Kinetics and Mechanism of Palladium Catalysed Electron Transfer Reaction between Glutathione (Reduced) and Pyridinium Chlorochromate in Acid Medium

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Abstract: The palladium $[Pd^{+2}]$ catalysed electron transfer reaction between glutathione (reduced) (GSH) and pyridinium chlorochromate (PCC) has been studied spectrophotometrically over the range $2.00 \leq 10^3 [GSH] \leq 6.00$, $0.01 \leq [H^+] \leq 0.03$ mol dm^{-3} , $2.83 \leq 10^5[Pd^{+2}] \leq 14.15$ and $20\ ^0C \leq t \leq 40\ ^0C$. The rate of reaction was found to increase with the increase in $[GSH]_T$, $[H^+]_T$ and $[Pd^{+2}]$. The reaction was found to exhibit first order dependence in $[GSH]_T$, $[H^+]_T$ and $[Pd^{+2}]_T$. The $\Delta H^{\neq}$ (kJ/mol) and $\Delta S^{\neq}$ (JK^{-1} mol^{-1}) for the electron transfer reaction were found to be -27.7 and -243.9. The product of the reaction was found to be glutathione disulfide (GSSG) as indicated by infrared spectrum. The negative values of activation parameters favour the formation of the ordered transition state.

Keywords: Palladium, Glutathione (Reduced), Pyridinium chlorochromate and Electron transfer

Introduction

Glutathione, a tri peptide (γ-*L*-Glutanyl-*L*-cysteinylglycine) is a molecule that occurs in plants and animals (Figure 1). It is an antioxidant, preventing damage to important cellular components caused by reactive oxygen species such as free radical and peroxides[1]. The thiol group of glutathione reduces disulphide bonds formed within cycloplasmic protein to cysteines by serving as an electron donor. In the process glutathione is oxidized to its oxidized form glutathione disulphide (GSSG). Pyridinium chlorochromate (PCC) is a mild oxidizing agent. The electron transfer reactions of PCC with various molecules have been studied[1-11]. PCC is a mild oxidizing agent. The compound has been used extensively for the study of redox reactions of many biomolecules, but the electron transfer reaction of PCC with peptides GSH in presence of $[Pd^{+2}]$ catalyst has not been studied. However the redox reactions of [GSH] with other oxidant have been studied[12-15]. The γ-*L*-glutanyl-*L*-cysteinylglycine or GSH is the major low molecular mass thiol compound in plants and animals and its peptide γ–linkage is thought to protect it from degradation by aminopeptidases. It plays a role in signal transduction, gene expression, apoptosis, protein glutathionylation and NO metabolism. Palladium(II) is known to catalyse effectively several redox reactions. In order to understand the role of $[Pd^{+2}]$ in the electron transfer reaction, the work has been undertaken.
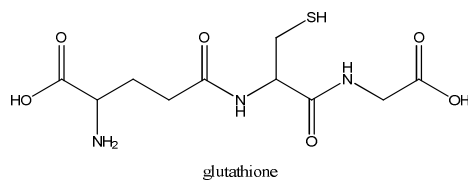
glutathione

Figure 1. Structure of glutathione

Experimental

Pyridinium chlorochromate has been synthesized by following the reported method[16]. The compound was characterized by estimating Cr(VI) iodometrically. The estimation of [Pd^{+2}] was carried out gravimetrically using dimethylglyoxime[17]. The acid strength of the medium was maintained by addition of HClO$_4$. Kinetic measurements were recorded on a sytronic 119 PC scanning UV-Vis spectrophotometer (Figure 2). Reaction progress was monitored at 435 nm. Pseudo first order condition were maintained though out the runs by using a large excess (>5 fold) of [GSH]. The constant (k$_{obs}$) were obtained from the slope of $-\ln(A_t - A_\infty)$ *versus* 't' plots.

$$- \ln (A_t - A_\infty) = k_{obs}\, t - C$$

Where A$_t$ and A$_\infty$ are the absorbances of the reaction mixture at time t and at the completion of the reaction. The reported rate data represented as an average of duplicate runs were reproducible within ±3% the correlation coefficient of the plots used determine k$_{obs}$ were found to be 0.99 in most of the cases.
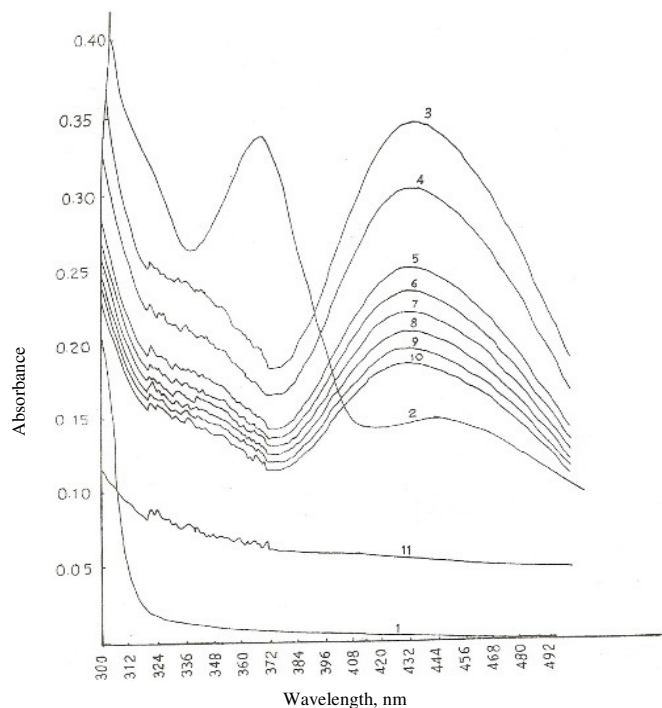

Figure 2. Repetitive spectral scan of PCC with GSH
(*Curve 2: [PCC] = 4×10^{-4} mol dm^{-3}, Curve 1:[GSH] = 2×10^{-3} mol dm^{-3}, [H$^+$] = 1.0×10^{-2} mol dm^{-3}, T = 30 ^{o}C, at different time intervals of 2 min (Curve 3-10), Curve 11 is after 24 H)*

Results and Discussion

The kinetic results obtained for the above reaction may be summarized as follows. With the varying concentration of 10^3 [GSH]$_T$ in the range 2.00 to 6.00 mol dm^{-3}, the 10^4 k_{obs} sec^{-1} (25 ^{0}C) increased from 6.03 to 11.35 when [H$^+$] = 0.01 mol dm^{-3}, [PCC] = 4x10^{-4} mol dm^{-3} and [Pd^{+2}] = 2.83x10^{-5} mol dm^{-3} (Table 1). The [GSH]$_T$/ [PCC]$_T$ was varied from 5.00 to 20.00. The k_{obs} *versus* [GSH]$_T$ plot (Figure 3) was linear at all reported [H$^+$]$_T$ indicating 1st order dependence of the reaction on [GSH]$_T$. At fixed [Pd^{+2}] and [H$^+$] and [GSH]$_T$, the k_{obs} does not change by changing [PCC]$_T$, hence the order of the reaction is one with respect to [PCC]$_T$. The rate law is therefore given by equation (1).

$$\text{Rate} = k_{obs} \text{ [PCC]}_T$$
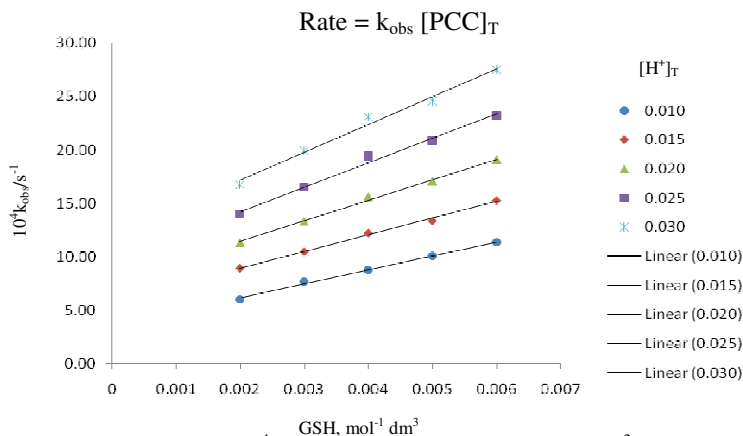
Figure 3. The plots of 10^4 k_{obs} / s^{-1} *versus* [GSH]$_T$ / mol dm^{-3} at different [H$^+$]
([PCC]$_T$ = 4.0×10^{-4} mol dm^{-3}, t = 25 ^{o}C, [H$^+$] was varied from 0.01 to 0.03 mol dm^{-3} and [GSH] was varied from 0.002 to 0.006 mol dm^{-3})

With [PCC]$_T$ = 4x10^{-4} mol dm^{-3} and [GSH]$_T$ = 2x10^{-3} mol dm^{-3},10^4 k_{obs} (25 ^{0}C) changed from 6.03 to 16.77 as [H$^+$]$_T$ was changed from 0.01 to 0.03 mol dm^{-3}. This behavior was repeated for the entire [GSH]$_T$ range 0.002 to 0.006 mol dm^{-3} (Figure 4). When [PCC]$_T$ = 4x10^{-4}, [GSH]$_T$ = 2x10^{-3}, [H$^+$]$_T$ = 0.01 mol dm^{-3}, by changing [Pd^{+2}]$_T$ from 2.83x10^{-5} to 14.15x10^{-5} mol dm^{-3}, 10^4 k_{obs}(s^{-1}) at 30 ^{0}C changes from 7.13 to 39.83 (Figure 5).
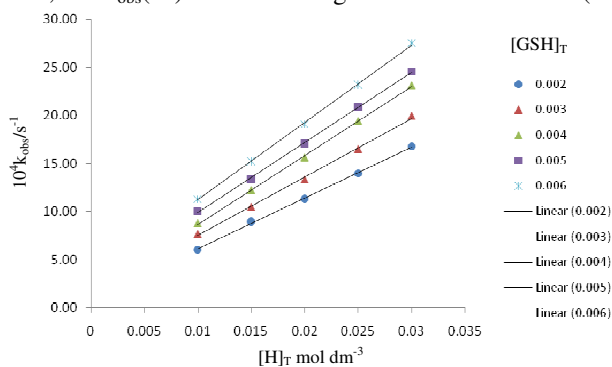
Figure 4. The plots of $10^4 k_{obs}$ / s^{-1} *versus* [H$^+$]$_T$ mol dm^{-3} at different [GSH$^+$]$_T$
([PCC]$_T$ = 4.0×10^{-4} mol dm^{-3}, t = 25 ^{o}C. [H$^+$] was varied from 0.01 to 0.03 mol dm^{-3} and [GSH] was varied from 0.002 to 0.006 mol dm^{-3})
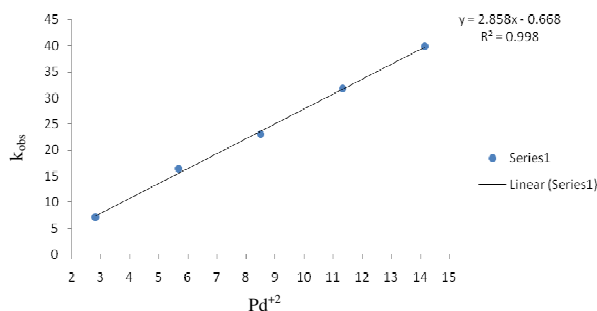
Figure 5. The plots of $10^4 k_{obs}$ / s^{-1} *versus* $[Pd^{+2}]_T$ mol dm^{-3} at different $[Pd^{+2}]_T$
($[PCC]_T = 4.0 \times 10^{-4}$ mol dm^{-3}, $t = 30\ ^oC$. $[Pd^{+2}]$ was varied from 2.83×10^{-3} mol dm^{-3} to 14.15×10^{-3} mol dm^{-3}, $[H^+] = 0.01$ mol dm^{-3} and $[GSH] = 0.002$ mol dm^{-3})

The temperature variation was carried out in the range 20 ^0C to 40 ^0C. With the increase in temperature, k_{obs} was found to increase. With $[GSH]_T = 2 \times 10^{-3}$ mol dm^{-3} $[PCC]_T = 4 \times 10^{-4}$ mol dm^{-3}, $[H^+] = 0.01$ mol dm^{-3} and $[Pd^{+2}] = 2.83 \times 10^{-5}$ mol dm^{-3} $10^4 k_{obs}$ (s^{-1}) changed from 5.25 to 9.21 as the temperature was changed from 20 ^0C to 40 ^0C (Table 1).

Table 1. Rate constants for the oxidation of GSH by PCC in presence of Pd^{+2} at different temperature

| Temp ^oC	$10^3[GSH]_T$ mol dm^{-3}	$10^4 k_{obs}$, s^{-1}				
		$[H^+]$, mol dm^{-3}				
		0.010	0.015	0.020	0.025	0.030
20	2.0	5.25	7.66	10.01	12.58	15.28
25	2.0	6.03	8.94	11.33	13.98	16.77
30	2.0	7.13	9.78	12.56	15.39	18.25
35	2.0	8.07	10.72	13.70	16.63	20.53
40	2.0	9.21	12.06	15.19	18.40	22.90
20	3.0	6.55	9.22	12.01	15.07	18.47
25	3.0	7.69	10.50	13.33	16.49	19.92
30	3.0	8.92	11.81	14.92	18.42	21.62
35	3.0	9.77	12.79	16.19	19.79	23.79
40	3.0	10.84	14.06	17.66	21.46	25.46
20	4.0	7.68	10.94	14.44	17.94	20.44
25	4.0	8.77	12.23	15.63	19.43	23.13
30	4.0	10.56	14.12	17.60	21.40	25.10
35	4.0	11.39	15.15	18.93	22.93	27.23
40	4.0	12.23	15.99	19.77	23.77	28.07
20	5.0	8.83	12.09	15.59	19.19	22.59
25	5.0	10.07	13.38	17.08	20.88	24.58
30	5.0	11.98	15.49	19.39	23.19	26.89
35	5.0	12.93	16.64	20.84	25.44	29.14
40	5.0	14.22	18.00	22.28	26.98	30.88
20	6.0	9.85	13.11	16.61	20.21	23.61
25	6.0	11.35	15.30	19.10	23.20	27.50
30	6.0	13.71	17.91	22.55	26.65	30.35
35	6.0	14.72	18.92	23.72	28.12	32.02
40	6.0	15.03	19.29	23.93	28.36	33.06

Stoichiometry and characterization of product

The stoichimetry of the reaction was studied at 30 ^{0}C, where $[PCC]_T$ was kept constant at 4.00×10^{-4} mol dm^{-3} and $[GSH] = 6.00 \times 10^{-3}$ mol dm^{-3}, the $[H^+] = 0.01$ mol dm^{-3} and $[Pd^{+2}]$ $= 2.83 \times 10^{-4}$ mol dm^{-3}. From the decrease in $[PCC]_T$ and $[GSH]_T$ the stoichiometry of the reaction can be written as

$$6GSH + 2Cr\ (VI) \xrightarrow{Pd^{+2}} 2Cr(III) + 3GSSG + 6H^+$$
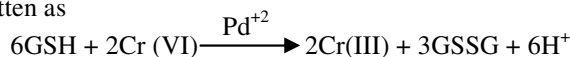
Since pK_1, pK_2, pK_3, pK_4 of GSH are 2.05, 3.47, 8.63 and 9.52. (Scheme 1), at higher concentration of the acid 0.03 mol dm^{-3}, the undissociated form of GSH will participate in the electron transfer reaction. The reaction sequence delineated below (Scheme 2) is consistent with the experimental data.
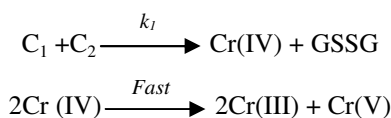
Deprotonation equilibria of GSH
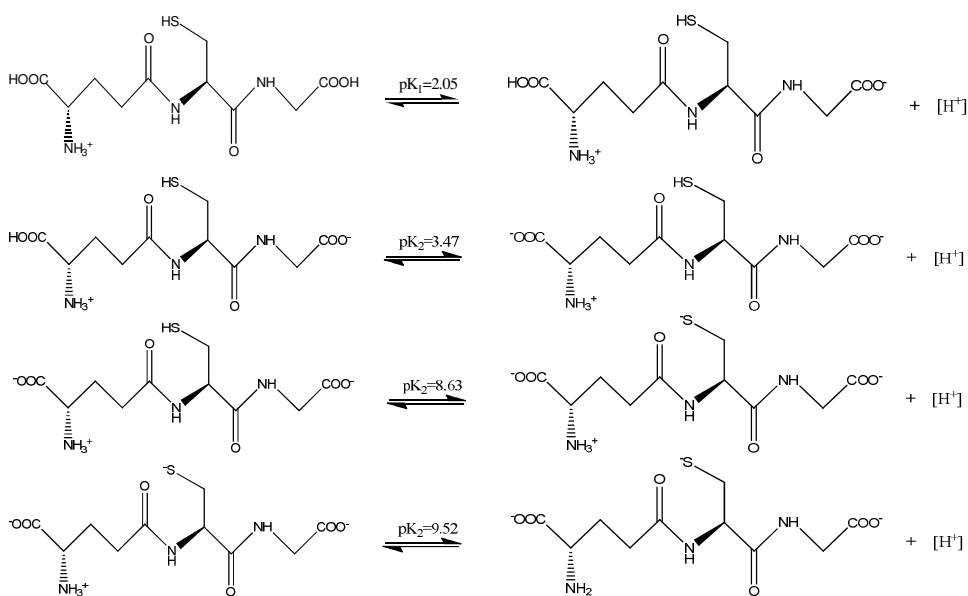
Scheme 1

Proposed mechanism for electron transfer

Scheme 2

$$C_1 + C_2 \xrightarrow{k_1} Cr(IV) + GSSG$$

$$2Cr\ (IV) \xrightarrow{Fast} 2Cr(III) + Cr(V)$$
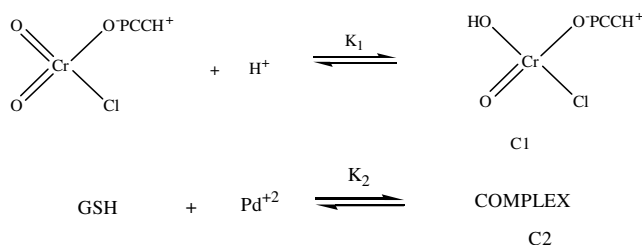
$$\text{Cr(V) + GSH} \xrightarrow{\textit{Fast}} \text{GSSG + Cr(III)}$$

$$\text{Rate} = k_1 [C_1][C_2]$$

$$= k_1 K_1 K_2 [H^+][PCC]_e[Pd^{+2}]_e[GSH]_e$$

$$[PCC]_e = \frac{[PCC]_T}{1+K_1[H^+]}$$

$$\text{Rate} = \frac{k_1 K_1 K_2 [PCC]_T [H^+]_e [Pd^{+2}][GSH]_e}{1+K_1[H^+]_e}$$

$$\text{Rate} = k_{obs} [PCC]_T$$

$$k_{obs} = \frac{k_1 K_1 K_2 [GSH]_e [H^+]_e [Pd^{+2}]_e}{1+K_1[H^+]_e}$$

$$\frac{k_{obs}}{[GSH]} = k_2 = k_1 K_1 K_2 [Pd^{+2}]_T [H^+]_T, \quad k'_2 = k_1 K_1 K_2$$

k_2 is the second order constant for the electron transfer reaction.

The plot of $k_{obs}/[GSH]_T$ *versus* $[H^+]_T$ are found to be linear for every $[GSH]_T$ (Figure 6). From the plot the slope is found to be $k_1 K_1 K_2 (Pd^{+2})$. If $k_1 K_1 K_2$ taken as k'_2, then value of k'_2 can be stated as $\{Slope/(Pd^{+2})\}$.
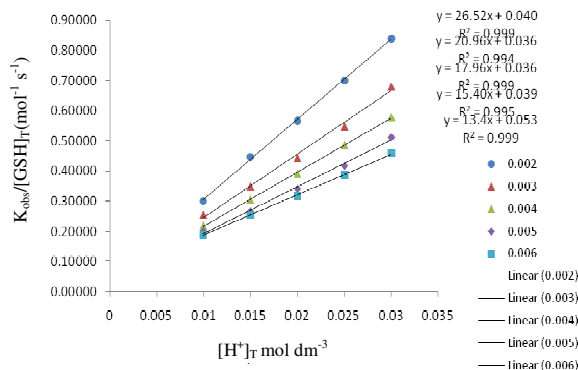
Figure 6. The plots of $\{K_{obs}/[GSH]_T\}$ *versus* $[H^+]_T$ mol dm^{-3} at different $[GSH]_T$

($[PCC]_T = 4.0\times10^{-4}$ mol dm^{-3}, t = 25°C. [H$^+$] was varied from .001 to .003 mol dm^{-3} and [GSH] was varied from 0.002 to 0.006 mol dm^{-3})

Now by plotting a graph between k'_2/T *versus* T^{-1} (Figure 7), a new slope and intercept is obtained. $\Delta H^{\neq}$ (kJmol^{-1}) and $\Delta S^{\neq}$ (JK^{-1} mol^{-1}) were calculate from the Eyring plot of (k'_2/T) *versus* (T^{-1}) and were found to be -27.7 kJmol^{-1} and -243.9 JK^{-1} mol^{-1}. The negative values of activation parameters favour the formation of the ordered transition state.

Characterization of product

The FT IR spectra of GSH (Figure 8 & 9) and the product were recorded with a Pekin Elmer (U.K) FT IR spectrophotometer. A broad peak at 3419 cm^{-1} in the product may be assigned to ν_{N-H} (NH$_3^+$), as compared to 3252 cm^{-1} and 3026 cm^{-1} in GSH. The shifting to higher frequency is probably due to an association of water molecules with the product. The NH$_3^+$ bending bands and a strong absorption peak of carboxylate ion are mixed up and a broad band

is observed at 1636 cm^{-1} in the product compared to 1600 cm^{-1}, 1538 cm^{-1} and 1395 cm^{-1} peaks in GSH. The weak band at 2526 cm^{-1} in GSH due to S-H stretching is absent in the product (Figure 8) suggesting the dimerization of GSH having S-S linkage. Strong and broad peak of 1089 cm^{-1} and a sharp peak of 628 cm^{-1} in the product corresponds to 1073 cm^{-1} and 691 cm^{-1} in GSH is due to the free NH_2 twisting & rocking[18].
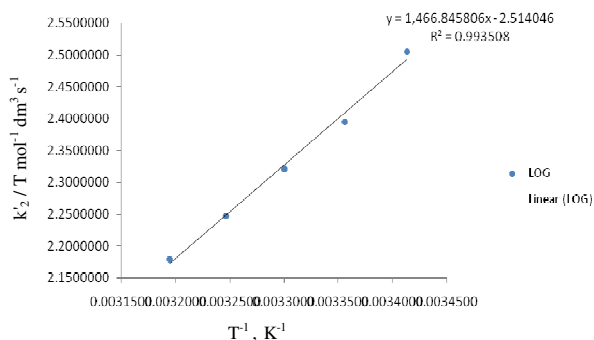

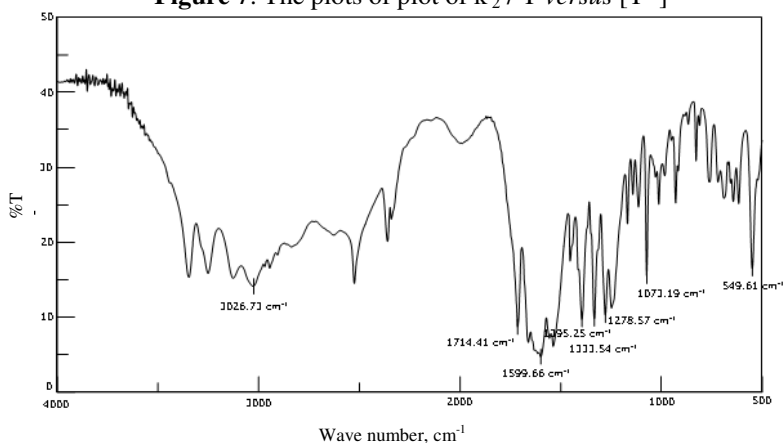**Figure 7**. The plots of plot of k'$_2$ / T *versus* [T^{-1}]

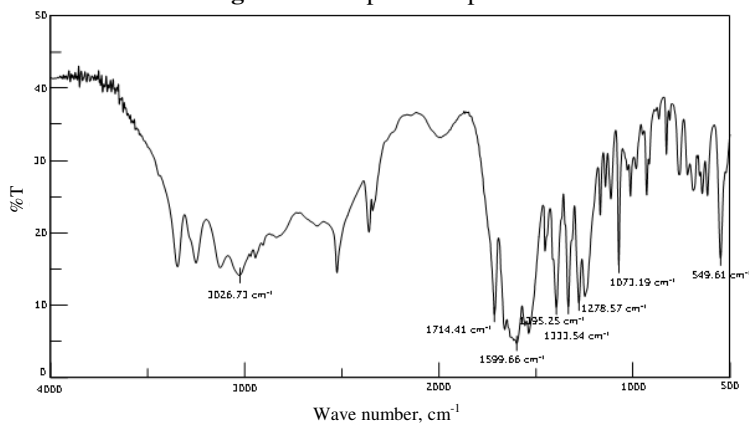**Figure 8.** IR spectra of pure GSH

Figure 9. IR spectra of the product

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