

# Synthesis and Structural Elucidation of a Nitro Substituted Ethynyl-thiourea Derivative (NETh) for Carbon Monoxide (CO) Detection

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A model compound of hybrid ethynyl-thiourea featuring nitro substitution at the *para*-position of the molecular framework was designed, synthesised and structurally elucidated. In this work, the characteristic response of the nitro-substituted ethynyl-thiourea derivative (NETh) towards carbon monoxide (CO) gas was evaluated via UV-Vis spectrophotometer under optimised absorbance response. NETh exposed to CO gas within the concentration range of 10-30 ppm exhibited the highest sensing response of 11.78% towards the lowest CO concentration (10 ppm). The calculated interaction distance and interaction energy between NETh and CO molecules were modelled using density functional theory (DFT) via Gaussian09 software, and the results revealed that the preferred active site of interaction between NETh and CO was at the alkene position (H atom at *cis* position to carbonyl, C=O).

**Keywords:** Thiourea; density functional theory; interaction with CO; organic synthesis; functional materials

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These days, the quality of air in Malaysia is affected by various toxic gases, including carbon monoxide (CO), which are released from numerous sources to the environment. The main sources of CO are vehicles, industrialisation, and open burning activities which represent 70-75% of the air pollution issues in Malaysia [1, 2]. Prevention and control measures for CO gas contamination are necessary to assure adequate protection of public health as well as to maintain natural habitats [3, 4]. In addition, since the development of technology in the industrialization era, there has been an increase in combustion processes. This development has negatively impacted the environment not only because of the increased combustion but also the diversity of toxic gases released. This phenomenon pollutes ambient air and affects the quality of clean air.

The development of an integrated system for detecting CO in the environment has always been an aim of chemists in this field. In this study, an organic molecule featuring a nitro-substituted ethynyl-thiourea derivative (NETh) for the purpose of CO detection was designed, synthesised, structurally elucidated, and examined for its interaction with CO. The NETh system is rich with  $\pi$ -electrons which may show a strong interaction towards CO gas, as it contains a high degree donor and acceptor system within its molecule. The molecular structure of NETh is as shown in Figure 1.

Moreover, optical sensing by UV-Vis analysis offers ease of detection as the structure is examined in terms of its electronic properties before and upon interaction with the gas analyte.

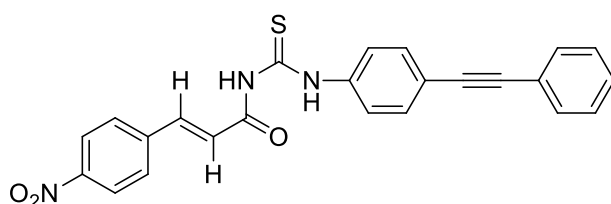


Figure 1. The molecular structure of NETh.

Absorbance, reflectance, fluorescence, refractive index properties, and both intensity and wavelength of absorbance and fluorescence can be analyzed simultaneously by an optical sensor to detect and differentiate the analyte [5]. In 2012, Gonçalves and co-workers studied the optical sensing of polythiophene derivatives towards volatile organic compounds (VOCs) and carbon monoxide gas by their absorption and refractive index changes [6].

The presence of rigid ethynyl moieties ( $C\equiv C$ ) provides the **NETh** molecule with a  $\pi$ -conjugated system which provides an abundance of electrons that allows electron delocalisation to occur along the **NETh** molecular framework [7]. Therefore, **NETh** is a molecular wire candidate that is capable of interacting with the CO gas analyte. Besides, the **NETh** system also provides an easy synthetic pathway and contains an electron-rich molecular framework with a D- $\pi$ -A system. As it acquires donor and acceptor functional groups, **NETh** is a versatile ligand that can be expected to interact with a CO gas analyte.

## MATERIALS AND METHODS

### Chemicals and Reagents

All chemicals, solvents, and materials were commercially purchased from standard suppliers and used as received without further purification. Chemicals used in this work, namely, 4-iodoaniline, ammonium thiocyanate, ethynylbenzene, and nitro cinnamoyl chloride were purchased from Sigma-Aldrich and Acrós Organics. Solvents such as acetone, acetonitrile, dichloromethane, diethyl ether, triethylamine, ethyl acetate, and hexane were purchased from Fisher Scientific, Merck and HmBG®. The catalyst  $Pd(PPh_3)_2Cl_2$ , used in the Sonogashira reaction was prepared by referring to the literature method [8]. For the gas-interaction studies, carbon monoxide (CO) gas with various concentrations of 10, 20, and 30 ppm were purchased from Gas Sensor Sdn. Bhd., UKM-MTDC Technology Centre, Bangi, Selangor, Malaysia.

### Instrumentation and Characterisation

Infrared (IR) spectra were recorded using a Perkin Elmer 100 Fourier Transform Infrared spectrophotometer within the spectral range of  $4000\text{--}450\text{ cm}^{-1}$ . Electronic transition analysis of the synthesised compound and its interaction with CO

was recorded using a Shimadzu 1601 series with  $1\text{ cm}^3$  path length quartz cell in acetonitrile at a concentration of  $1 \times 10^{-5}\text{ M}$ . The molecular structure of **NETh** was elucidated using  $^1H$  400.11 MHz and  $^{13}C$  100.6 MHz NMR analyses, recorded on a Bruker Avance III 400 in deuterated chloroform ( $CDCl_3$ ) at room temperature with the standard spectral ranges of  $\delta_H$  0-15 ppm and  $\delta_C$  0-200 ppm, respectively. Finally, time dependent density functional theory (TD-DFT) calculations at the theoretical level of B3LYP/6-31G (d, p) were carried out via Gaussian09 software to examine the molecular electronic characteristics and the sensing interactions between the synthesised molecules and carbon monoxide gas at a minimum potential.

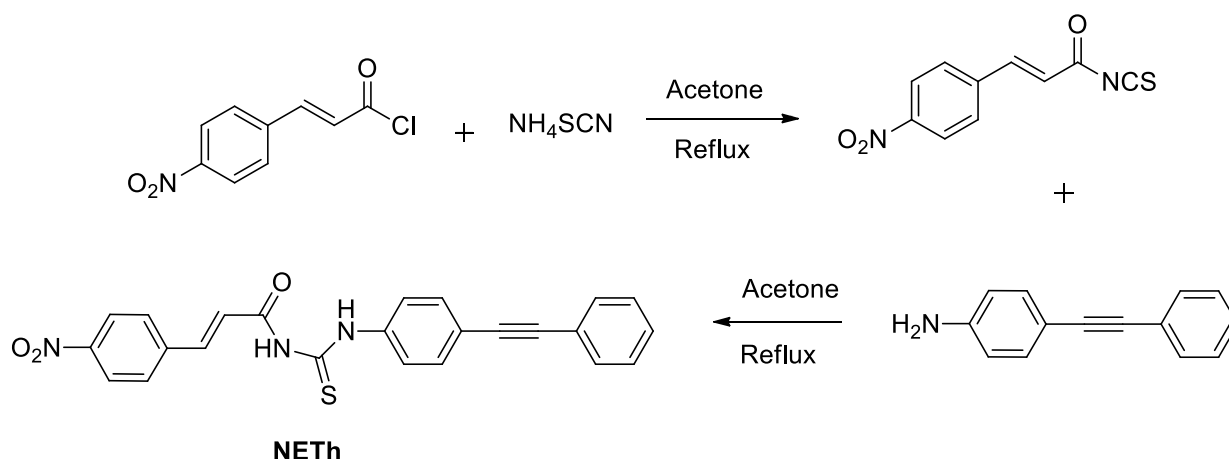
## EXPERIMENTAL

### Synthesis of N-(4-phenylethynylaniline)-N'-(nitrocinnamoyl)thiourea (NETh)

The general reaction for the synthesis of **NETh** is shown in Scheme 1. 4-nitrocinnamoyl chloride (1 mmol) and ammonium thiocyanate (1 mmol) were dissolved in acetone and refluxed for approximately 3 hours until the formation of a white precipitate salt (nitrocinnamoyl isothiocyanate) was observed. The nitrocinnamoyl isothiocyanate was treated with an equimolar amount of 4-phenylethynylaniline (1 mmol) to yield N-(4-phenylethynylaniline)-N'-(nitrocinnamoyl) thiourea (**NETh**), the targeted final compound. The obtained compound was then recrystallised from acetonitrile, yielding the yellowish amorphous solid **NETh** (85 % yield). IR (KBr):  $\nu = 3436.11$  (N-H),  $2365.92$  ( $C\equiv C$ ),  $1682.35$  (C=O),  $732.67$  (C=S)  $\text{cm}^{-1}$ ;  $^1H$  NMR ( $CDCl_3$ ),  $\delta$  (ppm): 8.74 (s, H), 12.52 (s, H), 7.21-8.25 (m, 13H), 6.77 (p-d, 11 Hz, H), 7.72 (p-d, 11 Hz, H);  $^{13}C$  NMR ( $CDCl_3$ ),  $\delta$  (ppm): 89.1, 90.4, 122.5-146.9, 173.4, 181.2.

### Response Towards Carbon Monoxide (CO) Gas: Solution Studies

**NETh** at a concentration of  $1 \times 10^{-5}\text{ M}$  was used to study its response towards carbon monoxide gas at room temperature using a UV-Vis spectrophotometer. The absorption of **NETh** was first used as a control without the presence of CO gas. Later, different concentrations of CO gas (10, 20, and 30 ppm) were purged into the cuvette for 10 minutes for the CO molecules to interact with **NETh**.



**Scheme 1.** The **NETh** synthetic pathway

### Density Functional Theory (DFT) Calculation

Time-dependent density functional theory (DFT) calculations were performed at the B3LYP/6-31G (d, p) for electronic excitation analysis and to assess the theoretical interactions between **NETh** and CO in terms of the effects of Mulliken charges, interaction and stabilisation energies, energy band gaps, and the prediction of a preferred site for the interaction to occur.

## RESULTS AND DISCUSSION

### Spectroscopic Analysis

The  $^1\text{H}$  NMR spectrum of **NETh** showed two distinctive singlet resonances for amide (N-H) protons at  $\delta_{\text{H}}$  8.74 ppm and  $\delta_{\text{H}}$  12.52 ppm, due to the presence of two different NH environments resulting from the intramolecular hydrogen bonding of N-H in the *trans*- and *cis*-conformations [9-11]. Among both amide resonances, the amide resonance of NH(C=S) was observed at a higher chemical shift compared to the amide proton of NH(C=O) due to deshielding effects and intramolecular hydrogen bonding. The aromatic protons were observed as multiplet resonances in the range  $\delta_{\text{H}}$  7.21 ppm –  $\delta_{\text{H}}$  8.25 ppm and the alkene protons (CH=CH) appeared as pseudo-doublet resonances at  $\delta_{\text{H}}$  6.77 ppm and  $\delta_{\text{H}}$  7.72 ppm. The  $^{13}\text{C}$  NMR spectrum of **NETh** showed resonances for C $\equiv$ C moiety at  $\delta_{\text{C}}$  89.1 and  $\delta_{\text{C}}$  90.4 ppm. The aromatic carbon resonances can be assigned in the range  $\delta_{\text{C}}$  122.5-146.9 ppm. The resonances of the carbonyl (C=O) and thiocarbonyl (C=S) were observed at  $\delta_{\text{C}}$  173.4 and  $\delta_{\text{H}}$  181.2 ppm, deshielded to a higher chemical shift due to intramolecular hydrogen bonding and electronegative effects from the oxygen and sulfur atoms, respectively [12, 13].

The FT-IR spectrum of **NETh** showed the

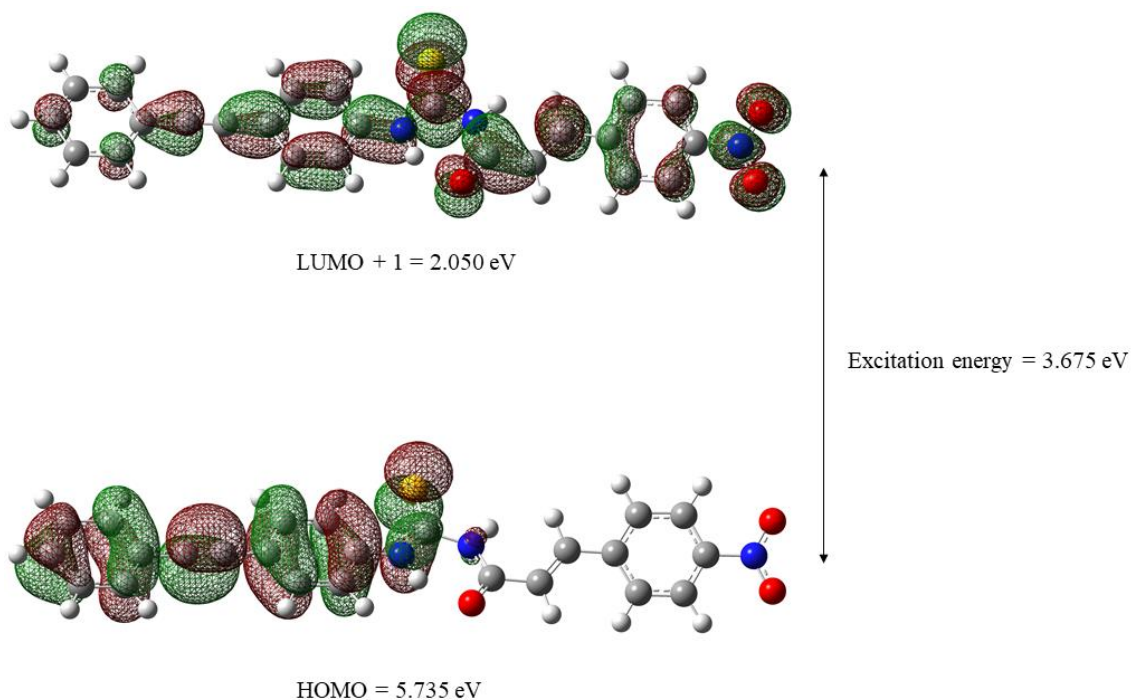
absorption of asymmetric and symmetric stretching vibrations of a secondary thioamide moiety (N-H) at 3436.11  $\text{cm}^{-1}$ . The (C $\equiv$ C) stretching vibration in **NETh** occurred at 2365.92  $\text{cm}^{-1}$  as a medium intensity absorption peak. The carbonyl (C=O) strong absorption band for **NETh** appeared at 1682.35  $\text{cm}^{-1}$ . This absorption band was decreased in frequency due to the presence of a conjugated resonance with the phenyl ring and NO $_2$  as an electron withdrawing group and inter-molecular hydrogen bonding with thioamide (N-H). Furthermore, the vibrational absorption of C=S was observed at 732.67  $\text{cm}^{-1}$  which is in tune with other literature [14-16].

### Electronic Transition Analysis

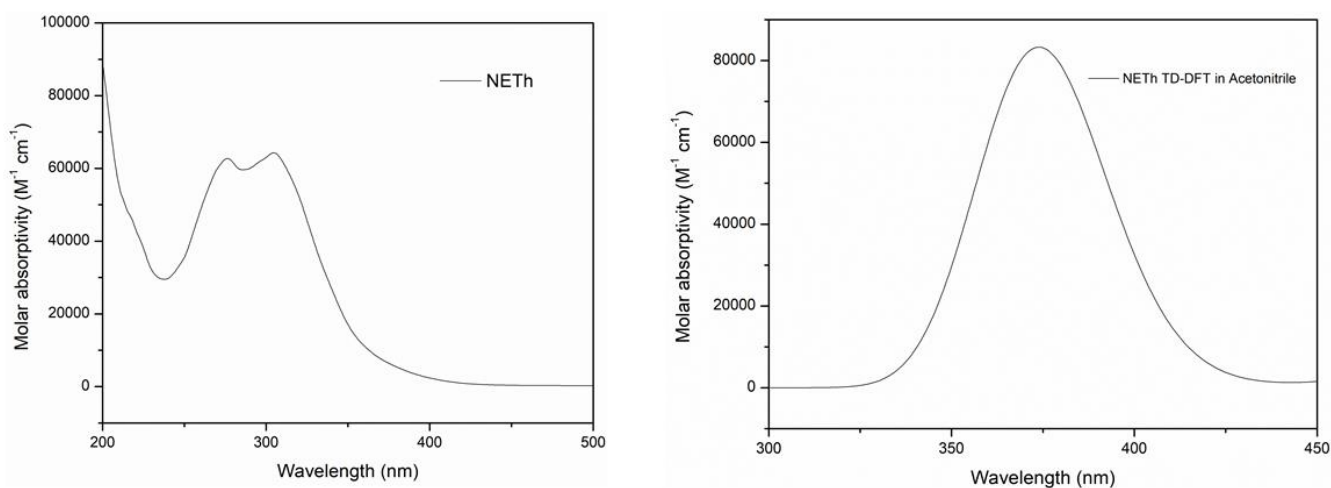
The UV-Vis analysis for **NETh** was recorded in acetonitrile ( $1 \times 10^{-5}$  M). The reported experimental and calculated absorption wavelengths, theoretical electronic excitation energy, and oscillator strength of **NETh** are listed in Table 1. The calculated absorption bands were obtained using B3LYP 6-31 G (d, p) using IEF-PCM formalism in acetonitrile. The experimental absorption at 300 nm for **NETh** corresponded to the mixed transitions of  $\pi \rightarrow \pi^*$  and  $n \rightarrow \pi^*$ . Figure 2 illustrates the interfrontier orbitals obtained from TD-DFT calculations at the contour value 0.02 which are used to determine the possible electronic transitions mentioned in Table 1. The experimentally and theoretically predicted UV-Visible spectra are visualized in Figure 3. In Table 1, the calculated absorption maxima value for **NETh** was found to be 373 nm, whilst the oscillator strength was one of the parameters to determine the strength of an electronic transition. The oscillator strength for the transition at 373 nm was the highest in magnitude and it corresponded to the experimental value observed at 300 nm and assigned to the transition from HOMO  $\rightarrow$  LUMO+1 orbital and predicted for the mixed transitions of  $n \rightarrow \pi^*$  and  $\pi \rightarrow \pi^*$ .

**Table 1.** Theoretical electronic absorption spectra of **NETh** calculated at B3LYP/6-31 G (d, p) level of theory in gas phase.

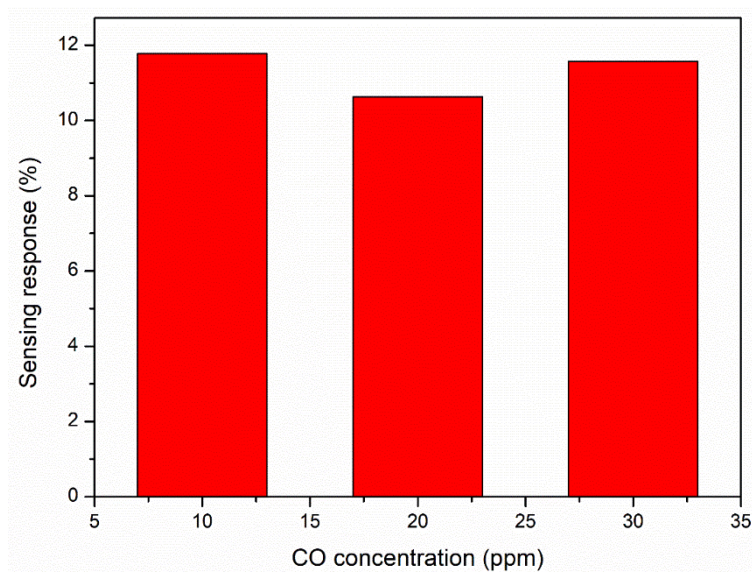
Excited state	Wavelength (nm)		Excitation energy (eV)	Oscillator strength ( <i>f</i> )	Transition assignment
	Theoretical	Experimental			
1	373	300	3.675	1.1495	HOMO → LUMO + 1



**Figure 2.** The interfrontier orbitals of HOMO and LUMO obtained from TD-DFT calculations at the contour value 0.02



**Figure 3.** The experimental and theoretical UV-Visible spectra of **NETh**.



**Figure 4.** The sensing response of **NETh** towards 10-30 ppm CO

#### Interaction Response Towards Carbon Monoxide via UV-vis Spectroscopy: Solution Studies

**NETh** as molecular sensor was investigated at three different CO concentrations (i.e., 10, 20, and 30 ppm). The absorption spectra of the **NETh** at different CO concentrations were analysed to determine the response and sensitivity of the synthesised molecule to the detection of CO. The absorption spectra showed that significant changes occurred in the electronic transitions of the synthesised **NETh** in solution before and after exposure to different CO concentrations. The sensing response from the UV-Vis analysis shows that the absorption of **NETh** before and after exposure to CO produced similar trends in the electronic transition at the same wavelength. The obvious and most changed bands can be observed at  $\lambda_{\text{max}} = 300$  nm, which was used to monitor and evaluate the response of the molecular sensor to different CO concentrations. The changes in absorbance after exposure to different CO concentrations indicated an interaction of **NETh** with CO.

Results showed that the sensing response of **NETh** with an electron withdrawing substituent ( $\text{NO}_2$ ) exhibited a higher response towards 10 ppm

and 30 ppm of CO gas with 11.78% and 11.57% respectively. However, **NETh** exhibited the lowest sensing response of 10.63% towards 20 ppm of CO concentration. Overall, **NETh** could only provide a moderate sensing response towards 10-30 ppm CO due to the nature of **NETh** with electron withdrawing groups that lack the electron density to enable the interaction with the  $\pi$ -molecular orbital of CO. This finding is similar to those reported previously [6, 17]. Figure 4 illustrates the sensor response towards various CO concentrations in the form of a bar chart.

#### Theoretical Calculations: Density Functional Theory (DFT)

The **NETh** molecule (free-sensor molecule) and the sensor-CO complex were optimised to the minimal potential energy using the Gaussian 09 quantum mechanical software package at the theoretical level of DFT B3LYP 6-31G (d, p). From the calculated results, **NETh** showed promising interactions with CO in terms of the stabilisation energy and the interaction distance of the sensor-CO complex. The calculated Mulliken charges on the selected atoms of **NETh** as well as the interaction energy and the possible interaction distance are listed in Table 2.

**Table 2.** The calculated Mulliken charges, interaction distance and interaction energy of free **NETh** and the complex with CO.

Molecular sensor	Mulliken charges			Interaction distance between <b>NETh</b> and CO ( $\text{\AA}$ )	Interaction energy (kJ/mol)
	O (C=O)	S (C=S)	HC=CH ( <i>cis</i> to C=O)		
<b>NETh</b>	-0.527	-0.254	0.128	2.62	-6.67

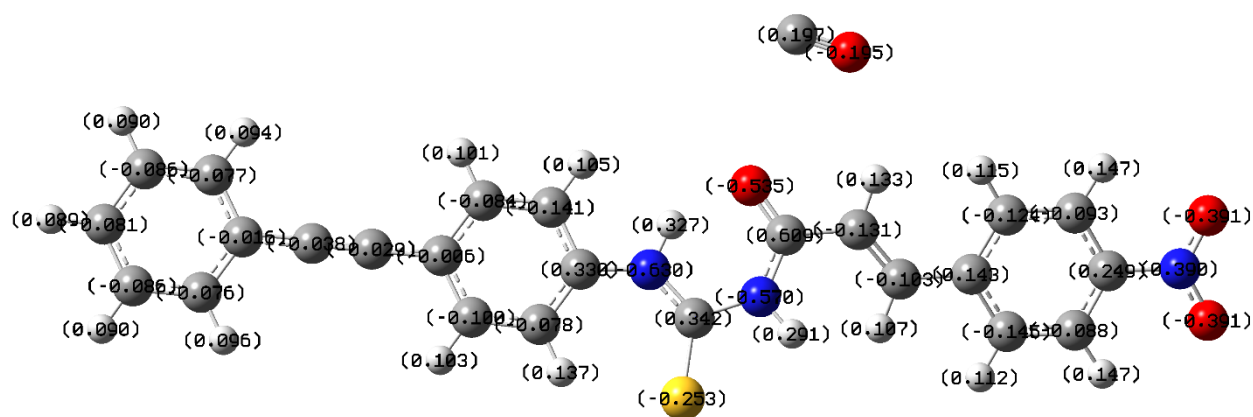


Figure 5. The distribution of Mulliken charges on NETH atoms.

These results show that the charge on the oxygen atom of the C=O amide (-0.527) are about two times higher compared to that on the sulphur atom of C=S (-0.254) in the NETH moiety. Due to the highly positive value of the charge on the H atom of the alkene at *cis* position to C=O, we believe that the interaction formed between NETH and CO occurred at the alkene (H at *cis* position to C=O). Figure 5 illustrates the molecular optimisation of the NETH-CO complex. It reveals that NETH is the most sensitive molecular sensor for CO detection with a stabilisation value of -6.67 kJ/mol compared to the previous reported literature [18]. The presence of the alkene (CH=CH) improves the sensitivity as well as the interaction ability of the NETH with CO. To understand the characteristics of the interaction between NETH and CO, the values of Mulliken charges on the selected atoms were measured (as illustrated in Figure 5). The charge on the H atom at the *cis* position to C=O was observed to be +0.133, and this is the most preferable site in the structure for H-bonding with CO as it has the least steric hindrance.

### CONCLUSION

A new model compound of N-(4-phenylethynylaniline)-N'-(nitrocinnamoyl) thiourea (NETH) was successfully designed, synthesised and physicochemically characterised as an active sensing molecular material for the determination of carbon monoxide (CO) gas at three different concentrations (10, 20, and 30 ppm). The response of NETH in solution form towards CO gas at room temperature was investigated by comparing differences in its UV-Vis spectral characteristics prior to and upon interaction with CO gas. The NETH molecular structure with D- $\pi$ -A system in solution form exhibited an ideal response towards low CO concentration of 10 ppm with 11.78%. In addition, the theoretical calculations from DFT analysis proved that NETH demonstrated an interaction energy of -6.67 kJ/mol for the NETH-CO complex. Therefore, NETH provides an alternative molecular sensing

material that has possible interactions with CO gas. In future, NETH may be used as a dopant in a polymer host to enhance the interaction of NETH with CO.

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