

ORIGINAL ARTICLE

# Synthesis, characterization and *RHF/ab initio* simulations of 2-amino-1,3,4-thiadiazole and its annulated ring junction pyrimidine derivatives

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## KEYWORDS

Thiadiazolo[3,2-*a*]pyrimidine;  
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*RHF/ab initio* calculations

**Abstract** Michael addition reaction of the 2-amino-1,3,4-thiadiazole to chalcone as biselectrophile afforded 5,7-diphenyl-6-[1,3-diphenylpropan-1-on-3-yl][1,3,4]thiadiazolo[3,2-*a*]pyrimidine (**3**) instead of 5,7-diphenyl-5*H*-[1,3,4]thiadiazolo[3,2-*a*]pyrimidine (**5**) *via* further Michael addition at C<sub>5</sub> in pyrimidine moiety. The structure **3** was established through the aspect of *ab initio* calculations, elemental analysis and spectral data.

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## Introduction

The diverse and interesting biological activity of thiadiazoles has been reported [1–4]. It is well known that these heterocycles are valuable building blocks. Many methods for preparation of these heterocyclic ring systems and their fused

analogues have been described in the literature [5,6]. 2-Amino-1,3,4-thiadiazoles as amidine moiety provided a useful method for the synthesis of thiadiazolopyrimidine [7]. Also, the *N*-alkylation could occur either on the endocyclic or on the exocyclic nitrogen atom [8].

The objective of this work is directed to annulate compound **1** *via* sequential cycloaddition followed by cyclocondensation reaction with enones as biselectrophile, in order to synthesize 5,7-diphenyl-5*H*-[1,3,4]thiadiazolo[3,2-*a*]pyrimidine (**5**). Formation of compound **5** was unsuccessful and instead, we obtained 5,7-diphenyl-6-[1,3-diphenylpropan-1-on-3-yl][1,3,4]thiadiazolo[3,2-*a*]pyrimidine (**3**), this result persuaded us to use *RHF/ab initio* calculations with the aim to explore the chemical reactivity of the interacted compounds including the investigation of different reaction processes on the basis of their expected quantum mechanical behavior and to envisage why compound **5** reacted with another equivalent mole of chalcone.

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## Experimental

The melting point is in degree centigrade (uncorrected) and was determined on Gallenkamp electric melting point apparatus. The IR spectrum ( $\text{cm}^{-1}$ ) was recorded using KBr discs on a Mattson 5000 FTIR Spectrophotometer at Microanalytical Center, Faculty of Science, Mansoura University. The  $^1\text{H}$  NMR spectrum was carried out on a Varian Spectrophotometer at 300 MHz, using TMS as an internal reference and  $\text{DMSO-}d_6$  as solvent at Chemistry Department, Faculty of Science, Cairo University. High Resolution Mass Spectra (HRMS) were recorded using both a Bruker HCT ultra and a high resolution (Bruker Daltonics micrOTOF) instruments from methanol or dichloromethane solutions using the positive Electrospray Ionization Mode (ESI). The *RHF/ab initio* quantum mechanical level of computation was employed in all calculations of molecular orbitals and quantum chemical parameters. The 6-31G\*\* basis set was used for carbon, nitrogen, hydrogen atoms, whereas the 6-31++G\*\* diffuse function basis set for Sulfur atom. All calculations were performed *in vacuo*, and no solvent effect was considered. The HyperChem ver 8.06 software package, accommodated on Core-Due 2 PC was employed.

### 5,7-Diphenyl-6-[1,3-diphenylpropan-1-on-3-yl][1,3,4]thiadiazolo[3,2-a]pyrimidine (**3**)

A mixture of 2-amino-1,3,4-thiadiazole (**1**) (0.5 g, 0.5 mmol) and benzalacetophenone (0.5 mmol) in ethanol/glacial acetic acid mixture (1:1, 10 mL) was refluxed for 15 h and then left to cool. The formed precipitate was filtered and recrystallized ethanol/DMF mixture (1:1) to afford the corresponding thiadiazolopyrimidine derivative **3** as yellow crystals; yield (43%);

**Table 2** Calculated atomic charge densities and the HOMO atomic orbital coefficients for the amine **1a**.

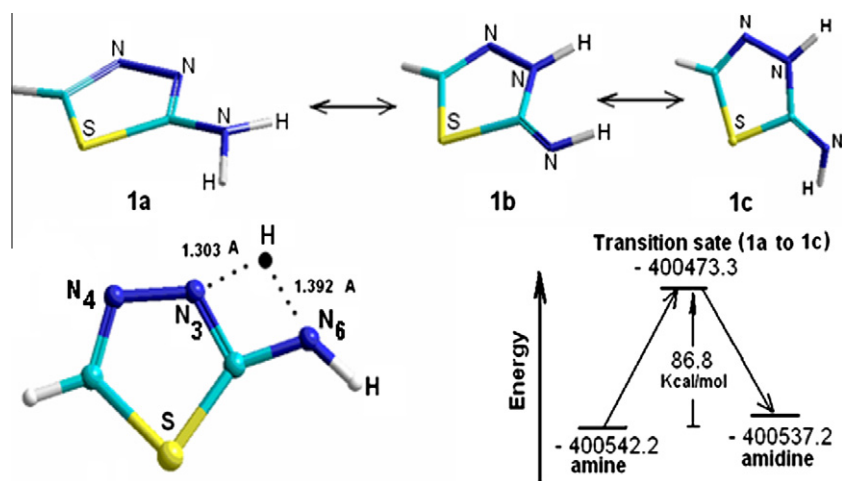
Atom	Charge	Atomic orbital coefficients			
		2s	2p <sub>z</sub>	2p <sub>y</sub>	2p <sub>x</sub>
S	+0.2163	0.0060	-0.1101	0.0018	0.0044
N <sub>3</sub>	-0.3633	-0.0661	-0.2289	0.0022	0.0199
N <sub>4</sub>	-0.2274	-0.0030	0.1776	0.0098	-0.0265
N <sub>6</sub>	-0.7227	-0.0499	0.3055	0.0239	0.0566

**Table 3** Charge densities and LUMO<sup>a</sup> atomic orbital coefficients of the chalcone **2**.

Atom	Charge	LUMO coefficients			
		2s	2p <sub>z</sub>	2p <sub>y</sub>	2p <sub>x</sub>
O	-0.630	-0.0001	0.2462	-0.12781	-0.1249
C <sub>1</sub>	+0.852	-0.0014	-0.2428	0.1246	-0.2428
C <sub>2</sub>	-0.548	-0.0013	-0.3357	0.1729	0.1692
C <sub>3</sub>	+0.328	0.0104	0.5196	-0.2679	-0.2652

<sup>a</sup> Orbital energy = +3.437 eV.

mp 285 °C;  $R_f$  = 0.6 [pet. ether (40–60): ethyl acetate (3:2.5)]; IR (KBr) ( $\text{cm}^{-1}$ ), 3097 (CH, str.), 1666 (C=O), 1575 (C=C);  $^1\text{H}$  NMR (300 MHz,  $\text{DMSO-}d_6$ )  $\delta$  (ppm): at 4.57 (br, 1H), 4.91 (br, 1H), 5.91 (br, 1H), 6.61–7.84 (m, 21H, CH, Ar–H), 8.79 (s, 1H, C–H<sub>7</sub>, pyrimidothiadiazole); (ESI, -98.7v) (+)-ESI mass spectrum showed three quasi-molecular ion peak at 500 ( $\text{MH}^+$ ), 523 ( $\text{MH}^+ + \text{Na}$ ) and 539 ( $\text{MH}^+ + \text{K}$ ) pointing 399 as the molecular mass of **5**; HRMS(micrOTOF):  $m/z$  for  $\text{C}_{32}\text{H}_{26}\text{N}_3\text{OS} + \text{Na}$ , Calcd.:



**Fig. 1** Possible tautomeric forms of 2-amino-1,3,4-thiadiazole and the transition state for their conversion (**1a** → **1c**).

**Table 1** Calculated energies of the tautomeric forms of 2-amino-1,3,4-thiadiazoles (**1a–c**, Fig. 1).

Character	Amine <b>1a</b>	Amidine <b>1b</b>	Amidine <b>1c</b>	Transition State ( <b>1a</b> → <b>1c</b> )
Total energy (kcal/mol)	-400542.16	-400535.93	-400537.22	-400373.34
$E$ (HOMO) (eV)	-9.595	-8.922	-8.891	-8.760
$E$ (LUMO) (eV)	2.333	2.506	3.395	2.292
Dipole moment (debye)	3.737	2.436	1.979	2.596

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