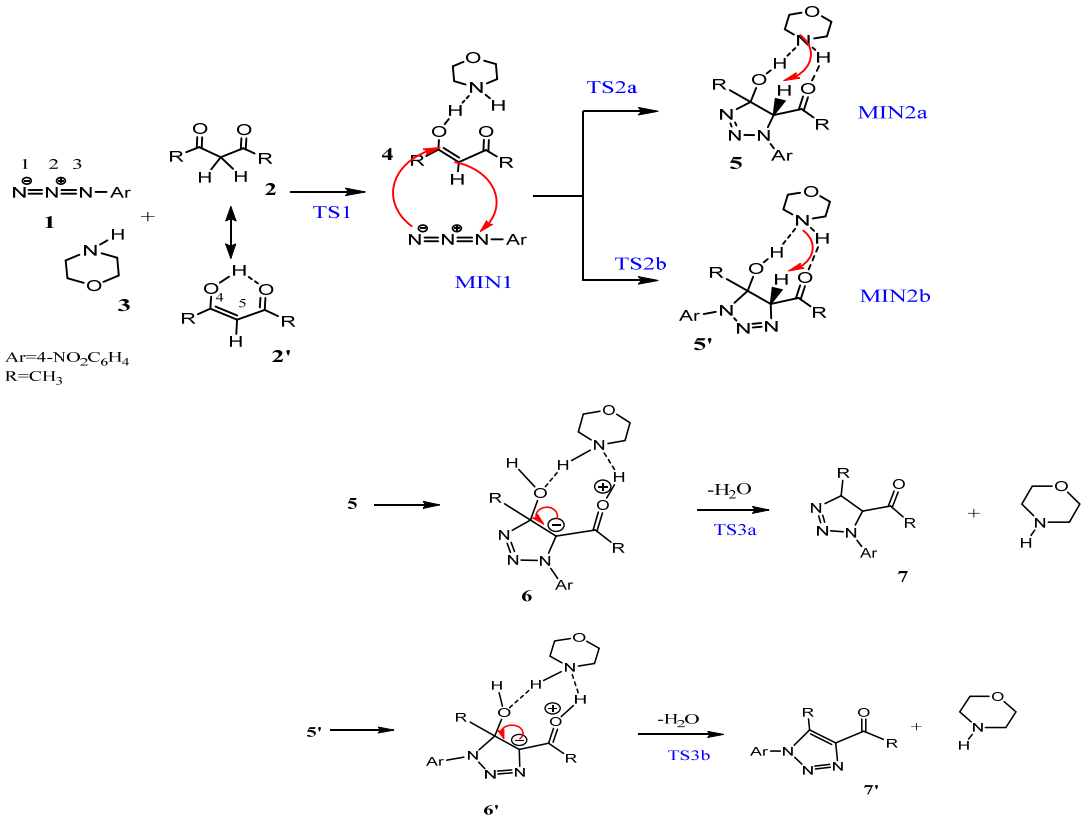
3.2. DFT Study of the Domino Reactions of Acetylacetone Compounds with 4-Nitrophenyl Azide

The thermal reactions between acetylacetone compounds 2 and 4-nitrophenyl azide 1 are domino processes that involve three consecutive reactions (Scheme 1):

A. Tautomeric equilibrium between acetylacetone compounds 2 and their enol forms 4.
B. The 1,3-dipolar cycloaddition (13DC) reaction between the enol compounds 4 and 4-nitrophenyl azide 1, resulting in the formation of 4,5-dihydro-1,2,3-triazoles 5.
C. The dehydration process facilitated by the morpholine base to yield the final 1,2,3-triazoles 7 (see Scheme 2).

The first reaction in this domino process is a tautomeric equilibrium between the keto and enol forms of the carbonyl compounds 2. The enols 2′ can adopt an E or Z configuration at the C-C double bond (see Figure 1). The Z isomers without morpholine have an energy of −3.16 kcal/mol (Z), which is more stable than their corresponding E isomers (7.96 kcal/mol). The addition of morpholine stabilizes the E isomer due to the

formation of an intramolecular hydrogen bond in the E isomers and slightly destabilizes the Z isomer, but the Z isomer remains more stable than the E isomer (Table 2).



Scheme 2. The two regioisomers obtained from the domino reaction of 4-nitrophenyl azide 1 with (Z)-4-hydroxy-3-penten-2-one 2′ and morpholine 3.

Table 2. Relative energy B3LYP/6-311++G(d,p) of the enol form for both Z and E isomers without and with morpholine.

Reactants	ΔE (kcal/mol)	Reactants	ΔE (kcal/mol)
Acetylacetone + Morpholine	0.00	Acetylacetone	0.00
(Z)-4-hydroxy-3-penten-2-one + Morpholine	−0.99	(Z)-4-hydroxy-3-penten-2-one	−3.63
(E)-4-hydroxy-3-penten-2-one + Morpholine	0.75	(E)-4-hydroxy-3-penten-2-one	7.96

In the context of the 1,3-dipolar cycloaddition (13DC) reaction between the enols 2′ and 4-nitrophenyl azide 1, two regioisomers can form due to the asymmetry of these compounds. These regioisomers are associated with the approach of nitrogen N1 of 4-nitrophenyl azide 1 to the carbon atoms C5 or C4 of the enols 2′. They are respectively referred to as (a) and (b) (see Scheme 2).

To understand the regioselectivity of this reaction, it is important to study the mechanism of the two isomers.

Regioisomer (a): In this case, nitrogen N1 of 4-nitrophenyl azide 1 attacks carbon C5 of the enol 2′. This mechanism may be favored if carbon C5 of the enol has a higher electron density or better steric accessibility for nitrogen N1.

Regioisomer (b): Here, nitrogen N1 of 4-nitrophenyl azide 1 attacks carbon C4 of the enol 2′. This mechanism may be favored if carbon C4 of the enol has a higher electron density or better steric accessibility for nitrogen N1.

According to the natural bond orbital (NBO) values in the transition state of the 1,3-dipolar cycloaddition reaction, the NBO value for the formation of the N1-C4 bond in the

transition state of regioisomer (a) is 1.12. And for the formation of the N1-C5 bond in the transition state of regioisomer (b), it is 6.19. These NBO values indicate that the formation of the N1-C5 bond is more favorable than the formation of the N1-C4 bond in the transition state. Therefore, regioisomer (b) is favored over regioisomer (a).

In this case, the higher NBO value for the formation of the N1-C5 bond suggests better stability and a higher probability of forming this isomer (b) compared to isomer (a).

According to the data provided in Table 3 and Figure 2, the activation energies for the 13DC reactions between the enols 2′ and 4-nitrophenyl azide are lower for regioisomer (b) compared to regioisomer (a). For the transition state TS1b associated with regioisomer (b), the activation energy $\Delta G^{\neq}$ is 18.09 kcal/mol. And for regioisomer (a), the activation energy $\Delta G^{\neq}$ is 26.52 kcal/mol.

Table 3. Relative energy, free energy, activation energy, and free energy of activation for the domino reaction of 4-nitrophenyl azide 1 with (Z)-4-hydroxy-3-penten-2-one 2′ and morpholine 3.

		ΔE (kcal.mole^{-1})	**ΔG (kcal.mole^{-1})**	**ΔE$^{\neq}$ (kcal.mole^{-1})**	**ΔG$^{\neq}$ (kcal.mole^{-1})**
	Reactant	0.00	0.00	10.85	12.54
Enolization	TS1	10.85	12.54		
	MIN1	2.55	3.81	26.21 18.17	26.52 18.09
Cycloaddition	TS2a TS2b	28.76 20.72	30.33 21.90		
	MIN2a MIN2b	−10.92 −11.51	−8.65 −9.42	11.77 17.1	24.68 18.33
Dehydration	TS3a TS3b	0.85 5.59	16.03 8.91		
	Product-a Product-b	−38.14 −42.20	−27.53 −29.90		

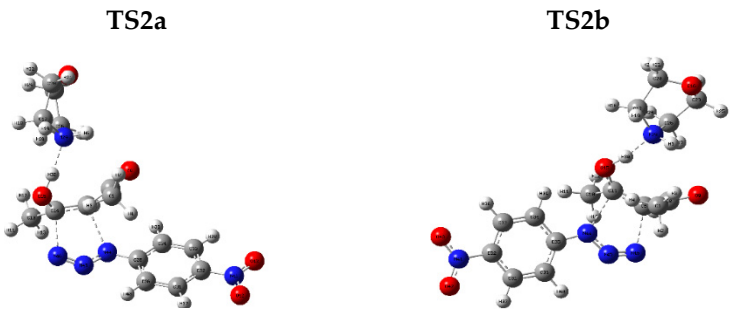


Figure 2. The transition states corresponding to the two regioisomers of the 1,3-dipolar cycloaddition reaction between the enols 2′ and 4-nitrophenyl azide in the presence of morpholine.

These activation energy values indicate that regioisomer (b) is kinetically favored over regioisomer (a). In other words, the 1,3-dipolar cycloaddition reaction between the enols 2′ and 4-nitrophenyl azide has a lower energy barrier and is more likely to occur with regioisomer (b).

The final step of this domino process is the dehydration of the cycloadducts 7 and 7′ in the presence of morpholine. This dehydration occurs in three steps:

A. Deprotonation of carbon atom C5: morpholine will deprotonate the carbon atom C5 of the cycloadduct, creating a carbanion on this carbon atom.
B. Protonation of the ketone oxygen: The ketone oxygen in the cycloadduct will be protonated, usually by a proton from morpholine itself. This step will stabilize the negative charge formed during deprotonation.

C. Elimination of a water molecule and formation of the C5=C4 double bond: Under dehydration conditions, a water molecule will be eliminated. This elimination reaction will lead to the formation of a double bond between the carbon atoms C5 and C4 of the cycloadduct (see Scheme 2).

From Figure 3, it can be observed that the water elimination step is kinetically more favored for isomer (b) than for isomer (a). This means that the dehydration reaction occurs more rapidly for isomer (b) than for isomer (a). Additionally, it can be noted that the triazole product formed from isomer (b) is thermodynamically more stable than the one formed from isomer (a).

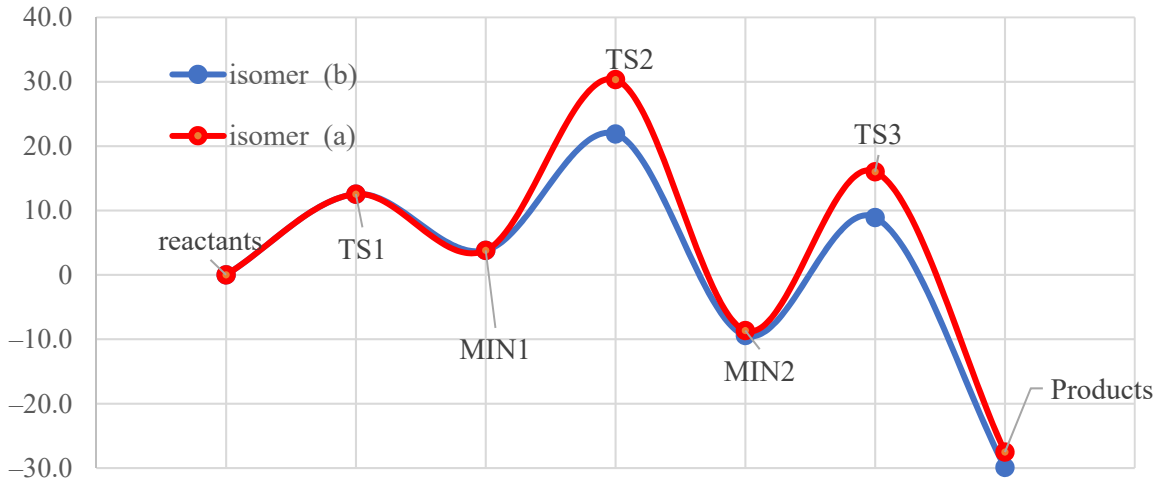


Figure 3. Energy profile of the domino reaction between 4-nitrophenyl azide 1, (z)-4-hydroxy-3-penten-2-one 2′, and morpholine 3.

4. Conclusions

The DFT theoretical investigation shows that the reaction proceeds effectively with morpholine as a catalyst, resulting in 100% regioselectivity towards a specific isomer. This method offers a significant advantage as it enables a practical one-step synthesis of a wide range of mono-, bi-, or tricyclic 1,2,3-triazoles using readily accessible active methylene compounds.

Regarding triazoles 7 and 7′, a DFT calculation study was conducted to compare various approaches involving dipole/dipolarophile interactions. This study involved calculating the energies associated with different transition states.

Author Contributions: Conceptualization, A.A. and H.H.M.; methodology, A.A. and O.B.; software, A.A. and A.N.; validation, O.B. and H.H.M.; formal analysis, A.A. and A.N.; investigation, A.A.; data curation, H.H.M.; writing—original draft preparation, A.A., H.H.M. and O.B.; writing—review and editing, A.A., H.H.M. and A.N. All authors have read and agreed to the published version of the manuscript.

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References

1. Imperio, D.; Pirali, T.; Galli, U.; Pagliai, F.; Cafici, L.; Canonico, P.L.; Sorba, G.; Genazzani, A.A.; Tron, G.C. Replacement of the lactone moiety on podophyllotoxin and steganacin analogues with a 1,5-disubstituted 1,2,3-triazole via ruthenium-catalyzed click chemistry. *Bioorg. Med. Chem.* **2007**, *15*, 6748–6757. [CrossRef]
2. Akselsen, Ø.W.; Odlo, K.; Cheng, J.J.; Maccari, G.; Botta, M.; Hansen, T.V. Synthesis, biological evaluation and molecular modeling of 1, 2, 3-triazole analogs of combretastatin A-1. *Bioorg. Med. Chem.* **2012**, *20*, 234–242. [CrossRef]
3. Duan, Y.-C.; Ma, Y.C.; Zhang, E.; Shi, X.J.; Wang, M.M.; Ye, X.W.; Liu, H.M. Design and synthesis of novel 1,2,3-triazole-dithiocarbamate hybrids as potential anticancer agents. *Eur. J. Med. Chem.* **2013**, *62*, 11–19. [CrossRef]
4. El Akri, K.; Bougrin, K.; Balzarini, J.; Faraj, A.; Benhida, R. Efficient synthesis and in vitro cytostatic activity of 4-substituted triazolyl-nucleosides. *Bioorg. Med. Chem. Lett.* **2007**, *17*, 6656–6659. [CrossRef]
5. Hupe, D.J.; Boltz, R.; Cohen, C.; Felix, J.; Ham, E.; Miller, D.; Soderman, D.; Van Skiver, D. The inhibition of receptor-mediated and voltage-dependent calcium entry by the antiproliferative L-651,582. *J. Biol. Chem.* **1991**, *266*, 10136–10142. [CrossRef] [PubMed]
6. Bascal, Z.; Holden-Dye, L.; Willis, R.; Smith, S.; Walker, R. Novel azole derivatives are antagonists at the inhibitory GABA receptor on the somatic muscle cells of the parasitic nematode Ascaris suum. *Parasitology* **1996**, *112*, 253–259. [CrossRef] [PubMed]
7. Pet, C.; Batta, G.; Györgydeák, Z.; Sztaricskai, F. Glycoside Synthesis with Anomeric 1-N-Glycobiosyl-1,2,3-triazoles1. *J. Carbohydr. Chem.* **1996**, *15*, 465–483.
8. Buckle, D.R.; Rockell, C.J.; Smith, H.; Spicer, B.A. Studies on 1,2,3-triazoles. 13.(Piperazinylalkoxy)-[1] benzopyrano [2,3-d]-1, 2, 3-triazol-9 (1H)-ones with combined H1-antihistamine and mast cell stabilizing properties. *J. Med. Chem.* **1986**, *29*, 2262–2267. [CrossRef] [PubMed]
9. Kurumi, M.; Sasaki, K.; Takata, H.; Nakayama, T. Synthesis and Chemiluminescent Activity of Pyridazino [4,5-b] indole-1,4 (2H, 3H)-diones. *Heterocycles* **2000**, *53*, 2809–2819.
10. Costa, M.S.; Boechat, N.; Rangel, E.A.; Da Silva, F.d.C.; De Souza, A.M.; Rodrigues, C.R.; Castro, H.C.; Junior, I.N.; Lourenço, M.C.S.; Wardell, S.M. Synthesis, tuberculosis inhibitory activity, and SAR study of N-substituted-phenyl-1,2,3-triazole derivatives. *Bioorg. Med. Chem.* **2006**, *14*, 8644–8653. [CrossRef]
11. Arora, B.S.; Shafi, S.; Singh, S.; Ismail, T.; Kumar, H.S. A novel domino-click approach for the synthesis of sugar based unsymmetrical bis-1,2,3-triazoles. *Carbohydr. Res.* **2008**, *343*, 139–144. [CrossRef] [PubMed]
12. Boddy, I.K.; Briggs, G.G.; Harrison, R.P.; Jones, T.H.; O'Mahony, M.J.; Marlow, I.D.; Roberts, B.G.; John Willis, R.; Bardsley, R.; Reid, J. The Synthesis and Insecticidal Activity of a Series of 2-Aryl-1,2,3-triazoles. *Pestic. Sci.* **1996**, *48*, 189–196. [CrossRef]
13. Buechel, K.; Gold, H.; Frohberger, P.; Kaspers, H. German Patent 2407305. *Chem. Abstr.* **1975**, *83*, 206290.
14. Reisser, F. British Patent 8101239. *Chem. Abstr.* **1981**, *96*, 69006.
15. Kaushik, C.; Kumar, K.; Singh, S.; Singh, D.; Saini, S. Synthesis and antimicrobial evaluation of 1, 4-disubstituted 1, 2, 3-triazoles with aromatic ester functionality. *Arab. J. Chem.* **2016**, *9*, 865–871. [CrossRef]
16. Abdennabi, A.; Abdulhadi, A.; Abu-Orabi, S.; Saricimen, H. The inhibition action of 1 (benzyl) 1-H-4, 5-dibenzoyl-1, 2, 3-triazole on mild steel in hydrochloric acid media. *Corros. Sci.* **1996**, *38*, 1791–1800. [CrossRef]
17. Voitekhovich, S.V.; Filippova, J.V.; Sukhanova, A.G.; Lyakhov, A.S.; Ivashkevich, L.S.; Sukhanov, G.T.; Grigoriev, Y.V. Selective complexation of 1-ethyl-5-nitro-1,2,3-triazole (entz) with copper (II) salts: Preparation and characterization of $[Cu(entz)_2Cl_2]$ and $[Cu(entz)_4(H_2O)_2](ClO_4)_2$. *Inorg. Chem. Commun.* **2012**, *24*, 77–80. [CrossRef]
18. Gil, M.V.; Arévalo, M.J.; Lopez, O. Click chemistry-what's in a name? Triazole synthesis and beyond. *Synthesis* **2007**, *2007*, 1589–1620. [CrossRef]
19. Krivopalov, V.P.; Shkurko, O.P. 1,2,3-Triazole and its derivatives. Development of methods for the formation of the triazole ring. *Russ. Chem. Rev.* **2005**, *74*, 339. [CrossRef]
20. Katritzky, A.R.; Zhang, Y.; Singh, S.K. 1,2,3-Triazole formation under mild conditions via 1,3-dipolar cycloaddition of acetylenes with azides. *Heterocycles Int. J. Rev. Commun. Heterocycl. Chem.* **2003**, *60*, 1225–1239. [CrossRef]
21. Anastas, P.; Warner, J. *Green Chemistry: Theory Ant Practice*; Oxford University Press: New York, NY, USA, 2000.
22. Lancaster, M. *Green Chemistry: An Introductory Text*; Royal Society of Chemistry: London, UK, 2020.
23. Totobenazara, J.; Burke, A.J. New click-chemistry methods for 1,2,3-triazoles synthesis: Recent advances and applications. *Tetrahedron Lett.* **2015**, *56*, 2853–2859. [CrossRef]
24. Chassaing, S.; Bénéteau, V.; Pale, P. When CuAAC'click chemistry'goes heterogeneous. *Catal. Sci. Technol.* **2016**, *6*, 923–957. [CrossRef]
25. De Proft, F.; Geerlings, P. Conceptual and computational DFT in the study of aromaticity. *Chem. Rev.* **2001**, *101*, 1451–1464. [CrossRef] [PubMed]
26. Frisch, M.J.; Trucks, G.; Schlegel, H.; Scuseria, G.; Robb, M.; Cheeseman, J.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. *Gaussian 09, Revision D. 01*; Gaussian Inc.: Wallingford, CT, USA, 2009.
27. Grimme, S. Accurate description of van der Waals complexes by density functional theory including empirical corrections. *J. Comput. Chem.* **2004**, *25*, 1463–1473. [CrossRef]
28. Grimme, S. Semiempirical GGA-type density functional constructed with a long-range dispersion correction. *J. Comput. Chem.* **2006**, *27*, 1787–1799. [CrossRef] [PubMed]
29. Hariharan, P.C.; Pople, J.A. The influence of polarization functions on molecular orbital hydrogenation energies. *Theor. Chem. Acc. Theory Comput. Model. (Theor. Chim. Acta)* **1973**, *28*, 213–222. [CrossRef]

30. Cossi, M.; Scalmani, G.; Rega, N.; Barone, V. New developments in the polarizable continuum model for quantum mechanical and classical calculations on molecules in solution. *J. Chem. Phys.* **2002**, *117*, 43–54. [CrossRef]
31. Hadj Mokhtar, H. Application de la Réaction Multicomposés à la Synthèse de Triazolines. Ph.D. Thesis, University of Oran 1, Oran, Algeria, 2018.
32. Reed, A.E.; Weinstock, R.B.; Weinhold, F. Natural population analysis. *J. Chem. Phys.* **1985**, *83*, 735–746. [CrossRef]
33. Reed, A.E.; Curtiss, L.A.; Weinhold, F. Intermolecular interactions from a natural bond orbital, donor-acceptor viewpoint. *Chem. Rev.* **1988**, *88*, 899–926. [CrossRef]