



Deep eutectic solvents (Reline) and Gold Nanoparticles Supported on Titanium Oxide (Au–TiO₂) as New Catalysts for synthesis some substituted phenyl(substituted-3-phenyloxiran)methanone Enantioselective Peroxidation



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Abstract

Background: The eco-friendly power of hydrogen peroxide oxidant produced water that was the only by-product after oxidation. Unfortunately, its oxidation power towards chalcones and chalcones analogs was substantially low, and therefore, it was normally used together with a catalyst or converted to hydroperoxides in order to improve its oxidation power. **Objective:** This research aimed to study epoxidation chemistry. Hence, hydrogen peroxide was used as a potential oxidant for epoxidation with different techniques and catalysts.

Methodology: Advantageous effects of (reline) (derived from two moles of choline chloride and one mole of urea) as a deep eutectic solvent (DES) or the gold (Au) catalyst nanoparticles (NPs) supported on titanium oxide (Au–TiO₂) on the chalcone derivatives of peroxidation was studied under several procedure conditions using hydrogen peroxide/sodium bicarbonate to produce novel oxiranes (I–VI).

Results and Discussion: Acceptable results were obtained by method (B) using hydrogen peroxide/sodium bicarbonate – (reline) mixture, which gave 87- 90% peroxidation results in a short time (4 h) in comparison with less than 86% and 24 h of the conventional method (A), while using the Au NPs supported on titanium oxide (Au–TiO₂); that is, Method (C) gave the best percentage yield of 90-95 % and time (about 2 h), which is about half of that of (Reline) mixture. Such a condition may be due to high activation of hydrogen peroxide by Au and titanium oxide nanoparticles and low viscosity of the reaction mixture.

Conclusions: The chalcones epoxidations would convince chemists that using the deep eutectic solvent (Reline) and the Au-supported on titanium oxide NPs for catalysing these reactions are techniques of great importance in various branches of oxidation.

Keywords: Catalysts, Deep eutectic solvents (DESs), Gold nanoparticles supported on titanium oxide, Hydrogen peroxide, Peroxidation, Reline, Tert-butyl hydroperoxide, α -Ketoperoxide

1. Introduction

As a result of the significant ring strain (~ 27 kcal mol⁻¹) and polarity of the two oxygen-carbon bonds in the three-membered ring system, oxiranes (according to the Hantzsch–Widman system or 1,2-epoxide that is used interchangeably, as well as ethylene oxide that is the most systematic method of naming heterocyclic compounds) were the most studied ring in heterocyclic compounds, in addition to wide-ranging ring-opening reactions, which usually occur with expectable stereospecificity [1].

These three-membered rings can be prepared by using reagents and/or catalyst systems by direct or indirect peroxidation procedures. The catalysts were

the mercury (II) ions catalyzed by cyclization or the presence of Lewis acid (anhydrous copper (II) sulfate) in the reaction of oxiranes with carbonyl compounds to the synthesis of 1,3-dioxolanes, which were proceeded with inversion of stereochemistry of the oxirane [2]. Owing to the high reactivity of this ring toward the amino function under mild conditions, it was used for the conjugation of bioactive substances [3]. Investigation of the configurations of these Spiro epoxy ketones indicated that they have trans-configurations, which were verified by mean of IR, UV, and NMR spectra [4]. Later, the olefinic double bond with various oxidizing agents was successfully oxidized via the reaction of arylidene tetralones with

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hydrogen peroxide in a basic medium. The reaction involved formation of an intermediate via addition of 1,4 – in the first step, followed by intramolecular cyclization of the intermediate to form the final product of keto oxiranes in good yield [5]. Moreover, a novel series of biphenyl keto oxiranes have been synthesized using sodium hypochlorite, which have been evaluated as antimicrobial and insect antifeedant activities of all synthesized oxiranes [6]. While chalcones were exposed to be reduced antioxidants, 7,8-methylenedioxy-3(4-hydroxybenzyl) chroman, as one of the tested homoisoflavonoids, showed a strong antioxidant activity comparable to that of the strongest flavanol antioxidant, quercetin [7]. In addition, a new and effectual chiral catalyst lanthanum-tris(4-fluorophenyl) phosphine oxide-cumene hydroperoxide was used for oxidation of chalcones analogs in order to synthesize enantioselective epoxy ketones with good to excellent yields at room temperature [8]. Furthermore, sodium hypochlorite was used as an oxidizing agent in toluene under mild phase-transfer conditions, which gave oxirane derivatives with an excellent yield and high enantioselectivity [9]. Therefore, various vinyl metallic can be used, including palladium-catalyzed vinyl Grignard reagents, vinylstannanes, vinyl-manganese compounds, and vinyl mercury compounds [10]. Researchers also used guanidine-urea bifunctional enantioselective catalyst with hydrogen peroxide for peroxidation of α,β -unsaturated olefin moieties [11]. Then, they employed trans-3,5-dihydroperoxy-3,5-dimethyl-1,2-dioxolane, as an efficient oxygen source, using a basic medium to synthesize epoxy ketones with excellent yields [12]. Despite the potential of chiral peroxides to induce enantioselectivity, it was successfully developed with the simple use of the available α,β -unsaturated ketones and hydroperoxides, and thus an easily accessible cinchona alkaloid catalyst did not appear to modify the subject of this novel reaction [13]. Consequently, visible light enabled photocatalytic generation of acyl radicals, tert-butyl hydroperoxide, and cesium carbonate. In fact, it was a technique used to form α,β -epoxy ketones by the reaction of a range of styrene and benzaldehydes [14]. Therefore, using the above range as well as conjugated and nonconjugated olefins, epoxyketones were synthesized by the visible-light-driven hydroacylations and epoxyacylations in water using methylene blue as the photo redox catalyst and persulfate as the oxidant [15]. The use of catalyst in the oxidation reactions is commercially and technically important because it facilitates the eco-friendly oxidant and hydrogen peroxide used for several oxidations, especially chalcones peroxidation by increasing yield and selectivity [15,16]. It is notable that DESs were the systems formed

from Lewis or Brønsted acids and bases, which can contain a variety of anions and/or cations. However, unusual properties of these ionic solvents were their melting points, which were much lesser than either of the individual components from they made [17].

According to a study in the field, important types of the used eutectic solvents were quaternary ammonium salt with metal chloride, metal chloride hydrate, hydrogen bond donor, or even metal chloride hydrate with hydrogen bond donor [17]. It is well-known that DESs are a new group of solvents that can balance the major drawbacks of common ionic liquids, which have high toxicity, non-biodegradability, complex synthesis requiring refinement, and expensive starting materials. In fact, DESs were obtained by mixing safety, inexpensiveness, renewability, and biodegradability components. This eutectic mixture termed deep eutectic solvent has been created mainly to differentiate them from true ionic liquids as well as to reflect the big depression of several hundred degrees in the freezing point of the eutectic mixture [18]. It was found that reline is an organic salt with very interesting and valuable properties such as nonflammability, thermal and chemical stability, and infinitely low vapor pressure. Therefore, researchers used 1-butyl-3-methylimidazolium chloride as ionic liquid with high-pressure homogenization to isolate CNF from sugarcane bagasse [19]. Moreover, DES was used as the solvent and catalyst in the H_2O_2 oxidation reaction due to:

- i) Radical species, which stabilized the charged reactive intermediate [20].
 - ii) Ionic environment, which strongly immobilized the actual catalyst [21].
 - iii) Recovery and reuse of the catalyst, which improved the product yield and selectivity [22].
- Some researchers found that ionic liquids (ILs), especially DESs, such as reline, have been highly investigated as the reaction media and as catalysts in oxidation processes due to their exceptional properties of safety, low vapor, and chemical stability [23]. Therefore, experts in the field have considered the use of the ionic liquids as a catalyst in oxidation reactions by hydrogen peroxide as an oxidant.

In addition, oxidation of unsaturated alkenes using ionic liquids gave unpretentious products. Thus, strategies that permit for multiple uses of the catalyst systems and simple reaction conditions with the possibility to run reactions without any transition metal catalyst were evaluated [21]. In their study, described a well-organized technique for epoxidation of electron deficient olefins, with basic aqueous solutions of hydrogen peroxide in different ionic liquids at ambient temperature. The epoxide yield was

80-99%, which has been affected by important factors in addition to the recovery and reuse of ionic liquid [24]. Furthermore, activity of the Au-titanium oxide NPs was tested and used as the best oxidation catalyst [25]. Researchers also found that catalytic activity of Au was strongly dependent on the Au particle size, and smaller particles produced higher turnover frequencies so that modification of metal dispersion occurred during the reaction, leading to minor activity [26]. Some heterocyclic compounds, including 1, 2, 3-selenadiazole derivatives from ketones (acetophenone (A), cyclohexanone (B), and menthone (C)) were also synthesized [27]. As a part of a continuous program directed toward the enantioselective epoxidation of chalcones or their analogous [4,28] several techniques have been investigated to be used for facilitating conventional low-temperature enantioselective peroxidation reactions by decreasing the reaction time, increasing the yields, and reducing the amount of catalyst with the use of the DES (reline) or Au catalysts supported on titanium oxide (Au-TiO₂) NPs.

2. MATERIALS and METHODS

2.1. All the reagents and solvents were of analytical grade. They were purchased from a commercial source and used directly. Moreover, DES (reline) was prepared and the Au catalysts NPs (of sizes <5 nm) supported on titanium oxide (Au-TiO₂) were provided by the School of Chemistry, the University of Manchester. According to the research design, IR spectra (ν_{max} in cm⁻¹) were recorded using a Bruker Alph FTIR Germany spectrophotometer using the KBr technique. Then, ¹H NMR spectra of the synthesized compounds were recorded on a spectrophotometer of Bruker-Avance II 400 (400 MHz), using DMSO-d₆ solvent and TMS as an internal standard.

2.2. SYNTHESIS PROCESS OF EPOXIDES (I-VI). Method (A): [27, 29]

A hot ethanolic solution of (0.01 mole) of proper chalcone derivative was added to the mixture of (1 gm/10 ml) sodium carbonate and 30% hydrogen peroxide (1 ml). Then, the mixture was allowed to stand at room temperature for 24 h. The solid was

removed by filtration, washed with water to be neutralized, dried, and finally crystallized from aqueous ethanol to give oxiranes (I-VI). Table (1) presents the methods, percentage yields, and physical and spectral data.

2.3. PREPARATION OF DEEP EUTECTIC SOLVENTS (RELIN): [30]

A glass rod was used to mix choline chloride (0.1 mole) and urea (0.2 mole) in a test tube by heating at 100-120 °C until a clear solution began to form. Then, the product was cooled and used without any purification. The freezing point of the product was 12 °C.

2.4. ENANTIOSELECTIVE EPOXIDATION USING (RELIN) CATALYST, METHOD (B): [31]

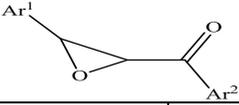
In this step, 30% hydrogen peroxide (1 ml) was added to a solution of proper chalcones derivatives (0.1 mole) and sodium carbonate in (reline). The resulting mixture was stirred at room temperature for 4 h and then 5 ml of water was added to the solid, which was formed in the workup stage as in method (A). Table (1) reports the methods, percentage yields, and melting points and Table (1) lists the I.R. spectral data.

2.5. ENANTIOSELECTIVE EPOXIDATION USING Au NANOPARTICLES SUPPORTED ON TITANIUM OXIDE (AU-TIO₂), METHOD (C):

A hot ethanolic solution of (0.01 mole) of proper chalcone derivatives was added to a mixture of (1 gm/10 ml) sodium carbonate, 30% hydrogen peroxide (1 ml), and Au NPs supported on titanium oxide (0.1 gm). Then, the mixture was stirred at 80 °C for 2 h.

After that, the product mixture was cooled, and the solid was removed by filtration, and workup as in method (A). Table (1) presents the percentage yields.

Table (1): Methods, percentage yields, and melting points of oxiranes (I-VI).

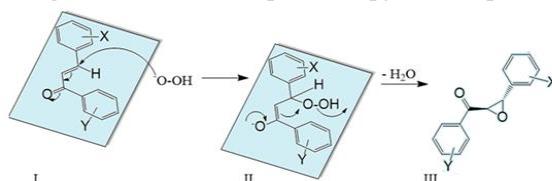


Comp. no.	Chemical structure		% Yields			m.p. °C
	Ar ¹	Ar ²	A	B	C	
I	4-NO ₂ C ₆ H ₅ -	3-ClC ₆ H ₄ -	85	90	90	(102-104)
II	2-NO ₂ ,4MeO-C ₆ H ₃ -	3-ClC ₆ H ₄ -	85	90	95	(210-212)
III	2,4-DiMeOC ₆ H ₃ -	4-NO ₂ C ₆ H ₄ -	82	78	95	(245-247)
IV	3-MeC ₆ H ₄ -	3-NO ₂ C ₆ H ₄ -	82	87	95	(123-125)
V	3-MeC ₆ H ₄ -	3-Pyridinyl-	85	87	95	(221-222)
VI	C ₆ H ₅ -	C ₆ H ₅ -	85	90	92	(87-90)

Table (2): I.R. spectral data of oxiranes (I-VI).

Comp. no.	CH aromatic	CH Aliphatic	C=O	Sym. & assym. NO ₂	C-O-C Cyclic	Others
I	3072	2920	1687	1523, 1347	1284, 1090	732 C-Cl
II	3003	2971, 2837	1679	1571, 1410	1259, 1158	1158, 1103 C-O-CH ₃ , 767 C-Cl
III	3098	2971, 2837	1672	1521, 1350	1259, 1103	1158, 1010 C-O-CH ₃
IV	3050	2970, 2885	1686	1525, 1350	1254, 1077	--
V	3060	2950, 2850	1686	1523, 1354	1254, 1106	--
VI	3060	2955, 2905	1686	--	1254, 1077	--

Show Figure (III & IV) IR spectroscopy for compounds (5 & 6)



3. RESULTS AND DISCUSSIONS

Hydrogen peroxide (H₂O₂), which was the only peroxidizing agent in this work, was reactive oxygen species (ROS) and converted to hydroperoxide -OOH in an alkaline medium, which acts as a nucleophile ready for attacking the electron-deficient chalcone substrates via Michael-type mechanism [32]



It should be noted that these mildly basic conditions (NaHCO₃) were used as the activator because hydrogen peroxide itself was a slow oxidant due to the poor leaving tendency of the hydroxide or lakeside ion and thus their uses without an activator or catalyst was very limited, because bicarbonate-activated peroxide (BAP) system (the active oxidant formed from hydrogen peroxide and carbonate ion) was a shortly living peroxy monocarbonate ion [33] and needed catalysts to increase the yields and decrease the reaction time.

According to Scheme (1), the Michael addition mechanism of nucleophilic HOO⁻ attacks the electron-deficient chalcone substrate.

Scheme (1). The nucleophilic HOO⁻ attacks chalcone at the electron-deficient beta-carbon substrate (I) via Michael addition mechanism. Note that oxirane for (II) is trans-configuration.

All these oxirane ketones were trans-configuration [29] because trans isomers were more likely to form than the cis isomer due to its more stability that may be caused by later isomer having both function groups on the same side of a double bond that can produce steric hindrance [34].

These results can be verified by IR spectra, which show frequency of C-O str. (1254-1284 cm⁻¹) specific for trans-epoxides. Moreover, disappearance

of the aliphatic double bond frequency and relative increase of the carbonyl frequency to 1669-1689 indicated the absence of conjugation (see Table (1)).

The ¹HNMR (CDCl₃) spectra of these trans-epoxy ketones (I-VI) showed a characteristic signal (2.25-2.49δ) for protons at carbon atom number 2 of the oxirane ring and signal (2.55-3.64 δ) for protons at carbon atom number 3 of the oxirane ring. This increased values and a significant downfield about 0.30-1.5 δ was due to the deshielding of the carbonyl anisotropic effect. All aromatic protons also showed the characteristic signals (6.96-8.87 δ) and the aromatic rings protons were shifted downfield.

According to the analyses, the ten protons in the two benzene rings of unsubstituted oxirane number (VI) show figure (II) were magnetically and chemically equivalent and appeared multiplet at (6.69-8.10 δ). The farther downfield of pyridinyl protons of compound (V) show figure (I) in comparison to phenyl, which appeared down to (8.87δ) was due to the 2- and 4-protons resulting from the lower electron density due to the inductive effect of electronegative nitrogen atom as shown by the resonance structures (Scheme (2)).

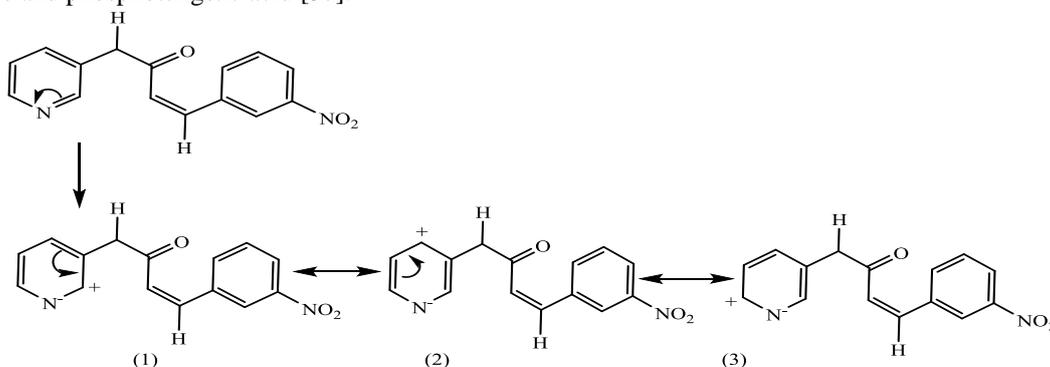
In addition to the monosubstituted benzene, this contained an electron-withdrawing group -NO₂ to make the adjacent protons shift slightly downfield of the other aromatics [35].

The methoxy protons of compounds (II and III) showed the characteristic signals (4.06-4.54 δ) for respectively three and six protons of methoxy group, all these ¹HNMR spectra were in agreement to the published data [36].

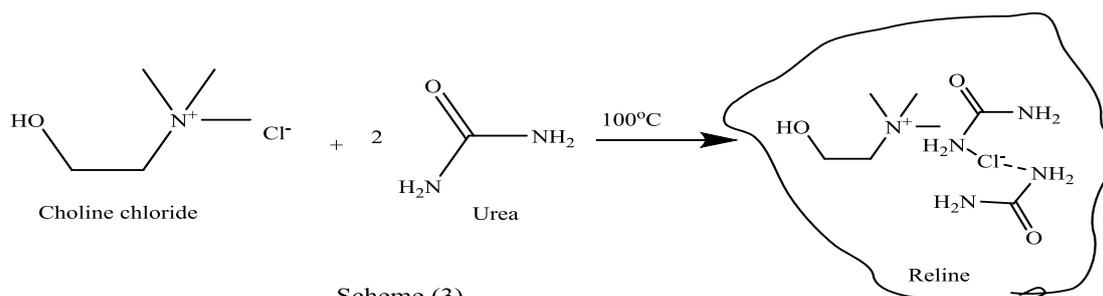
Therefore, this reaction could be catalyzed by a variety of agents such as ionic solvents (especially DESs) [31] and heavy metals or under the presence of ionizing radiation.

Researchers also used DESs such as reline comprising 1:2 choline chloride/urea with hydrogen peroxide and phosphotungstic acid [37].

The DES (reline) was produced by heating choline chloride (2-hydroxyethyltrimethylammonium chloride) with urea to about 100 °C or until the formation of a clear liquid product [38,39] (Scheme (3)).

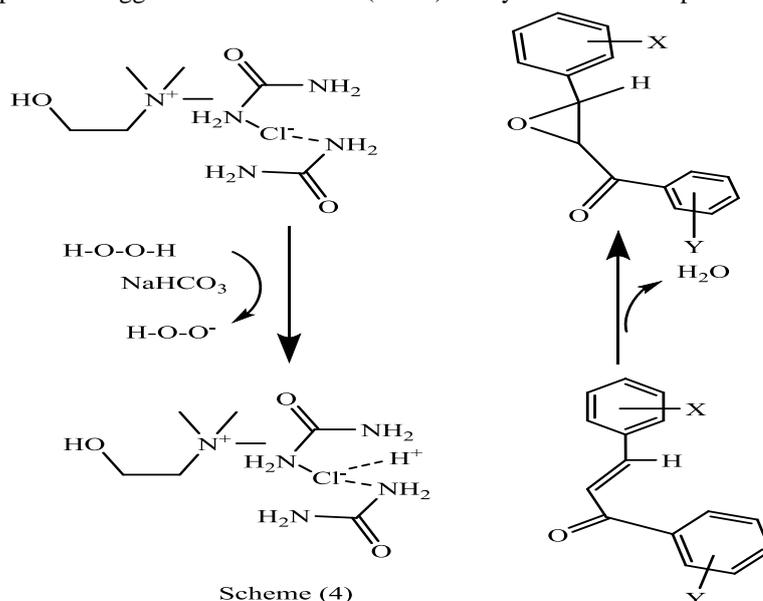


Scheme (2)
Compound (V) pyridinyl resonance structures (1-3):
only positions 2- (in both sides) and 4-positions result from the lower electron density because of inductive effect of electronegative nitrogen atom



Scheme (3)
Formation of deep eutectic solvent (Reline)

Scheme (4) depicts the suggested mechanism of (reline) catalyst of chalcones peroxidation.



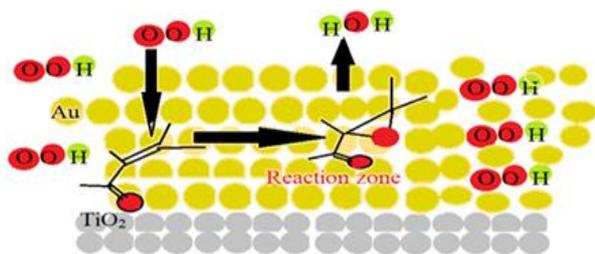
Scheme (4)
The suggested mechanism of Reline catalyst of chalcones peroxidation

Advantages of the adduct form between hydrogen peroxide with urea (percarbamide), which was more active than hydrogen peroxide itself [40], encouraged the use of reline, which is one of the deep DESs, as a solvent and catalyst consisting of choline chloride and urea to form the adduct with hydrogen peroxide. Acceptable results was observed by this method (B), which gave 90% peroxidation results in a short time (4 h).

The most recently catalysts used for peroxidation of the organic substrates were transition metal salts such as titanium, vanadium, nickel, platinum, and palladium. The catalytic effects were due to their electronic configurations, which helped them to exchange their partially filled d-orbitals electrons with the reacting species [30].

Other studies have extensively investigated the best prominent catalysts and good capability of TiO₂ nanoparticles to promote the formation of reactive oxygen species (ROS), which in combination with the heterogenous Au NPs (of sizes <5 nm) for room-temperature oxidation reactions may help oxygen dissociation on their nano-surface area. It could fully reduce the metallic Au NPs on a reducible support (TiO₂) form activated Au-oxygen complexes, which was an active component in peroxidation [23,25,37].

Scheme (5) schematically represents the peroxidation pathway for chalcones.



Scheme (5). Schema of the peroxidation pathway for chalcones.

Au catalyst NPs supported on titanium oxide (Au–TiO₂) was the most extensive form of heterogeneous catalysts. The major role of the support was firstly recognized to be the stabilization of the active component or increase of the metal diffusion and surface area. However, it was recognized that physicochemical interactions between the Au and titanium oxide can also influence catalytic presentation through the so-called carrier effects. For this reason, the Au- titanium oxide support interface has a long history of controlling catalyst structure and reactivity [31].

A definite form of these supported effects came to importance in the late 1970s when an uncommon interaction was detected between platinum metal and TiO₂, which distinctly blocked adsorption of the small molecules (such as CO and H₂) following the

high-temperature reduction treatments. This was called strong metal–support interaction and such effects have been the topic of intensive studies. Although suppressed H₂ and CO adsorption were initially recognized to be the electronic perturbation of the atoms by an interaction with Ti cations, an agreement has now been reached on the fact that this effect originates from metal encapsulation by a titanium overlayer. Hence, catalytic performance has been modified in diverse reactions and has been exploited to improve the catalyst constancy, identify the reaction mechanisms, and enhance activity. Thus, research into the catalyst systems that can manifest these effects has undergone rapid expansion. However, to date, classical effects has never been reported for Au/TiO₂ catalysts, and there was only one such example showing indirect effects for any group metal based on x-ray photoelectron spectroscopy and ion-scattering spectroscopy measurements of Ag/TiO₂ [26].

As mentioned earlier, oxide-supported Au catalysts have attracted the attention of the experts in the field to the epoxidation of chalcones and chalcones analogs, so that Au/TiO₂ has been probably the most extensively investigated analogue [41]. Supported Au NPs have revealed ability for some peroxidation procedures because of their unique catalytic performance; however, useful uses have been hindered by poor on-stream stability. Initiation of the strong metal–support interaction between Au and titania would offer a route to stabilize Au NPs, but surface science studies of the model catalysts have found no evidence for this phenomenon. In addition, electron transfer between Au and TiO₂ upon reduction was accompanied by increased CO adsorption, contrary to the classical strong metal–support interaction [42]. Finally, Au NPs were not believed to undergo the strong metal–support interaction with titanium.

As illustrated by the above discussion, the strong Au-TiO₂ support interaction (SMSI) gave a procedure to control the structural properties of Au and, hence, their reactivity and stability. Conventionally, the supported Au could not manifest a classical SMSI, which was characterized by reversible metal encapsulation by the support upon oxidation –reduction treatments. Furthermore, a classical SMSI for Au/TiO₂ was evidenced by suppression of chalcones adsorption, electron transfer from TiO₂ to Au NPs, and Au encapsulation by a TiO_x overlayer following the oxidation [42,43].

Results showed the increased speed of peroxidation process by using the catalysts of Au NPs supported on the titanium dioxide NPs, which gave the best percentage yield results of more than 90-95% and time of 2 h and 5 min, about half of that of (reline) mixture, which could be due to the high activation of

hydrogen peroxide by Au and titanium oxide NPs and low viscosity of the reaction mixture.

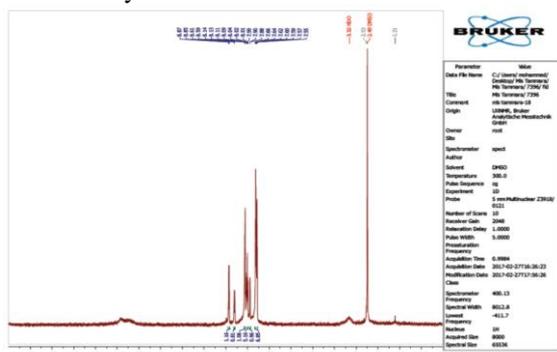


Figure (I)

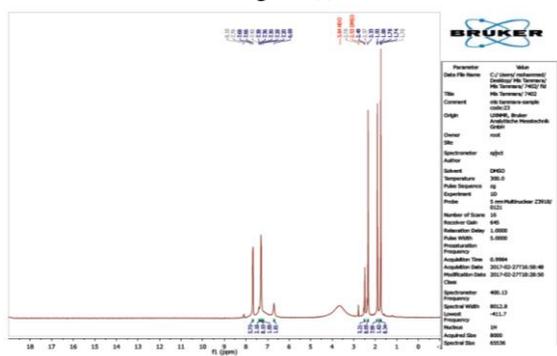


Figure (II)

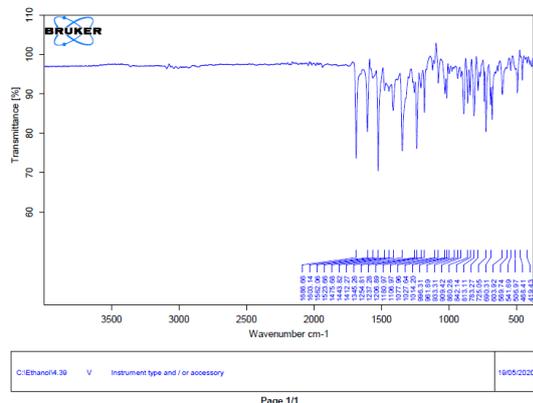


Figure (III)

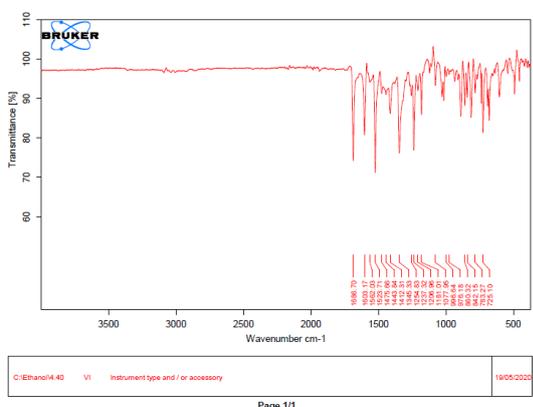


Figure (IV)

4. CONCLUSIONS

It was concluded that chalcones epoxidations would convince chemists that the use of DESs (reline) and the Au-supported on titanium oxide NPs for catalysts of these reactions are techniques of great importance in various branches of oxidation. In fact, hydrogen peroxide itself is an interesting environment-friendly raw material due to its high reactivity and low toxic effects and hence can be used even without catalyst.

As mentioned in previous studies, reline has a strong and complex hydrogen-bonding network as a catalyst between the hydrogen bond donor molecule urea and the chloride anion.

This set of interfaces caused the formation of a radially coated sandwich structure where choline and urea worked to bond with chloride and maximized their own weaker interaction.

This sandwich structure could also be catalysed by peroxidation and visualized as a charge delocalized. Moreover, Au NPs supported on the titanium dioxide NPs gave the best percentage yield results about half of that of (reline) mixture, which may be due to the high activation of hydrogen peroxide by Au and titanium oxide NPs as well as low viscosity of the reaction mixture.

5. ACKNOWLEDGEMENT

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