STUDIES TOWARDS GREEN OXIDATION OF ALCOHOLS WITH VISIBLE LIGHT

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ABSTRACT

STUDIES TOWARDS GREEN OXIDATION OF ALCOHOLS WITH VISIBLE LIGHT

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Conversion of alcohols to the corresponding carbonyl compounds is one of the key reactions in organic chemistry. For this, numerous methods have been developed. However, most of these methods produce environmentally hazardous waste. With this in mind, an environmentally benign method was attempted to be developed. The idea was borrowed from Dye Sensitized Solar Cells (DSSC); electron relay mechanism in DSSC to be replaced with oxidation of alcohols. First, TiO_2 as metal oxide and O_2 as electron acceptor were used. The benzyl alcohol was added to the dye and TEMPO included TiO_2/O_2 system to yield benzaldehyde, but the method failed in our hands. However, when ZnO as metal oxide and Ag^+ as electron acceptor were used, the reaction converted alcohols to the corresponding aldehydes. Our contribution in this thesis is reducing the diffusion control to increase the rate of reaction. To this end, TEMPO incorporated dyes were developed and synthesized.

Keywords: Alcohol, aldehyde, oxidation, oxidant, light, metal oxide

ÖZ

ÇEVRECİ BİR YÖNTEMLE GÖRÜNÜR IŞIKTA ALKOLLERİN YÜKSELTGENMESİ

AKKAŞ, Kıvanç

Yüksek Lisans, Kimya Bölümü

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Alkollerin karbonillere dönüştürülmesi organik kimyanın temel tepkimelerinden biridir. Bu bağlamda birçok metot geliştirilmiştir ve geliştirilmektedir. Fakat bu metotların çoğu çevreye zarar veren atıklar üretmektedir. Bu nedenle, bu çalışmada çevreye zarar vermeyen yeni bir metot geliştirilmek istendi. Boya ile uyarılan güneş pillerinden esinlenerek düşünülen bu metotta, bu güneş pillerinin çalışma prensibindeki elektron aktarım mekanizmasını alkollerin yükseltgenme reaksiyonları için uygulanmak istenildi. Öncelikle, metal oksit olarak TiO_2 ve elektron alıcı olarak O_2 kullanıldı. Boya ve TEMPO içeren TiO_2/O_2 sistemine yükseltgemek için benzil alkol eklendi ancak bu metot alkol yükseltgemesinde başarılı olamadı. Fakat ZnO ve Ag^+ kullanıldığında, reaksiyonun alkolleri aldehite yükseltgediği görüldü. Bu tezdeki alkol oksidasyonuna katkımız difüzyon kontrolünü azaltarak reaksiyon hızını arttırmış olmamızdır. Bu amaçla TEMPO ile birleştirilmiş boyalar geliştirilmiş ve sentezlenmiştir.

Anahtar Kelimeler: Alkol, aldehit, yükseltgenme, yükseltgen, metal oksit

To My Family

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CHAPTER 1

INTRODUCTION

1.1 OXIDATION AND HISTORY OF OXIDATION

Oxidation terms appeared with the discovery of oxygen. Oxygen was discovered by three people, Scheele, Priestley and Lavoisier, but Priestley is mostly credited as the discoverer of the oxygen.[1] However, Lavoisier made great contribution to the discovery and description of the oxygen.

Lavoisier performed experiments on oxidation reactions and mentioned about these reactions in his book.[2] He did not mention as oxidation reaction but these reactions were oxidation reactions. In his reactions, he was heating the metal in a closed vessel. He observed no change in total mass but remains mass was increasing (that means formation of metal oxide). So, he performed oxidation reaction actually.

Oxidation has been defined as removal of hydrogen(s) or addition of oxygen(s). However, removal of electron(s) is most convenient description of the oxidation nowadays.

1.2 OXIDATION OF ALCOHOLS

1.2.1 REAGENTS AND CATALYST

In the literature, there are many types of metal based reagents and catalysts used for oxidizing alcohols to corresponding aldehydes, ketones or carboxylic acids. The major ones are listed and explained below.

1.2.1.1 METAL BASED OXIDANTS

1.2.1.1.1 CHROMIUM BASED OXIDANTS

One of the most used metals in oxidation of alcohols is chromium. Compounds containing chromium at its sixth oxidation state [Cr(VI)] have been facilitated to oxidize alcohols (Eqn. 1).[3]

$$3\ RCH_2OH + K_2Cr_2O_7 + 4\ H_2SO_4 \rightarrow 3\ RCHO + Cr_2(SO_4)_3 + K_2SO_4 + 7H_2O$$ **Eqn. 1**

Sodium or potassium dichromate in dilute sulphuric acid was explored to oxidize alcohols at relatively high temperatures. With this method, oxidation of alcohols was attained. This oxidation takes an alcohol to an aldehyde which is then further oxidized to a carboxylic acid. If aldehydes are the desired compounds, aldehydes were separated by steam distillation from the reaction medium.[3]

Also dichromates were used as phase-transfer reagents to oxidize alcohols.[3] In this system, tetraalkylammonium dichromate, soluble in the organic solvents, was obtained from alkaline dichromate.

The other known dichromates were tetrabutylammonium dichromate and pyridinium dichromate (PDC), $(C_5H_5NH)_2Cr_2O_7$.[3] The former was obtained, *in situ*, from sodium dichromate and tetrabutylammonium bisulfate in 3M sulfuric acid and dichloromethane and it was used at room temperature. PDC was obtained as a precipitate from chromium trioxide in pyridine. The oxidations with pyridinium dichromate result in different products depending on the solvent. While the reaction was performed in the dicholoromethane, product was an aldehyde. On the other hand, when dimethylformamide was used as solvent, carboxylic acid was obtained.

3- and 4-carboxypyridinium dichromate and silver dichromate were also used to oxidize benzylic alcohols to aldehydes.[3]

Chromic acid was employed as substitute of dichromates to oxidize alcohols.[3] Chromic acid can be produced by dissolution of chromium trioxide in sulfuric acid or acetic acid. It can be also obtained by dissolving of potassium dichromate, sodium dichromate, potassium chromate or sodium chromate in sulfuric acid **(Scheme 1)**.

*Aldehydes may react with water and form hydrate. It will overoxidized to carboxylic acids.

Scheme 1 Mechanism of chromium based oxidation

To oxidize alcohols, Jones reagent was developed by Jones' group.[3] It was a derivative of chromic acid. Jones reagent is a solution of chromium trioxide in dilute sulphuric acid in acetone. Also diethyl ether and hexamethylphosphoric triamide (HMPA) were used as solvent.[4] This oxidation occurs at room temperature and it can be applied to both saturated and unsaturated alcohols. This method oxidizes primary and secondary alcohols to corresponding aldehydes or ketones. With changing conditions, aldehydes may be overoxidized to carboxylic acids **(Scheme 2)**.

Scheme 2 Examples for Jones oxidation

Collins reagent, another well-known reagent to oxidize alcohols; was improvement over Jones reagent.[3] It is a complex of chromium trioxide and pyridine (CrO_3.2Py). It

works best in dichloromethane (DCM). Its solubility is very good in DCM, yet easily converted into dipyridinium dichromate $Py_2Cr_2O_7$, insoluble in DCM, very effective at room temperature. However, it has some disadvantages. Its most important drawback is that 1:6 ratio of substrate to reagent is needed. Other drawback is that saturated alcohols are oxidized in low yield. Collins reagent is very appropriate for acid sensitive alcohols due to basic properties of the reagent (**Scheme 3**).

Scheme 3 Using Collins reagent in alcohol oxidation

Pyridinium chlorochromate (PCC) is another chromium-based reagent developed for oxidation of alcohol.[3] In early days of PCC, it was seen as advanced version of Collins reagent. Important advantage over Collins reagent is that almost stoichiometric amounts of PCC were required to oxidize an alcohol (**Scheme 4**).

Scheme 4 Alcohol oxidation with PCC

PCC is slightly acidic, thus acid sensitive substrates cannot be oxidized with PCC. Although stoichiometric amounts of PCC is required, Hunsen et al. reported that they used catalytlic amounts of PCC to convert alcohols into aldehydes or ketones, where periodic acid was used as a secondary oxidant (**Scheme 5**).[7]

Scheme 5 Using of PCC in catalytic amounts

Poly(vinylpyridinium)chlorochromate, tetrabutylammoniumchlorochromate, chromyl chloride, di-tert-butyl chromate were also used as oxidizing agents.[3]

Oxidation of alcohols with Jones reagent is a very useful method but overoxidation primary alcohols to carboxylic acid is a major concern. Therefore, Jones reagent is used when carboxylic acids are in need. Moreover, it does not require anhydrous conditions. Meanwhile, Collins reagent needs anhydrous conditions and high reagent loading. In addition to this, its selectivity is lower than PDC and PCC reagents. Therefore, PCC based reagent have been commonly employed to get aldehydes from alcohols.

1.2.1.1.2 COPPER BASED OXIDANTS

Copper is a very versatile metal to oxidize alcohols catalytically due to its reduction potential, which is enough to oxidize most of the alcohols. Therefore, nature employes copper as an oxidizing agent in enzymes.[8]

The first Cu-catalyzed aerobic alcohol oxidation was reported by Sammelhack et al.[9] They used cuprous chloride in combination with TEMPO in DMF. In this system, Cu^+ oxidizes TEMPO to activated TEMPO which, in turn, oxidizes an alcohol to an aldehyde. This could oxidize allylic and benzylic primary alcohols.

Then, Marko's group worked on Cu-catalyst development to oxidize alcohols. They developed a system that constitute 5 mol% CuCl, 5 mol% phenantroline, and 5 mol% di-tertbutylazodicarboxylate (DBAD) to oxidize alcohols.[10] However, the system needed to use 2 equivalent of base and it did not give good results with primary alcohols. Moreover, catalyst was thought as heterogenous and adsorbed on the base.

Switching solvent from toluene to fluorobenzene caused a decrease in the amount of base to catalytic level.[11] However; a system was needed to be developed due to the insufficiency for the primary alcohols. Catalytic usage of N-methylimidazole (NMI) increased the activity of the procedure to oxidize primary alcohols (**Scheme 6**).[12]

Scheme 6 Marko's alcohol oxidation catalyzed by copper

In addition to Marko; Sheldon, Sekar, Stahl, Ansari and Gree, and Knochel have made contribution to such Cu-catalyzed alcohol oxidations.[8a]

Sheldon et al. used $CuBr_2$ and TEMPO with 2,2'-bipyridine (bpy) as a ligand to oxidize primary alcohols (**Scheme 7**).[13] This system provides no overoxidation and it does not require pure oxygen. It works in air and gives very good conversion.

Scheme 7 Sheldon's alcohol oxidation catalyzed by copper

Stahl's group improved Sheldon's Cu-catalyst.[14] They designed a new (bpy)Cu^I/TEMPO system in the presence of NMI. This system provides selectivity for primary alcohols with no reaction with other functional groups, such as alkynes, heterocycles, ethers and thioethers. Moreover, it could oxidize diols and secondary alcohols as well (**Scheme 8**).

Scheme 8 Stahl's procedure for alcohol oxidation

Sekar et al. reported that they developed a catalyst for kinetic resolution of secondary alcohols.[15] This catalyst can oxidize one enantiomer selectively, while the other one was not oxidized (**Scheme 9**).

Scheme 9 Sekar's Cu-catalyzed enantioselective alcohol oxidation

Ansari and Gree, in 2002, developed a new system to oxidize secondary alcohols in an ionic liquid as solvent.[16] This system provides an easy isolation of product. The product could be separated by simple extraction. Therefore, ionic liquid could be recycled but catalyst could not be (**Scheme 10**).

Scheme 10 Alcohol oxidation catalyzed by Cu in ionic solvent

Knochel reported a new Cu(I)-catalyzed aerobic oxidation of alcohols in the presence of TEMPO.[17] They used fluorous biphasic and bipyridine ligand. A wide variety of alcohols were converted into the carbonyl compounds. In this oxidation, the –OH moiety on axial position is oxidized more rapidly than the equatorial one (**Scheme 11**).

Scheme 11 Knochel's procedure for alcohol oxidation catalyzed by copper

1.2.1.1.3 COBALT BASED OXIDANTS

The first report of the oxidation of alcohols with Co-based catalyst was published by Tovrog's group.[18] They used Co-nitro complexes for alcohol oxidations in the presence of Lewis acid. After this publication, several procedures have been developed with some handicaps such as requirement of high temperatures or high loadings of catalyst.[8a]

Ishii reported that N-hydroxyphtalimide(NHPI)/Co(III) complexes oxidize primary and secondary alcohols to carboxylic acid and ketones respectively.[19] These Co-complexes oxidize a wide variety of alcohols. However, oxidation of vicinal diols (one being primary) gave the carboxylic acids with one carbon less. It was also reported that adding small amount of benzoic acid accelerated the reaction (**Scheme 12**).

Scheme 12 Ishii's Co-catalyzed alcohol oxidation

Also Iqbal and Sain developed very similar Co(III)-Schiff-base system simultaneously.[20,21] Both procedures were developed for oxidation to secondary aliphatic and benzylic alcohols. The main difference of these two reactions is the using iso-butanal, provide selective oxidation of benzyl alcohol to benzaldehyde in the presence of olefins and alkenes. Sain and co-workers reported that secondary α-hydroxyketones could also be oxidized to diketones (**Figure 1)**.

Iqbal's Ligand: R_1=CH_2OH, R_2=CO_2Me
Sain's Ligand: R_1=Ph, R_2=Me

Iqbal's method:	Sain's method:
2 equivalent iso-butenal 5 mol% $Co(L_1)_2$ 3A MS, MeCN, O_2, rt	5 mol% $Co(L_2)_2$ 3A MS, MeCN, O_2, rt

Figure 1 Procedures developed by Iqbal and Sain

On the other hand, three component catalytic system was developed by Jing et al.[22] $Co(NO_3)_2$/dimethylglyoxime (DH_2)/TEMPO (1:4:1 molar ratio) system was very successful to oxidize both primary and secondary alcohols, however, it required quite ungentle conditions such as 0.4 MPa O_2 atmosphere at 70°C.

1.2.1.1.4 OSMIUM BASED OXIDANTS

Osmium based catalysts are very strong catalyst to dihydroxylate olefins and to convert alcohols into corresponding aldehydes, ketones or carboxylic acids.[8a] With low catalyst loading, it gives very good yields for alcohol oxidations.

Beller et al. reported a procedure for alcohol oxidation with Os-catalyst.[8a] They used small amount of catalyst, and observed very good conversion and yields from both primary and secondary aromatic alcohols. Its turnover number (TON) can reach 16600 under optimized conditions (**Scheme 13**).

Scheme 13 Beller's Osmium catalyst

Osmium has been also used with other metals in a combination, such as Os-Cu, Os-Cr. In these, osmium was used in small ratio as compared to other metals. Osmium is the active metal while other metals re-oxidize the reduced osmium.

Although osmium is a powerful oxidizing agent, some aliphatic alcohols could not be oxidized with osmium containing reagents.

Ozkar group reported that heterogeneous Os catalytic system work for alcohol oxidation.[23] They used Os(0)-Y(zeolite-Y) at 80 ^{o}C under 1 atm O_2 pressure or air to oxidize alcohols. This system gives good yields for aliphatic alcohols also.

1.2.1.1.5 RUTHENIUM BASED OXIDANTS

Ruthenium oxidation chemistry is similar to that of Osmium.[24] Ruthenium and osmium are in the same group, and they have similar properties. Thus RuO_4 acts like OsO_4, very good oxidation reagent. Moreover, RuO_4 has more powerful oxidation property than OsO_4. RuO_4 is cheaper with less toxicity than OsO_4.

Due to the strong oxidizing properties, RuO_4 has been used in different organic oxidation reactions. In appropriate conditions, alcohols can be oxidized by RuO_4. Thus solvent must be chosen carefully due to the high reactivity of RuO_4. Highly halogenated organic solvents must be used such as CCl_4, $CHCl_3$.

Oxidation reaction with RuO_4 occurs at room temperature in couple of minutes. With the oxidation product in hand, RuO_4 is needed to RuO_2 which precipitate.

With using RuO_4, secondary alcohols can be converted into ketones while primary ones are oxidized to carboxylic acids. RuO_4 is convenient for highly hindered alcohols, especially secondary alcohols.

Although RuO_4 is very strong oxidizing agent, it has been used rarely. Other ruthenium compounds, in which ruthenium has lower oxidation state than +8, have been used to oxidize alcohols. This compounds act as milder oxidant such as $RuCl_3.H_2O$ and $Ru(PPh_3)_3Cl_2$ (**Scheme 14**).

Scheme 14 An example for alcohol oxidation with Ru-catalyst

Ruthenium oxidation states, between +2 to +8, provide large variety of oxidation. To increase activity of ruthenium compounds, they are used in ionic liquid.[8a] In the literature, there are many examples of alcohol oxidation with Ru-compounds, some of the relevant ones are discussed below.

Bäckvall et al. reported one of the fastest Ru-catalyst systems to oxidize alcohols.[25] They used benzoquinone and a cobalt-Schiff's base complexes. However it needs high loading of 2,6-dimethyl-1,4-benzoquinone. In order to overcome this obstacle, scientists used a new reagents.[26] For example, Shvo's Ru version catalyst was employed.[27] This method decreased the amount of benzoquinone and gave excellent conversion of alcohols to aldehydes (**Scheme 15**).

Scheme 15 Bäckvall's Ru-catalyzed aerobic oxidation of alcohol

Ishii and co-workers improved Bäckvall's method for primary alcohols.[28] They showed benzoquinone could be regenerated in $PhCF_3$ used as a solvent, even if there is no cobalt co-catalyst in the system. Moreover, chemoselective oxidation of primary alcohols was achieved in the presence of secondary alcohols (**Scheme 16**).

Scheme 16 Ishii's Ru/hydroquinone system

Sheldon and co-workers reported a very efficient system.[29] They could oxidize non-activated primary and secondary alcohols with using Ruthenium/TEMPO catalyst. TEMPO prevents overoxidation of primary alcohols to carboxylic acids. However the system has some difficulties. The system needs high pressure of O_2. Moreover,

some heteroatom containing (N, O, S) alcohols cannot be oxidized by this procedure. Its reason is probably their coordination with Ruthenium (**Scheme 17**).

Scheme 17 Sheldon's Ru-catalyzed alcohol oxidation

Marko and Ley independently reported that tetrapropylammonium perruthanate (TPAP), a high valent perruthenate catalyst, is able to oxidize alcohols aerobically.[30] However these procedures had handicaps. Marko's system needed high temperature while Ley's one needed high catalys loading in chlorinated solvents. Both systems were not sufficient to oxidize aliphatic alcohols (**Scheme 18**).

Scheme 18 Methods for alcohol oxidation developed by Marko and Ley

Katsuki et al. worked on Ru-salen based catalayst.[31] Their catalyst was very effective for oxidizing primary aliphatic alcohols photoinducedly and chemoselectively in the presence of another alcohols with high enantioselectivity. Also, Ru-salen catalyst, not need further irradiation; was developed by Katsuki et al (**Scheme 19**).[32]

Scheme 19 Alcohol oxidation catalyzed by Katsuki's Ru-salen catalyst

Ruthenium-based catalysts are very effective catalyst but further studies are needed to optimize conditions.

1.2.1.1.6 MANGANESE BASED OXIDANTS

Manganese dioxide has been utilized to transform alcohols into corresponding aldehydes, ketones, or carboxylic acids.[3] The oxidant is used in different solvents at room temperature generally. The yields varied with respect to substrates, substrate/oxidant ratio, solvent, and reaction time **(Scheme 20)**.

Scheme 20 Different product of alcohol oxidation with MnO_2

Alcohols have been also oxidized with using manganates and permanganates that are barium manganates[36] ($BaMnO_4$), potassium permanganate[37] ($KMnO_4$), sodium permanganate[38] ($NaMnO_4$), copper permanganate octahydrate[39] [$Cu(MnO_4)_2.8H_2O$], tetrabutylammonium permanganate.[40] Manganates or permanganates were not used to oxidize primary alcohols to aldehydes generally because the oxidation does not stop at aldehyde stage and aldehydes are oxidized to carboxylic acids by permanganate. However, there are some procedures for oxidation of primary alcohols to aldehydes by permanganates in the literature.[37]

Feringa et al. reported that a novel method to oxidize alcohols with using dinuclear Mn-complex as a catalyst.[41] They developed the catalyst in **Scheme 21** that converted benzylic alcohols into aldehydes or carboxylic acids selectively depend on amount of oxidant (hydrogen peroxide or tert-butyl hydroperoxide). This provides high selectivity, high turnover number in short period.

Scheme 21 Alcohol oxidations with Feringa's oxo-bridged Mn-catalyst

1.2.1.1.7 PALLADIUM BASED OXIDANTS

Palladium is one of the most useful reagents to convert alcohols into corresponding aldehydes, ketones, or carboxylic acids. Although many researchers have been interested in Pd-based oxidations, many unknowns about using Pd as an oxidizing agent.[8b] Eventhough many mechanisms were suggested for its working principle, one of them is widely accepted nowadays.[8a] According to the mechanism; alcohol binds to the Pd^{II}-catalyst and it gives intermediate B which forms Pd^{II}-alkoxide intermediate C with deprotonation by an exogenous base. Associated with β-hydride elimination, C forms Pd^{II}-hydride intermediate D and alcohols are oxidized to

corresponding aldehydes, ketones, and so on. Catalytic cycle completes with reductive elimination of Pd^{II}-hyride intermediates D and reoxidation of Pd(0) species E to active Pd(II)-compounds A **(Scheme 22)**.

Scheme 22 Mechanism of Pd-catalyzed alcohol oxidation

The first alcohol oxidation with Pd-catalyst was reported by Schwartz and Blackburn.[42] They used $Pd(OAc)_2$ and NaOAc mixture but the procedure needed some development. Two decades later, other Pd-catalyst procedures were reported by Larock, Uemura, and Sheldon for oxidations.[43-45]

Larock et al. used $Pd(OAc)_2$ and $NaHCO_3$ as a base in DMSO.[43] This system gave good results for oxidation of primary and secondary allylic and benzylic alcohols. Seddon et al. improved this by using imidazole-type ionic liquid as solvent to replace DMSO increasing Pd-catalyst activity but conversion was very low.[44]

Uemura's group developed a new system to oxidize alcohols.[45] With using 5 mol% $Pd(OAc)_2$, pyridine, molecular sieves in toluene, they converted aliphatic, allylic, and benzylic alcohols into corresponding aldehydes or ketones.

Sheldon et al. developed a new Pd-complex,[46] which did not need organic solvent to oxidize alcohols except solid alcohols. Oxidized product could be obtained by simple extraction. Their oxidation method works for primary alcohols. Primary alcohols are oxidized to carboxylic acids without his often employed TEMPO **(Scheme 23)**.

Scheme 23 Sheldon's Pd-catalyzed alcohol oxidation without solvent

In Pd-based oxidation procedures, Pd black formation is a problem. To prevent Pd black (Pd metal) formation, substituted pyridines were used as ligands by Tsuji.[47] This works under air atmosphere and with low catalyst loading. Meanwhile, Sigman et al. developed new $Pd(OAc)_2$/TEA system to oxidize alcohols effectively.[48]

Pd(II) catalysts could also be used for oxidative kinetic resolution of racemic secondary alcohols, oxidative desymmetrization of meso-diols (**Scheme 24**).[49]

Scheme 24 Oxidative desymmetrization of meso diols

1.2.1.1.8 IRON BASED OXIDANTS

Iron is the most abundant metal in the earth crust. It has very vital role in living organisms; it provides oxygen and electron transportation and it reduces molecular oxygen.[8a] This property of iron is the simple explanation of oxidation and it was thought to be mimicked for oxidation reactions.

The first Fe-catalyzed alcohol oxidation was reported by Martin and Suarez.[50] They used $Fe(NO_3)_3$ in combination with $FeBr_3$ under aerobic conditions at room temperature. This provided selectivity for the oxidation of secondary and benzylic alcohols. However, primary alcohols could not be oxidized by this method **(Scheme 25)**.

Scheme 25 An example from Martin and Suarez's work

Liang and co-workers developed a novel procedure to oxidize alcohols.[51] They used $Fe(NO_3)_3$ with $NaNO_2$/TEMPO as co-catalyst. This oxidizes the most of the alcohols selectively yet primary aliphatic alcohols are oxidized to aldehydes in modest selectivity with carboxylic acid and esters as by-products. To overcome this problem, 4-substituted TEMPO derivatives as co-catalysts were used.[52] They achieved oxidation of alcohols to aldehydes with high selectivity. They developed a more green method to prevent using non-green solvents such as trifluorotoluene or dichloromethane.[53] They used $Fe(NO_3)_3.9H_2O$ as catalyst and 4-hydroxy-TEMPO as co-catalyst in acetonitrile. This system gave good results for the oxidation of wide variety of alcohols **(Scheme 26)**.

Scheme 26 Liang's optimized Fe-catalyzed alcohol oxidation

Ma's group explored $Fe(NO_3)_3$/TEMPO catalyzed alcohols oxidation system.[54] They used NaCl was used as additive, however its role is not known exactly. This works for alcohols which contains unsaturated C-C bonds, which are untouched at the end of the reaction **(Scheme 27)**.

Scheme 27 Ma's $Fe(NO_3)_3$/TEMPO catalyzed alcohol oxidation system

Zhang and He also reported that a new Fe-based oxidation method for aromatic alcohols.[55] They used bimagnetic imidazolium salt, $NaNO_2$ in water as solvent. Also air can be used instead of oxygen. The catalyst could be recovered by an extraction with ether and it could be re-used at least five times without loss of activity (**Scheme 28**).

[Imim-TEMPO][$FeCl_4$]:

Scheme 28 Zhang and He's bimagnetic catalyst

1.2.1.1.9 GOLD BASED OXIDANTS

Gold, as homogeneous oxidation catalyst, has been used to oxidize alcohols rarely.[8a] Shi and co-workers reported first Au-catalyzed alcohol oxidation.[56] They used 5 mol% AuCl, 6.3 mol% ligand in toluene at high temperature. This gave high conversions for the oxidation of both primary and secondary benzylic or allylic alcohols. On the other hand; primary aliphatic alcohols are oxidized slowly and aldol products occurred as by products **(Scheme 29)**. The optimized procedure, make use of gold(I)-neocuproine in aqueous basic solution under O_2 atmosphere. [57]

Scheme 29 Shi's alcohol oxidation with Au(I)-complex

1.2.1.1.10 VANADIUM BASED OXIDANTS

In the first studies of V-catalyzed alcohol oxidation, α-hydroxycarbonyl compounds[58] and propargylic alcohols[59] were oxidized **(Scheme 30-31)**.

Scheme 30 V-catalyzed aerobic oxidation of α-hydroxycarbonyls

Scheme 31 $VO(acac)_2$-catalyzed oxidation of propargylic alcohols

1 mol% $VOCl_3$ was used in acetonitrile at room temperature to oxidize α-hydroxycarbonyl compounds, while 1 mol% $VO(acac)_2$ was used in acetonitrile at 80 ^oC to oxidize propargylic alcohols **(Scheme 30)**. This procedure was applied to other alcohols such as benzylic, aliphatic unsuccessfully.

Velusamy and Punniyamurphy reported that they use 5 mol% V_2O_5 as the catalyst to oxidize broad range of alcohols.[60] According to the study, 0.5 equivalent K_2CO_3 in toluene was used, and good results were obtained for secondary alcohol oxidation, while primary alcohols gave average yields.

Jiang and Ragauskas used $VO(acac)_2$ in combination with DABCO (1,4-diazobicyclo[2.2.2] octane) to oxidize benzylic and allylic alcohols in ionic liquids.[61] The catalyst can be recovered and used again three times with no significant loss of catalyst activity.

1.2.1.2 ORGANIC OXIDANTS

Although researchers oxidized alcohols in high yields by employing metals, the main concern is that reactant or catalyst, used in these reactions, must be compatible with environment. Thus new oxidizing systems must be with reduced toxicity, decreased waste products. Therefore researchers diverted their attention to organic oxidants to

convert alcohols into corresponding carbonyl compounds. Main organic oxidants, used in oxidation of alcohols, are discussed below.

1.2.1.2.1 HYPERVALENT IODINE COMPOUND

2-iodoxybenzoic acid (IBX), also named as 1-hydroxy-1,2-benziodoxole-3(1H)-one-1-oxide, was synthesized by Hartmann and Meyer in 1883.[62] Its solubility in organic solvents is very low. Thus, IBX has not been used in organic reactions frequently **(Figure 2)**.

2-iodoxybenzoic acid
(IBX)

Dess-Martin Periodinane
(DMP)

Figure 2 2-Iodoxy benzoic acid and Dess-Martin Periodinane

A century later, Dess and Martin synthesized a new hypervalent iodine compound by treating IBX with acetic anhydride, named as Dess-Martin Periodinane (DMP). DMP is soluble in organic solvents. It was used to convert alcohols to the corresponding carbonyl compounds.[63] It has been used to oxidize alcohols before IBX. It is a mild and chemoselective reagent for alcohol oxidation, however IBX is cheaper and more stable than DMP.

After revealing solubility of IBX in DMSO, IBX has been used in organic reactions.[24] First alcohol oxidation with IBX was reported by Frigero and Santagostino.[64] The proposed mechanism of the alcohol oxidation with IBX was shown in **Scheme 32**. They achieved the oxidation of primary and secondary alcohols with a great tolerance to other functional groups. Moreover they could convert 1,2-diols to α-hydroxyketones or 1,2-diketo derivatives with the absence of cleavage of the glycol C-C bond. They also revealed that 1,2-diols are oxidized chemoselectively in the presence of other 2° alcohols.[65]

Scheme 32 Proposed mechanism of IBX oxidation

Corey et al. showed that 1,4-bisprimary or 1,4-primary-secondary diols can be oxidized selectively to γ-lactols.[66] **(Scheme 33)**.

Scheme 33 Corey's alcohol oxidation with IBX

On the other hand, α,β-unsaturated esters can be obtained by oxidation of alcohols with IBX. Maiti and Yadav reported that IBX converts alcohols; benzylic, allylic, propargylic and diols, into esters in the presence of stabilized Wittig ylides **(Scheme 34)**. [67]

Scheme 34 IBX oxidation tolerates Wittig reaction

Giannis et al. reported that the first oxidation of alcohols to the corresponding carboxylic acid with using IBX.[68] They used IBX in combination with certain o-nucleophiles, i.e. 2-hydroxypyridine (HYP), N-hydroxysuccinimide (NHS), in DMSO at room temperature. By using this method, aminoacids can be synthesized from corresponding amino alcohols without racemization **(Scheme 35)**.

Z: Protecting group

Scheme 35 Carboxylic acid synthesis with IBX

Finney et al. achieved oxidation of alcohols in different solvents with using IBX as a suspension.[69] This method was a very simple method to convert alcohol into corresponding carbonyl compounds. It includes only simple heating, filtration and evaporation of solvents. The oxidant could be regenerated and reused by this method. Although many solvent can be employed, EtOAc and DCE have been found to be superb **(Scheme 36)**.

Solvents: EtOAc, $CHCl_3$, DCE, acetone, benzene, CH_3CN, THF, toluene

Scheme 36 Alcohols oxidation with IBX in different solvents

To oxidize alcohols, IBX was used in ionic liquid [bmim]Cl and water.[70] Alcohols were converted to corresponding carbonyl compound mildly and efficiently: the oxidant and ionic liquids could be recycled and reused **(Scheme 37)**.

Scheme 37 IBX oxidation in ionic liquids

Rao and co-workers reported that a new alcohols oxidation system with IBX in combination with β-cyclodextrin.[71] They obtained very good yields in water/acetone mixture as solvent. This procedure is very selective for vicinal diols; only secondary hydroxyl group are oxidized **(Scheme 38)**.

Scheme 38 IBX oxidation catalysed by β-cyclodextrin

Nicolau et al. reported that oxidation of saturated alcohols or carbonyl compound into α, β-unsaturated carbonyl compounds (**Scheme 39**).[72]

Scheme 39 Nicolau's α,β-unsaturated carbonyl compounds' synthesis with IBX

Quideau et al. developed stabilized IBX (SIBX), which is composed of benzoic acid (22%), isophtalic acid (29%) and IBX (49%) and non-explosive form of IBX.[73] SIBX oxidized alcohols in EtOAc and THF **(Scheme 40**).

Solvents: EtOAc, CH_2Cl_2, NMP, DMSO, CH_3CN, THF, toluene

Scheme 40 Alcohol oxidation with SIBX

Also different IBX analogues (other than DMP) were developed to increase solubility, to decrease explosive property and to regenerate the catalyst (**Figure 3**).[74] They were used to oxidize alcohols and give good results.

Figure 3 IBX analogues

On the other hand, DMP (synthesized from IBX) was also used to convert alcohols into the carbonyl compounds. It was very selective oxidant for alcohols with a great tolerance to most of the other functional group (**Scheme 41**).

Scheme 41 DMP synthesis from IBX

Meyer and Schreiber accelerated the DMP oxidation with water addition.[75] Water addition decreased the reaction time sharply (**Scheme 42**).

Scheme 42 DMP oxidation accelerate with water addition

Myers et al. reported that DMP oxidation of optically active N-protected β-amino alcohols to corresponding aldehydes without loss of enantiomeric excess while loss of enantiomeric purity in Swern oxidation or TEMPO catalyzed oxidation **(Figure 4)**.[76]

Figure 4 Oxidation of optically active N-protected β-amino alcohols

Barret and co-workers reported a method to synthesize Wittig adducts from alcohols in one pot reaction.[77] This method includes DMP oxidation of diols in the presence of ester ylides and Wittig homologation of aldehydes *in situ*. They also used benzoic acid as additive to increase the reaction rate and E:Z selectivity (**Scheme 43**).

Scheme 43 Synthesis of Wittig adduct

Parlow et al. developed a method to isolate byproducts and excess starting material from reaction mixture.[78] This method was very simple and efficient. A thiosulfate resin was employed to purify products of oxidation of alcohols with DMP (**Scheme 44**).

Scheme 44 Purification of byproducts of alcohol oxidation with DMP

Arseniyadis and coworkers reported that a stable tricyclic enol ether with oxidation of bicyclic 1,2-diols through the tandem glycol cleavage-intermolecular [4+2] cycloaddition[79] **(Scheme 45)**.

Scheme 45 Oxidation of bicyclic 1,2-diols

1.2.1.2.2 ACTIVATED DMSO

DMSO was not only used as a solvent but it is also used as an oxidant for alcohol oxidation. However, DMSO must be activated by some activators, this form of DMSO is named as "activated DMSO".[24] "Activated DMSO" was firstly reported by Pfitzner and Moffat.[80] They used protonated DCC to activate DMSO. Then, they oxidized 3-acetoxy-2-deoxy-thymidine to the corresponding aldehyde with activated DMSO in the presence of phosphoric acid **(Scheme 46)**. They also activated DMSO with DCC in the presence of pyridinium trifluoroacetate or pyridinium phosphate and they worked well also.

Scheme 46 First alcohol oxidation with activated DMSO

Moffatt[81] and Allbright[82] proposed similar mechanisms concurrently. The only difference is the activators for the activation of DMSO **(Scheme 47)**.

Scheme 47 Mechanism of oxidation with activated DMSO

According to the Moffatt's mechanism; protonated DCC reacts with DMSO to form "activated DMSO". Alcohol attacks "activated DMSO" **A** and alkoxydimethyl sulfonium salt **B** is produced. Then base abstracts a proton to give sulfur ylide compounds, which decompose into the carbonyl compound and dimethyl sulphide.

However, “activated DMSO” can be eliminated to $H_2C{=}S^+{-}CH_3$, very reactive species, at high temperature. Then it can react with alcohol to form compound **D** as the side product. To prevent side product forming; solvents must be chosen with low polarity and reaction must be performed at low temperature **(Scheme 47)**.

Albright et al. used acetic anhydride (Ac_2O) as an activator.[82] It was observed that primary and secondary alcohol oxidized with “activated DMSO” at room temperature. They also tried different electrophiles as the activator, then they reported that phosphorous pentoxide (P_2O_5), benzoic anhydride and polyphosphoric acid could also be utilized as activators with relatively less yields **(Scheme 48)**.

Scheme 48 DMSO activated by Ac_2O

Onodera[83] et al. used P_2O_5, while Doering and Parikh[84] used SO_3.Py complex as the activator. On the other hand, Swern made a great contribution to the activation of DMSO. Firstly, Omura, Sharma and Swern reported that trifluoroacetic anhydride (TFAA) was very good activator although Albright et al. discarded it.[85] They mixed DMSO and TFAA, form trifluoroacetoxydimethylsulfonium trifluoroacetate *in situ*, and alcohol yields alkoxydimethylsulfonium trifluoroacetates, which decompose to carbonyl compound, alkyl trifluoroacetates and alkylmethylthiomethyl esters **(Scheme 49)**.

*Yield increase in order of primary, secondary, allylic and benzylic alcohols.

Scheme 49 DMSO activated by TFAA

Later, Swern reported a new oxidation system, known as Swern oxidation, with using oxalyl chloride to activate DMSO.[86] This "activated DMSO" is very reactive and reacts with alcohols in CH_2Cl_2 at low temperature to form alkoxysulfonium salts in short time, then transformed into corresponding carbonyl compounds after addition of triethylamine. The yields depended on the addition of triethylamine. This method gave best results for DMSO activation, the most of research groups use this method to activate DMSO nowadays **(Scheme 50)**.

Scheme 50 Swern Oxidation mechanism

According to the mechanism, oxalyl chloride attacked by DMSO to form complex A, which decompose rapidly to B with evolving CO and CO_2 even at very low temperature. If the temperature is higher than -20 °C, B can be transformed to chloromethyl methyl sulfide as side product. Below -60 °C, B reacts with alcohols, then complex D was formed. When reaction temperature goes to room temperature, triethylamine is added. Depending on the triethyl amine addition, carbonyl compounds are formed **(Scheme 50)**.

Briefly, “activated DMSO” shows different reactivity by changing the activators.[24] Strong activators; TFAA and oxalyl chloride, give highly reactive “activated DMSO”, which works well at low temperature, while mild activators DCC, SO_3.Py, Ac_2O and P_2O_5, forms less reactive one, which works well at room temperature.

Corey and Kim developed a new oxidation system, which is based “activated DMSO” a modified Swern oxidation.[87] The difference of this method is that DMSO was not used to obtain “activated DMSO”. They obtained “activated DMSO” by oxidizing dimethyl sulfide. They oxidized dimethyl sulfide with chlorine or N-chlorosuccinimide (NCS) **(Scheme 51)**.

Scheme 51 Corey-Kim oxidation

The active specie is same with the specie that is present Swern oxidation **(Scheme 52)**. Although Corey and Kim reaction has not been employed as much as the Swern oxidation, it provides some advantages like performing above -25°C.[24] In Swern oxidation, methylthiomethyl ethers can be formed as side product. This can be decreased by using apolar solvents.

Scheme 52 The active specie of Corey-Kim and Swern oxidations

1.2.1.2.3 TEMPO OXIDATION

The first alcohol oxidation with oxoammonium salts was reported by Golubev and co-workers in 1965.[88] They treated 4-hydroxy-2,2,6,6-tetramethyl-1-oxo piperidinium chloride with excess ethanol to yield acetaldehyde **(Scheme 53)**.

Scheme 53 First alcohol oxidation with oxoammonium salts

Cella et al. reported the conversion of the amine in 4-hydroxy-2,2,6,6-tetramethylpiperidine into nitroxide by m-chloroperbenzoic acid (mCPBA).[88] With doing that they also observed that the alcohol part of the piperidine was oxidized to the ketone **(Scheme 54)**.

Scheme 54 Oxidation of 4-hydroxy piperidine with mCPBA

After this observation, they thought that alcohol oxidation occurred due to the presence of nitroxide, not peracids, because peracids were not reactive to convert alcohols to the carbonyl compounds.[89] They used TEMPO in catalytic amount and mCPBA was used as secondary oxidant. mCPBA oxidized piperidine to nitroxide, primary oxidant. This procedure had an important drawback. The secondary oxidant, mCPBA, was very strong oxidant and it could affect other functional groups **(Scheme 55)**.

Scheme 55 The first alcohol oxidation with TEMPO

Sammelhack et al. developed a new alcohol oxidation system with TEMPO.[90] They converted TEMPO into oxoammonium salt with electrooxidation **(Scheme 56)**.

Scheme 56 Electrooxidation of alcohol in the presence of TEMPO

Anelli et al. achieved converting primary alcohols into aldehydes and/or carboxylic acids in the presence of catalytic amount of a TEMPO derivative, 4-methoxy-TEMPO.[91] By using this method, they obtained aldehydes in a few minutes. If desired product is carboxylic acid, reaction was continued for more time. They also converted secondary alcohols into corresponding ketones with this method. This procedure was very important for the alcohol oxidation with TEMPO **(Scheme 57)**.

Scheme 57 Anelli oxidation of alcohol

In Anelli's method; overoxidation of aldehydes to carboxylic acids is very slow. To accelerate the oxidation of secondary alcohols into ketones, primary alcohols into aldehydes, or primary alcohols into carboxylic acid, quarternary ammonium salts could be added as a phase transfer catalyst.[24, 92]

Piancatelli and Margarita modified Anelli's method[93]: [bis(acetoxy)iodo]benzene (BAIB) was used as a secondary oxidant. Moreover, primary alcohols are selectively oxidized to aldehydes **(Scheme 58)**.

Scheme 58 Modified Anelli's method

Zhao et al. reported that they used sodium chlorite in stoichiometric amount and sodium hypochlorite (bleach) in catalytic amount.[94] This method decreased chlorination of product, which is result of sodium hypochlorite. This procedure converted primary alcohols into the carboxylic acids **(Scheme 59)**.

Scheme 59 Alcohol oxidation with TEMPO/ bleach system

Rychnovsky and co-workers reported that halide ions catalyzed TEMPO mediated alcohol oxidations.[95] They used Bu_4NCl and Bu_4NBr as additive. Former one increased the conversion from 54 to 92%, while latter increased the conversion to 100% **(Scheme 60)**.

Scheme 60 Effect of halides on the oxidation of alcohols with TEMPO

Danishefsky et al. employed Margarita and Piancatelli's TEMPO mediated alcohol oxidation in total synthesis[96] **(Scheme 61)**.

Scheme 61 Alcohol oxidation with TEMPO in total synthesis

Akdag et al. reported that oxidizing of primary alcohol with using a polymer (chlorinated polystyrene hydantoin beads) as co-catalyst in combination with TEMPO as the catalyst.[97] Polymers can be recovered and reused more than 10 times **(Scheme 62)**.

Scheme 62 Alcohol oxidation with TEMPO/hydantoin/NaOCl system

TEMPO has been used in combination with metals for alcohol oxidations. These are mentioned in Metal Oxidants part. TEMPO using in photooxidation of alcohols will be mentioned in next chapter.

TEMPO was also attached polymers and utilized to oxidize alcohols.[98]

1.2.1.3 OXIDATION WITH LIGHT

It is important that methods, used in chemistry, should be green due to the environmental concerns and sustainability of the nature. To achieve green alcohol oxidation, light has been used as secondary oxidant. In these oxidation reactions, the key point is to achieve electron transfer by excitation of the molecules with light. The oxidation of alcohols occurs due to the electron transfer. Although this is relatively new research area, there exist some procedures from the literature are discussed in the below.

Stenberg et al. reported that alcohols were converted to the carbonyl compounds with nitrobenzene derivatives under UV-irradiation.[99] In this study, the main concern was quantum yield of consuming reactant or forming product. They dissolved 1,3,5-trinitrobenzene in 2-propanol. While nitrobenzene was reduced under irradiation, alcohols were oxidized to acetone (**Scheme 63)**.

Scheme 63 Oxidation with nitrobenzene under UV-light

In 1981, Walling et al. reported a new photooxidation procedure for alcohols.[100] They used $Fe(ClO_4)_3$ solution to oxidize alcohols with UV-irradiation. They obtained very different product such as aldehydes, ketones, esters, alkenes.

In 1988, Yamagata and co-workers published a paper.[101] They studied the mechanism of photocatalytic oxidation of alcohols with TiO_2, semiconductor, under UV-light. They used three different techniques: spin trapping, photocurrent

measurement, and product analysis. In the product analysis, they observed the alcohols were oxidized.

Kemp et al. reported a photooxidation reaction of alcohols with hexachloro-metallate(IV) ions (Metals could be Pd, Pt, or Ir.).[102] This reaction occurs under visible light (λ>380 nm).

Bonchio et al. synthesized a tungstate catalyst.[103] The catalyst, decatungstate in polymeric membranes, could oxidize alcohols to the carbonyl compound in water under light (λ>345 nm).

Demessi et al. reported a procedure for alcohol oxidation with TiO_2.[104] They used corona, kind of a low energy (10-20 eV) electric discharge, account for UV-light source. During the reaction low power UV-light was produced by corona discharge. Also ozone was produced by oxygen in the reaction medium, it is also strong oxidizing agent. The procedure was selective for secondary and cyclic alcohols.

Itoh and co-workers reported an aerobic photooxidation method for alcohols with using lithium bromide.[105] They achieved convertion of primary alcohols into the corresponding carboxylic acids selectively with a 400 W high pressure mercury lamp. They proposed a mechanism for the reaction, however they could not understand the process clearly. They stated that the reaction needs to be studied more in depth (**Scheme 64**).

Scheme 64 Mechanism of photooxidation of alcohols with LiBr

Subsequently the same research group published another paper about photooxidation of alcohols into the corresponding carboxylic acid.[106] N-bromosuccinimide (NBS) was utilized in this time.

Nagata and co-workers developed a porphyrin/quinone/TEMPO system for photooxidation of alcohols.[107] They could convert primary alcohols into the carboxylic acids. The procedure worked for secondary alcohols but in slow rates. The rates depend on the forming of oxoammonium cation from TEMPO. They used zinc porphyrin as a photosensitizer **(Scheme 65)**.

Scheme 65 Photooxidation of alcohol with porphyrin/quinone/TEMPO system

Rocha et al. synthesized dinuclear Ru-complexes, which includes both chromophore and catalyst moieties, to utilize in photooxidation reactions of alcohols.[108] The catalyst worked under visible light to oxidize alcohol to corresponding aldehydes or ketones (**Figure 5**).

Figure 5 Rocha's Ru-complex catalysts

Tanaka et al. reported that they achieved photocatalytic oxidations of alcohols with TiO_2 covered with Nb_2O_5.[109] 3.5 mol% Nb_2O_5 is sufficient to cover TiO_2. By excess addition of Nb_2O_5 activity of catalyst was decreased while the selectivity was increased. They used 500W ultrahigh pressure Hg-lamp as the light source (UV).

Recently, TEMPO has been used in photooxidation of alcohols by Zhao and co-workers.[110] They developed a system for aerobic oxidation of alcohols with a dye (alizarin red)/TiO_2/TEMPO catalyst system under visible light (**Scheme 66**). This method was taken as a model study in this thesis. However, we were not being able to reproduce the results in this study.

Scheme 66 Photooxidation of alcohols with dye sensitized TiO_2

Robinson and Jeena reported a procedure for photooxidation of alcohols with dye sensitized ZnO under visible light inspired by Zhao's study.[111] They used ZnO as a semiconductor and $AgNO_3$ as an electron acceptor while Zhao et al. used TiO_2 and

O_2 respectively. Zhao's procedure seems to be greener method, but Robinson et al. reported that the reaction was not appropriate for alcohol oxidation (**Scheme 67**).

Scheme 67 Photooxidation of alcohols with dye-sensitized ZnO

All trying to develop new methods for synthesis in chemistry aims to reach green chemistry, Nirvana point of the chemistry. Green is chemistry is defined as design and development of chemical substance and processes that reduce or eliminate the use or generation of hazardous substances. There are 12 conditions of green chemistry:

- Prevent waste
- Atom economy
- Less hazardous synthesis
- Design safer chemical
- Safer solvents and auxiliaries
- Design for energy efficiency
- Use of renewable feedstocks
- Reduce derivatives
- Catalysis

- Design for degradation
- Real-time analysis for pollution prevention
- Inherently safer chemistry for accident prevention

CHAPTER 2

AIM OF STUDY

The general goal of the study is to oxidize alcohols to the corresponding carbonyl compounds in a green way. This process was envisioned to be performed with visible light (λ >350 nm). In the literature, there are several examples employing light to oxidize alcohols. The reaction, shown in **Scheme 67**, is an example for these type oxidations. This procedure consists of an absorbent (dye), a metal oxide (ZnO), an oxidant (TEMPO) and a co-oxidant ($AgNO_3$). The reaction started with absorbing light by dye molecules. Then the excited dye molecule gives an electron to conduction band of metal oxide by leaving an oxidized dye. This, in turn, oxidizes TEMPO to active TEMPO (oxoammonium cation form of TEMPO). This step is the crucial for our oxidation system.

Scheme 68 Model for electron transfer from TEMPO to the metal oxide

Specifically, our goal can be narrowed down to synthesize a catalyst, which includes dye and TEMPO moieties together. In other words, TEMPO was incorporated to the dye molecule. With TEMPO attached to the dye, we aim to increase efficiency of electron transfer by decreasing diffusion control process. For a multicomponent reactions; molecules must collide each other with right conditions such as; collision angle, collision rate. With the synthesis of our catalyst, less molecules are needed to collide with each other (**Scheme 68**). In our test reactions, we will be using ZnO, TiO_2 as metal oxides, O_2 and Ag^+ as electron acceptors.

CHAPTER 3

RESULTS AND DISCUSSIONS

3.1 LITERATURE SURVEY AND TEST PROCEDURES

The basic idea of this study is to mobilize electrons by light such that the TEMPO becomes active TEMPO for oxidizing alcohols to the corresponding carbonyl compounds as summarized in **Scheme 68**.

This idea was previously proposed by Fox[112] and executed by Zhao et al. [110] Zhao's proposal was illustrated in **Scheme 69**. According to this study, the end oxidant is oxygen. The study reported excellent conversions. Despite this fact, they used micro scale experimentation. Their study was completely diffusion controlled; that is, TEMPO radical has to diffuse to the dye to get oxidized, then alcohol has to diffuse nearby active TEMPO for this reaction to occur. Nevertheless, we used this reaction as a model study.

Scheme 69 Photooxidation of alcohols with dye-sensitized TiO_2

The exact procedure by Zhao (TiO_2/O_2/Alizarin Red/TEMPO system) was repeated for benzyl alcohol except for that air was bubbled continuously during the reaction instead of oxygen. Our first test reaction did not produce benzaldehyde, we recovered benzyl alcohol. Then, oxygen was bubbled continuously during the reaction. This, again, did not yield the aldehyde. The reaction was repeated under oxygen atmosphere, this did not give the aldehyde as well. The reaction was monitored by TLC, GC, and NMR.

With these results in hand, we decided to change the amount of additives. We increased the amount of alizarin red (form of sodium salt) to increase the absorption of light, yet the desired results were not observed. Then, to increase the solubility of alizarin red (AR) sodium salt, the sodium salt was converted to the acid form. This also did not change the result. Then we decided to go with different dyes such as methyl orange (MO), methyl red (MR) and indigo (In), but results were not pleasant (**Figure 6**).

Figure 6 The dyes used in the study

Although we increased amount of TiO_2 and TEMPO in reactions, we were not able to reproduce Zhao's yield. Then the particle size of TiO_2 was changed from powder to nanopowder one because nanopowder anatase TiO_2 (its particle size is smaller than 25 nm) has been used for the photooxidation reaction. We, however, did not see any change in the reaction outcome. Among all the reactions repeated, we only get as

high as 5% conversion of aldehyde. This is not reproducible. With these results in mind, we decided to continue with our version of dyes (catalyst), in which the dye is directly bind to TEMPO. The structures of target dyes are given in **Figure 7**.

4 **5**

Figure 7 Designed catalysts for the study

To synthesize **4**, the synthesis of the precursor for the catalyst **8**, reaction of 1,4,5,8-naphtalenetetracarboxylic dianhydride (NDA) with 4-amino-2,2,6,6-tetramethyl piperidine (ATMP), was attempted in DMF.[113] This reaction gave a complex mixture from which the desired product **8** could not be separated. Such a procedure was previously employed for primary amines on primary carbons. Even the original procedure resulted low yields **(Scheme 70)**.

6 **7** **8**

Scheme 70 Synthesis of naphthalene-N-(2,2,6,6-teramethylpiperidinyl)-imidodi carboxylicacid in DMF

With this failed result, we went back to the drawing board. Literature suggests that such a reaction could occur in DMF at 140 ^{o}C.[114] Based on this suggestion, NDA was suspended in DMF, and the temperature was brought to 140 ^{o}C. At this temperature, ATMP was added to the solution, and the temperature was kept at 140 ^{o}C for 18 h.

Then, the mixture was cooled to 4 ^{o}C and filtered. The filtrate was evaporated, and residue was chromatographed on SiO_2 to give the desired product. The product was obtained in 10% yield. This was not serving our purposes.

Back to back failures for this basic reaction pushed us to check the validity of the procedure we followed. Benzyl amine was used instead of ATMP. The reaction proceeded in an expected way that we got 50% yield. So a new procedure was needed (**Scheme 71**).

6 . **9** **10** **11**

Scheme 71 Synthesis of naphthalene-N-(benzyl)-imidodicarboxylicacid in DMF

A literature procedure was found that n-butylamine was treated with NDA in water.[115] This reaction produced good yields for the authors. Therefore, we decided to apply this procedure for our compound. First, NDA was suspended in water, and pH of the solution was brought to *ca.* 6.4 with help of NaOH and H_3PO_4. Then, 4-amino TEMPO was added to the solution which was heated to 100 ^{o}C for 18 h. The solution was cooled to room temperature, the pH was adjusted to 1.5, the precipitate was filtered out. The precipitate was dissolved in AcOH, then filtered. The filtrate was evaporated to give the desired compound in 41% yield **(Scheme 72)**. The product was characterized with IR and Electron Paramagnetic Resonance (EPR), also known as Electron Spin Resonance (ESR). In the IR-spectrum, N-O$^{\cdot}$ stretching appeared at around 1360 cm^{-1}, which is consistent with literature.[112] In EPR, the radical presence was confirmed with a first derivative peak around 3470 Gauss (**Figure 8**). Since we performed EPR on solid compound, the hyperfine coupling are not obvious.

Scheme 72 Synthesis of catalyst **4**

With this compound in hand, we decided to redo this reaction with ATMP since 4-amino-TEMPO is an expensive reagent. The reaction was performed with ATMP. The product was obtained over 90% yield and treated with H_2O_2 in the presence of sodium tungstate and EDTA to get **4** (**Scheme 73**).

Scheme 73 Oxidation of compound **8** to catalyst **4**

Figure 8 EPR spectrum of catalyst **4**

In order to ensure the characterization, compound **5** was also synthesized as described in **Scheme 74**.[116-118] Compound 5 was characterized by IR.

Scheme 74 Synthesis of catalyst **5**

Both compound **4** and **5** were used for our oxidation reactions. The use of these compounds in place of AR and TEMPO did not change the result, which is no alcohol oxidation was observed. The UV-vis spectrum of compound **4** shows that a small portion of light is absorbed for λ>350 nm. We also checked what wavelength of light is being cut off from the reaction, and found that λ<350 nm is being cut off.

Scheme 75 Modified procedure from Zhao procedure

3.2. DESIGN OF NEW CATALYSTS AND ATTEMPTED SYNTHESIS OF THEM

With the results given above in hand, to increase the light absorption of the dyes, we designed the following compounds to be synthesized **(Figure 9)**.

Figure 9 All designed catalyst during the study

To synthesize the catalyst **18**, we designed a reaction pathway shown in **Scheme 76**.[118b, 119] Naphtalic anhydride was brominated with bromine solution at C4 position. The anhydride was converted into imide derivative **28** by addition of ATMP. However the reaction of C-C coupling failed. Due to the time restrictions, we did not pursue this reaction further. This reaction is still in our list of future studies.

Scheme 76 Reaction pathway for catalyst **18**

Scheme 77 Reaction pathway for catalyst **19**

The attempts to synthesize two designed compounds **18** and **19**[120, 121] failed (**Scheme 76-77**). We decided to follow a route in which we will not have acidic hydrogen adjacent to the ring to avoid conjugation. This conjugation will interfere with the electron acceptor and donor properties of the chromophore. Therefore, we designed compound **20**, which constitute two electron withdrawing groups which makes the anthracene to accept electrons easily. The synthesis of **20** starts with chloromethylation of anthracene of 9 and 10 positions. Then, an S_N2 reaction of acetate in the presence of KI. After esters were saponificated, the resulting alcohols were oxidized to the carboxylic acids.[122] The carboxylic acid **36** was then treated with $SOCl_2$ in the presence of catalytic amounts of DMF.[123] The diacylchloride was treated with ATMP. Even though we did not isolate compound **37**, It was assumed that the chlorination reaction took place. However, the desired compound **38** was not observed **(Scheme 78)**. This is perhaps due to unreactivity of the acid toward $SOCl_2$

since **37** was not isolated. Then, we turned our attention to couple ATMP with dicarboxylic acid. This also failed to yield the monoamide.

Scheme 78 Synthesis of **20** starting from the anthracene

In the previous attempted synthesis of **20**, the scapegoat was that the carboxylic acid groups were connected directly to the anthracene which reduced the reactivity. Therefore, we designed the synthesis of **21.** The synthesis is started with **33** which was treated with ethyl malonate to give **39**. A saponification followed by a decarboxylation gave **41**. The decarboxylation step was problematic that very high temperatures were needed. Nevertheless, we obtained **41** in small amounts. These small amounts were subjected to esterification. The esterification reaction failed.[124] We had to go back to the starting material (p-formaldehyde), the author was found to

be allergetic to p-formaldehyde. Consequently, we abandoned this scheme **(Scheme 79)**.

Scheme 79 Reaction pathway for catalyst **21**

We turned our attention to **22** and **23** with the left over **40**. The idea was to couple **45** with **40** in the presence of H_2SO_4. The reaction was a modification of synthesis of Meldrum's acid (**Scheme 80**).[125, 126] This coupling did not proceed the way we wanted.

Scheme 80 Reaction pathway for catalysts **22** and **23**

While working on synthesis of **24**[112,127] (**48** was synthesized), we realized that an anthraquinone containing compound would better serve our purposes.

Figure 10 Compound **48** and catalyst **25**

The catalyst was synthesized starting with sodium salt of anthraquinone-2-sulphonic acid (ASA), **49**.[128] It is converted to anthraquinone-2-sulphonyl chloride (ASC)[129] and reacted with ATMP to obtain catalyst precursor, **51**, which was oxidized to catalyst **25 (Scheme 81)**.

Scheme 81 The synthesis of catalyst **25**

The results of benzyl alcohol oxidation were tabulated in Table 1. The table reveals that reaction did not proceed the way we wanted. Mostly alcohols were recovered. Then, we facilitated our catalyst in another TEMPO-mediated alcohol oxidation procedure. All catalysts acted like TEMPO and gave over 90% conversion.[130] Therefore, a new method was needed desperately.

Table 1: Maximum conversions from the TiO_2 based alcohol oxidation reactions

Alcohol	Solvent	Metal Oxide	Oxidant	Dye	Co-oxidant	Light	Conversion $_{(max)}$
15	BTF	TiO_2	TEMPO	AR	O_2	+	5%<<
15	BTF	TiO_2	TEMPO	MR	O_2	+	0.1%<<
15	BTF	TiO_2	TEMPO	MO	O_2	+	0.1%<<
15	BTF	TiO_2	TEMPO	In	O_2	+	0.1%<<
15	BTF	TiO_2	**4**	-	O_2	+	0.1%<<
15	BTF	TiO_2	**5**	-	O_2	+	0.1%<<
15	BTF	TiO_2	**26**	-	O_2	+	0.1%<<
54	BTF	TiO_2	**4**	-	O_2	+	0.1%<<

Then we searched the literature to find the problem. We found another paper like our system. In this procedure, Robinson and Jeena oxidized alcohols by using AR/ZnO/TEMPO in water.[111] Alcohols were oxidized to aldehydes or ketones in good to excellent yield without further oxidation to carboxylic acids. They used

TiO_2, used in Zhao's procedure,[110] instead of ZnO. Unexpectedly TiO_2 did not work as ZnO, because TiO_2 and ZnO are expected to behave similar.[131]

After that exact procedure was repeated with benzyl alcohol to test whether this system oxidizes alcohols or not. The reaction gave over 90% conversions in 2.5 hours. This result encouraged us and we tested the procedure with changing parameters to understand how the system works.

Table 2: Test reactions of Robinson's system

	Metal Oxide	**Dye**	**TEMPO**	**Co-oxidant**	**Light**	**Solvent**	**Conversion**
1	ZnO	AR	+	$AgNO_3$	+	H_2O	>95%
2	TiO_2	AR	+	$AgNO_3$	+	H_2O	<8%
3	-	AR	+	$AgNO_3$	+	H_2O	<8%
4	ZnO	-	+	$AgNO_3$	+	H_2O	50-55%
5	ZnO	AR	+	$AgNO_3$	-	H_2O	NR
6	ZnO	AR	+	O_2	+	H_2O	NR
7	ZnO	AR	+	O_2	+	BTF	NR
8	ZnO	ASA	+	$AgNO_3$	+	H_2O	>99%
9	ZnO	NDA	+	$AgNO_3$	+	H_2O	>98%
10	ZnO	**25**	-	$AgNO_3$	+	H_2O	<1%
11	ZnO	**4**	-	$AgNO_3$	+	H_2O	>95%
12	ZnO	**5**	-	$AgNO_3$	+	H_2O	15-16%
13	ZnO	AR	+	$FeCl_3$	+	H_2O	<1%
14	ZnO	AR	+	$FeCl_3$	+	H_2O (acidic)	<2%
15	ZnO	AR	+	-	+	HNO_3	Complex mixture

a) NR: No reaction

To find a cheaper co-catalyst, we utilized O_2 and $FeCl_3$ in the system instead of $AgNO_3$. However, the procedure did not produce aldehyde, we only recovered alcohol. Then, we used HNO_3 solution as solvent. Moreover, we expected that HNO_3 acted like an electron acceptor due to the acidity of reaction medium but we could

not observe any aldehyde (entry 6, 7, 13, 14, 15 in **Table 2**). We decided that $AgNO_3$ was the best co-oxidant for our system.

Besides we tested the reactants effect on the system with removing a reactant. We observed that the system gave reasonable conversion (50%) without dye, while the conversion was very low in the absence of other reactant (ZnO or light). These results were very surprising because the system was started with absorbance of the light under favor of dye.

In addition, we utilized NDA and anthraquione-2-sulphonic acid sodium salt as dye account for alizarin red. This provides a preview, because our catalysts consist of these molecules combined with TEMPO. Both reactions oxidize benzyl alcohol to benzaldehyde 100% conversion almost. After that, we tried the catalysts **4**, **5** and **25** without extra dye or TEMPO molecules. Only catalyst **4** gave the expected conversion. Catalyst **5** had low oxidizing ability with 15% conversion. However, this conversion is very low for the study. Catalyst **25** was also unsuccessful for oxidation of alcohols. The reason may be lack of a tethering group, which provides that catalyst easily attach to metal oxide, for catalyst **5** and **25**. All test reactions are tabulated in Table 2.

Then, we designed our reaction procedure shown in **Scheme 82**. Variety of alcohols were oxidized, and most of the benzylic alcohols gave excellent conversions to the aldehydes. Meanwhile we also tried to oxidize *n*-octanol but it is not oxidized to corresponding aldehyde. Aldehydes, obtained from the oxidation of alcohols in this study, and their conversions are shown in **Figure 11**.

Scheme 82 The designed procedure for the study

Figure 11 The aldehydes obtained from alcohols oxidation

Then we concentrated on the oxidation of benzylic alcohols and isolation of them. We obtained excellent conversion for alcohol oxidation however we could isolate half of the product. This is a great problem for the study. We thought that alcohols and/or aldehydes attached to ZnO and we could not isolate it. To control this suspect, we mixed alcohol and ZnO in water, then separated them. There was no loss of alcohol.

Probably the problem was aldehyde and ZnO was attached each other and the work-up process was not enough for the separation of aldehydes. To break the coordination of aldehydes and ZnO, the reaction solution was acidified with HCl. After the extraction, we obtained almost 50% of total mass. During the acidification, Ag^+ ions precipitated as AgCl and it formed a large granule with ZnO that may also decrease isolated product. The isolation of the aldehydes is still the major problem of the study and it must be solved. Although isolation is a problem, the system oxidizes alcohols to aldehydes selectively. GC-MS and NMR results shows that there is no further oxidation to carboxylic acids.

CHAPTER 4

CONCLUSIONS

At the beginning of the study, we planned to synthesize a catalyst in that dye and TEMPO moieties incorporated to utilize for alcohol oxidation in the presence of a metal oxide (TiO_2 or ZnO). In this regard, we synthesized three different compounds **4**, **5**, **25**. One of these compounds **4** functioned as expected. In our oxidation system, alcohols were oxidized by electron(s) transfer between the molecules. To complete electron transfer mechanism, electron(s) must be transferred from the dye moiety to metal oxide. At this point, we observed that dye and TEMPO moieties of the catalysts are not sufficient to oxidize alcohols. Dye moiety of the catalyst must contain a tethering group in order for the reaction to proceed smoothly. The compound without a tethering group failed to give the expected results..

Meanwhile, we expected that TiO_2/catalyst/O_2 system functioned as well as ZnO/catalyst/$AgNO_3$ system. However, we could not reproduce the results of TiO_2/O_2 system as reported.[110] This was not an expected result. This may be resulted from back electron transfer from TiO_2.[111]

We developed a ZnO/**4**/$AgNO_3$ system which oxidize alcohols efficiently as we expected. We decreased the diffusion-control with attached TEMPO molecule to dye molecule.

Although the system oxidizes benzylic alcohols, it needs further optimizations:

- The amount of co-catalyst can be decreased.
- A metal-free co-oxidant can be used to replace silver.
- Using of this oxidation system can be extended on variety of alcohols.

CHAPTER 5

EXPERIMENTALS

Methods and Materials: Structural determinations of compounds were done with the instruments as written below.

1H and 13C nuclear resonance spectra of compounds were recorded in CDCl3 and DMSO-d_6 with 400 MHz Bruker NMR spectrometer. Chemical shifts are given in parts per million (ppm) with TMS as internal reference. Spin multiplicities were specified as s (singlet), bs (broad singlet), d (doublet), dd (doublet of doublet), ddd (doublet of doublet of doublet), dq (doublet of quartet), t (triplet), m (multiplet) and coupling constants (*J*) were reported in Hertz (Hz). 1H and 13C NMR spectra of products are given in Appendix A. NMR spectrums were processed with ACD/NMR Processor Academic Addition.

HRMS data were detected at Central Laboratory of Middle East Technical University.

Infrared Spectra were recorded with Bruker Alpha Platinum ATR. Peak positions were reported in reciprocal centimeters (cm-1). IR spectra of products are given in Appendix B.

ESR spectra were recorded with Varian ESR spectrometer.

Melting points were determined by Stuart SMP11 melting point device.

All reactions were monitored by TLC (Merck Silica Gel 60 F254), visualized by UV-light.

Chromatography was performed on silica gel 60 with a particle size of 0.063–0.200 mm purchased from Merck.

All starting materials and solvents were purchased from Sigma-Aldrich and were used without further purifications.

All photo-oxidation reactions were performed in pyrex®-round bottom glass. 400 W halogen lamps were used as light source.

1,8-Naphtalic anhydride:[116] Acenaphtene (0.50 g, 3.25 mmol) was dissolved in AcOH (20 ml). $Na_2Cr_2O_7$ (2.12 g, 8.13 mmol) was added to solution in small portions. The reaction mixture was stirred at 70 ^oC for 4 hours. Cold water was added to the mixture. Then, the reaction mixture was filtered and residue was washed with water. After drying, 1,8-naphtalic anhydride (**14)** was obtained (0.51 g, 80%, yellowish solid). m.p.: >250 ^oC. ^1H NMR ($CDCl_3$) δ (ppm): 8.65 (dd, 2 H, J_1=7.3 Hz, J_2=1.0 Hz), 8.34 (dd, 2 H, J_1=8.5 Hz, J_2=1.0 Hz), 7.77 (m, 2 H). IR: 1768 cm^{-1} (C=O stretching), 1714 cm^{-1} (C=O stretching), 1008 cm^{-1} (C-O stretching).

14

N-(2,2,6,6-tetramethylpiperidinyl)-1,8-naphtalimide:[118] Compound **14** (0.98 g, 4.95 mmol) was suspended in *i*-propanol (10 ml). 2,2,6,6-tetramethyl piperidine (1.00 g, 6.40 mmol) was added to the suspension. The reaction mixture was refluxed overnight. The mixture was cooled to room temperature, and filtered. The residue was dissolved in 1 M KOH solution. Then, neutralized with AcOH and 1 spoon of charcoal was added and filtered (to decolorize the mixture). The residue was dried under vacuum. (The obtained solid can be used without further purification.)

15

Further purification: The residue was extracted with diethyl ether and washed with water. The combined ether phases were dried over $MgSO_4$, then filtered, and volatiles were evaporated to give **15** (1.25 g, 75%, white solid). m.p.: 169-172 ^oC. ^1H NMR ($CDCl_3$) δ (ppm): 8.58 (dd, 2 H, J_1=7.3 Hz, J_2=1.0 Hz), 8.21 (dd, 2 H, J_1=8.3 Hz, J_2=1.0 Hz), 7.76 (dd, 2 H, J_1= 8.3 Hz, J_2=7.3 Hz), 5.74-5.64 (m, 1 H), 2.50 (t, 2 H, J=12.7 Hz), 1.67 (dd, 2 H, J_1=12.6 Hz, J_2=3.3 Hz), 1.39 (s, 6 H), 1.25 (s, 6H). ^{13}C NMR ($CDCl_3$) δ (ppm): 164.9, 133.7, 131.4, 131.2, 128.3, 127.9, 123.2, 52.1, 47.16, 41.8, 34.8, 28.0. IR: 3282 cm^{-1} (N-H stretching, piperidine), 1691 cm^{-1} (C=O stretching), 1651 cm^{-1} (C=O stretching), 1235 cm^{-1} (C-N stretching, imide).

N-(2,2,6,6-tetramethylpiperidinoxyl)-1,8-naphtalimide:[118] Compound **15** (0.150 g, 0.446 mmol) was dissolved in CH_2Cl_2. *m*CPBA (0.224 g, 1.298 mmol) was slowly added to reaction mixture. The reaction was stirred at room temperature. After 3 hours, CH_2Cl_2 was evaporated. Then, residue was dissolved in diethyl ether and washed with $NaHCO_3$ solution and water. Then the organic phase was dried with Na_2SO_4 and filtered. The ether was evaporated to obtain **5** (0.11 g, 70%, yellowish solid). IR: 1373 cm^{-1} (N-O· stretching).

5

Naphtalene-N-(benzyl)imidodicarboxylicacid: 1,4,5,8-Naphthalenetetracarboxylic diandyride (0.40 g, 1.49 mmol) was dissolved in H_2O (65 ml) and 1 M KOH (7 ml, 7 mmol) was added. The reaction mixture was stirred until it was completely dissolved. Then, pH was set to *ca.* 6.4 with 1 M H_3PO_4 solution. Then benzyl amine (0.16 g, 1.49 mmol) was added into the solution. pH was adjusted to *ca.* 6.4. The reaction mixture was heated to 110 ^oC and stirred overnight. It was cooled to room temperature. The pH was set to 1-2 with 2 M HCl solution. Then cooled in the refrigerator for 1 hour and filtered. Residue was collected and dried to obtain **11** (0.45 g, 80%, pale brown solid). m.p.: >250 ^oC. ^1H NMR (DMSO-d_6) δ (ppm): 8.56 (d, 2 H, *J*=7.0 Hz), 8.17 (d, 2 H, *J*=7.3 Hz), 7.47-7.19 (m, 5 H), 5.25 (s, 2H). IR: 2947, 2544 cm^{-1}(O-H stretching), 1698, 1658 cm^{-1} (C=O stretching), 1223 cm^{-1} (C-N stretching).

11

Naphtalene-N-(2,2,6,6-tetramethylpiperidinyl)imidodicarboxylicacid: 1,4,5,8-Naphthalenetetracarboxylic dianhydride (1.03 g, 3.84 mmol) was dissolved in H_2O (100 ml) and 1 M KOH (20 ml, 20 mmol) was added. The reaction mixture was stirred until it was completely dissolved. pH was set to *ca.* 6.4 with 1 M H_3PO_4 solution. Then 4-amino-2,2,6,6-tetramethylpiperidine (0.60 g, 3.84 mmol) was added into solution. pH was reset to *ca.* 6.4. Reaction was heated to 110 ^oC and stirred overnight. It was cooled to room temperature. pH was set to 1-2 with 2 M HCl solution. Then it was cooled in the refrigerator for 1 hour. Precipitate was filtered out and filtrate was

8

dried in rotary evaporator. AcOH (50 ml) was added to residue and heated to solve residue. After cooled to room temperature; the mixture was filtered and filtrate was evaporated. Then the residue was washed with water and dried to obtain **8** (1.47 g, 90%, pale brown solid). It can be used without further purification.

Further purification: AcO_2 (30 ml) was added to the residue and refluxed for 2h. Then the solvent was evaporated and the product was obtained. m.p.: >250 ^oC. ^1H NMR (DMSO-d_6) δ (ppm): 9.75 (bs, 1 H), 8.69 (m, 4 H), 8.02 (s, 1 H), 5.52 (t, 1 H, *J*=12.6 Hz), 2.74 (t, 2 H, J_1=11.5 Hz, J_2=11.3 Hz), 1.86 (d, 2 H, *J*=13.1 Hz), 1.55 (s, 6 H), 1.48 (s, 6 H). ^{13}C NMR (DMSO-d_6) δ (ppm): 163.1, 159.7, 131.8, 130.4, 128.4, 127.5, 126.2, 123.7, 57.2, 44.1, 36.9, 29.9, 23.9. IR: 2979 cm^{-1} (N-H stretching, piperidine), 2901cm^{-1} (O-H stretching), 1784 cm^{-1}, 1765 cm^{-1}, 1746 cm^{-1}, 1711 cm^{-1} (C=O stretching). HRMS (ESI+): Calc'd for $C_{23}H_{24}N_2O_6^+$ 424.1634; found 424.1634.

Naphtalene-N-(2,2,6,6-tetramethylpiperidinoxyl)imidocarboxylicacid:

4

(a) 1,4,5,8-Naphthalenetetracarboxylic dianhydride (0.31 g, 1.17 mmol) was dissolved in H_2O (100 ml) and 1 M KOH (20 ml, 20 mmol) was added. The reaction mixture was stirred until dissolution was complete. pH was set to *ca.* 6.4 with 1 M H_3PO_4 solution. Then 4-amino-TEMPO (0.20 g, 1.17 mmol) was added to the solution. pH was adjusted to *ca.* 6.4. The reaction was heated to 110 ^oC and stirred overnight. It was cooled to room temperature. pH was set to 1-2 with 2 M HCl solution. Then it was cooled in the refrigerator. The precipitate was separated and dissolved in AcOH. After filtration of the solution, the filtrate was evaporated to give the product (0.21 g, 41%, brown solid). m.p.: >250 ^oC. IR: 1363 cm^{-1} (N-O$^{\cdot}$ stretching), 1291 cm^{-1} (C-N stretching, imide). HRMS: Calc'd for $C_{23}H_{27}N_2O_7^{\cdot}$ $[M]^+$: 439.1733 Found: 439.1505.

b) Compound **8** (250.0 mg, 5.89x10^{-4} mol) was added to water and the mixture was slightly basified with $NaHCO_3$. Then $Na_2WO_4.2H_2O$ (11.6 mg, 3.53x10^{-5} mol), 0.06 equivalent EDTA(10.3 mg, 3.53x10^{-5} mol) and 30% H_2O_2 (267.1 mg, 2.35x10^{-3} mmol) were added to the mixture. The reaction mixture was stirred vigorously. After 3 days, organic compounds were extracted with CH_2Cl_2 from the reaction solution.

Organic phase was separated and dried with $MgSO_4$ and CH_2Cl_2 was evaporated to obtain the product (232.8 mg, 90%).

4-Bromo-1,8-naphtalimide:[116] 1,8-Naphtalic anhydride (1.98 g, 0.01 mol) was dissolved in hot KOH solution (2.8 g in 12 ml H_2O) and cooled to room temperature. Br_2 was dissolved in water in excess amount. Br_2 solution was added dropwise. After the addition was complete, the solution was stirred at 60 ^oC. After 40 minutes; the mixture was cooled to 0 ^oC and acidified with 4 M HCl. After precipitation, the reaction mixture was filtered. The residue was collected and 5% NaOH solution was added to the residue and filtered. The filtrate was neutralized with 4 M HCl solution, filtered. The residue was washed with water. Drying of the residue gave **26** (2.21 g, 80%, pale brown). m.p.: 215-216 ^oC. ^1H NMR ($CDCl_3$) δ (ppm): 8.73-8.68 (m, 2 H), 8.47 (d, 1 H, *J*=7.8 Hz), 8.14 (d, 1 H, *J*=7.8 Hz), 7.94 (dd, 1 H, J_1=8.5 Hz, J_2=7.3 Hz). ^{13}C NMR ($CDCl_3$) δ (ppm): 197.7, 197.6, 171.1, 170.7, 170.0, 169.2, 168.1, 167.7, 167.5, 166.6, 157.4, 156.6. IR: 1769 cm^{-1} (C=O stretching), 1728 cm^{-1} (C=O stretching), 1015 cm^{-1} (C-O stretching).

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4-Bromo-N-(2,2,6,6-tetramethylpiperidinyl)-1,8-naphtalimide:[118] 4-bromo-1,8-naphtalic anhydride (0.83 g, 3.0 mmol) was suspended into ethanol (10 ml). **7** (0.55 g, 3.5 mmol) was added into the mixture and stirred at 70 ^oC for 4 hours. Cold water (25 ml) was added to the mixture. A precipitate appeared, the reaction mixture was filtered. The residue was washed with 10% aqeous Na_2CO_3 solution and water. Drying of the residue gave the product (0.87 g, 70%). ^1H NMR ($CDCl_3$) δ (ppm): 8.65-8.55 (m, 2 H), 8.39 (d, 1 H, *J*=7.8 Hz), 8.05 (d, 1 H, *J*=7.8 Hz), 7.87 (dd, 1 H, J_1=8.5 Hz, J_2=7.3 Hz), 5.70-5.61 (m, 1H), 2.49-2.40(m, 2 H), 1.67 (dd, 2 H, J_1=12.6 Hz, J_2=3.5 Hz), 1.37 (s, 6 H), 1.22 (s, 6 H).

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9,10-Dibromoanthracene:[120] Solution of Br_2 (9.05 g, 56.6 mmol) in $CHCl_3$ (50 ml) was added slowly to the solution of anthracene (5 g, 28.05 mmol) in $CHCl_3$ (100 ml) at room temperature. After stirring for 4 hours, solvent was evaporated. The residue was recrystallized in CH_2Cl_2 to get **30** (8.90g, 95%, yellow needle crystals). m.p.: 224-226 ^oC. ^1H NMR ($CDCl_3$) δ (ppm): 8.59 (dd, 4 H, J_1=6.8 Hz, J_2=3.3 Hz), 7.64 (dd, 4 H, J_1=6.8 Hz, J_2=3.3 Hz); IR: 577 cm^{-1} (C-Br stretching), 3028 cm^{-1} (C-H stretching).

30

9,10-Dichloromethylanthracene:[122a] Anthracene (1.83 g, 10.2 mmol), paraformaldehyde (1.56 g, 52 mmol) and 37% HCl (5 ml) was added into AcOH (30 ml). The solution was stirred at *ca.* 55 ^oC. After 18 hours, the reaction solution was cooled to room temperature and poured into water. After organic compounds were extracted with $CHCl_3$, the organic phase separated and washed with water. Then dried over $MgSO_4$ and $CHCl_3$ was evaporated. The residue was precipitated in Et_2O. Recrystalization of the residue in benzene gave **33** (1.40g, 50%, yellow solid). m.p.: >250 ^oC. ^1H NMR ($CDCl_3$) δ (ppm): 8.40 (dd, 4 H, J_1=6.8 Hz, J_2=3.3 Hz), 7.67 d, 4 H, J_1= 7.0 Hz J_2=3.3 Hz), 5.62 (s, 4 H). ^{13}C NMR ($CDCl_3$) δ (ppm): 130.2, 129.8, 126.7, 124.3, 38.8. IR: 782 cm^{-1} (C-Cl stretching).

33

9,10-Acetoxymethylanthracene:[122a] Compound **33** (0.35 g, 1.3 mmol), KOAc (0.41 g, 4.1 mmol), KI (3-4 crystals) was added into AcOH (20 ml). The mixture was refluxed at 120 ^oC for 1 day. It was cooled to room temperature and poured into ice water. Organic compounds were extracted with diethyl ether. Organic phase was washed with $NaHCO_3$ solution until the organic phase become neutral or slightly basic. Then ether phase was washed with brine and dried over $MgSO_4$. Ether was removed with rotary evaporator. Residue was recrystallized in EtOH to obtain **34** (0.34 g, 80%, yellow powder). m.p.: 220 ^oC. ^1H NMR ($CDCl_3$) δ (ppm): 8.40 (dd, 4 H, J_1=7.0 Hz, J_2=3.3 Hz), 7.63 (dd, 4H, J_1=7.0 Hz, J_2=3.3 Hz), 6.19 (s, 4H), 2.10 (s, 6 H). IR: 1725 cm^{-1} (C=O stretching), 1241 (C-O stretching, acyl), 1016 (C-O stretching, alkoxy).

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9,10-Anthracenedimethanol:[122a] Compound 34 (112 mg, 0.347 mmol) was added to KOH solution of EtOH (25 mg KOH in 20 ml EtOH). The solution was refluxed for 2 hours. Precipitation occurred by cooling the solution. The precipitate was collected and dried to obtain 9,10-anthracenedimetahnol (80 mg, 97%) ^{1}H NMR (DMSO-d_6) δ (ppm): 8.53 (dd, 4 H, J_1=7.0 Hz, J_2=3.3), 7.46 (dd, 4 H, J_1=6.8 Hz, J_2= 3.3 Hz), 5.41 (s, 4 H).

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9,10-Anthracenedicarboxylicacid: Chromium(III) oxide (1.638 g, 16.38 mmol) was dissolved in water (10 ml) and cooled to 0 ^{o}C. At this temperature, H_2SO_4 (1.7 ml) was added dropwise to obtain chromic acid solution. The solution was added dropwise into the solution of anthracene dimethanol (0.619 g, 2.6 mmol) in acetone (30 ml) at 0 ^{o}C. The reaction mixture was stirred overnight at room temperature. Excess oxidant was destroyed by addition of *i*-propanol (30 ml).The reaction was stirred for 30 minutes. Then, the volatiles were evaporated, the residue was acidified with 10 ml of 2 M HCl solution. The solution was cooled to 0 ^{o}C. The precipitates were collected with glass frit, washed with water, and dried to obtain **36** in (0.518 g, 75%, yellowish powder). m.p.: >250 ^{o}C. ^{1}H NMR (DMSO-d_6) δ (ppm): 8.25-8.20 (m, 4 H), 7.97-7.92 (m, 4 H). IR: 3320.82 cm^{-1} (O-H stretching), 1674.22 cm^{-1} (C=O stretching).

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2,2′-[Anthracene-9,10-diylbi(methylene)]dimalonicacidethylester:[136] Sodium (0.750 g, 32.6 mmol) and EtOH (100 ml) was added into dry flask. After solution completed, diethyl malonate (10.55 g, 66 mmol) was added to solution. Reaction temperature was set to 50 ^{o}C. At this temperature, dry benzene (150 ml) and **33** (0.207 g, 0.76 mmol) was added into the solution. The solution was refluxed for 4 hours and cooled to room temperature. Then the solution was neutralized with 10% HCl solution. Organic phase was separated and benzene was evaporated. The rest was diethyl malonate and product. The product precipitated in short time (0.318 g, 80%, yellow solid). Note: Excess diethyl

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malonate was stocked to precipitate. m.p.: 166-168 ^{o}C. ^{1}H NMR ($CDCl_3$) δ (ppm): 8.35-8.30 (m, 4 H), 7.56-7.50 (m, 4 H), 4.32 (d, 4 H, *J*=7.5 Hz), 4.13-3.98 (m, 8 H), 3.88-3.83 (m, 2 H), 1.06 (t, 12 H, *J*=7.2 Hz). IR: 1726 cm^{-1} (C=O stretching), 1215 (C-O stretching, acyl), 1026 cm^{-1} (C-O stretching, alkoxy).

2,2′-[Anthracene-9,10-diylbi(methylene)]dimalonicacid:[137] Compound **39** (400 mg, 0.766 mmol) was saponificated by the addition of 6 M NaOH solution (100 ml), MeOH (100 ml), $CHCl_3$ (5 ml). The reaction mixture was refluxed for 3 hours. Then pH was set to *ca.* 1. The precipitate was separated by filtration, and dried to obtain **40** (308 mg, 98%, pale yellow solid). m.p.: 249-251 ^{o}C. ^{1}H NMR (DMSO-d_6) δ (ppm): 12.85 (bs, 4H), 8.36 (m, 4 H), 7.56 (m, 4 H), 4.13 (d, 4 H, *J*=7.0 Hz), 3.65 (t, 2 H, *J*=7.0 Hz). IR: 2924 cm^{-1} (O-H stretching), 1698 cm^{-1} (C=O stretching).

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4-Oxo-2,2,6,6-tetramethylpiperidine:[138] NH_4SCN (0.33 g, 4.33 mmol) was added into acetone (47.46 g, 817 mmol). Gaseoues NH_3 was bubbled into the solution for 5 hours. During the first hour, the reaction was stirred in an ice bath, then stirred at room temperature. After 5 hours, nitrogen was passed through the solution. The solution was washed with 50% NaOH solution. Organic phase was separated and condensed below 35 ^{o}C to obtain acetonine **44**. ^{1}H NMR ($CDCl_3$) δ (ppm): 4.89 (bs, 1 H), 1.90 (s, 3 H), 1.81 (s, 2 H), 1.31 (s, 6 H), 1.05 (s, 1 H).

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Note: There was no need for further purification. It can be used in further reactions directly.

Acetonine (2.5 g, 16.2 mmol), $CaCl_2$ (2.4 g, 21.6 mmol), water (2 ml) and acetone (4.98 g, 85.8 mmol) was mixed and cooled to 0 ^{o}C. Then the reaction temperature was increased to 50 ^{o}C and reaction was stirred with reflux condenser for 22 hours. After cooling to room temperature, reaction mixture was washed with 50% NaOH (15 ml). Organic phase separated and dried over K_2CO_3. The organic phase was condensed below 50 ^{o}C to obtain 4-oxo-2,2,6,6-tetramethylpiperidine (1.5 g, 60%, oil) . ^{1}H NMR ($CDCl_3$) δ (ppm): 2.20 (s, 4 H), 1.17 (s, 12 H).

N,N'-bis(2,2,6,6-tetramethylpiperidin-4-yl)-1,4,5,8-naphtalenediimide:[112] NDA (100 mg, 0.375 mmol) and 2,2,6,6-tetramethylpiperidine (123mg, 0.780mmol) was added into DMF (15 ml). Reaction was refluxed overnight. After the reaction was completed, DMF was evaporated. The residue was washed with ether, and dried to obtain **48** (163 mg, 80%, pale brown powder). m.p.: >250 ^{o}C. ^{1}H NMR ($CDCl_3$) δ (ppm): 8.73 (s, 4 H), 5.66 (tt, 2 H, J_1=12.8 Hz, J_2=3.3 Hz), 2.46 (t, 4 H, J=12.3 Hz), 1.68 (m, 4 H), 1.39 (s, 12 H), 1.25 (s, 12 H).

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Anthraquinone-2-sulphonylchloride:[128] Anthraquinone-2-sulphonic acid sodium salt (5.05 g, 15.4 mmol), was covered by addition of sufficient $SOCl_2$ and DMF (0.5 ml) was added into the mixture. The reaction mixture was refluxed under N_2 atmosphere. After 2 hours, the reaction mixture was poured into ice-water mixture and filtered. The precipitate was collected. Column chromatography (EtOAc:Hex) gave **50** (4.01 g, 85%, pale yellow). m.p.: 177-179 ^{o}C. ^{1}H NMR ($CDCl_3$) δ (ppm): 8.99 (dd, 1H, J_1=2.0 Hz, J_2=0.5 Hz), 8.59 (d, 1 H, J=8.3 Hz), 8.43 (dd, 1 H, J_1=8.3 Hz, J_2=2.3 Hz), 8.41-8.36 (m, 2 H), 7.94-7.89 (m, 2 H). IR: 3097 cm^{-1}(C-H stretching), 1679 cm^{-1} (C=O stretching), 1585 cm^{-1} (C=C stretching), 1373 cm^{-1} (S-Cl stretching), 1287.8 cm^{-1} (S=O stretching).

50

Anthraquinone-2-sulphonyl-2,2,6,6-tetramethylpiperidine: Anthraquinone 2-sulphonyl chloride (1.79 g, 5.8 mmol) was dissolved in CH_2Cl_2. 4-amino-2,2,6,6-tetramethylpiperidine (0.90 g, 6.8 mmol) and pyridine (0.5 ml) was dissolved in CH_2Cl_2 in another erlenmeyer-flask and added into the reaction solution slowly. The reaction was stirred at room temperature overnight. CH_2Cl_2 was evaporated and the residue was washed with 10% HCl solution and water. Then, the residue was gave the protonated form of the product (1.98 g, 80%,

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brownish powder). The protonated product can be used for oxidation without further purification. m.p.: >250 ^{o}C. ^{1}H NMR (DMSO-d6) δ (ppm): 9.28-9.17 (m, 1 H), 8.56-7.99 (m, 8 H), 3.67-3.53 (m, 1 H), 1.62 (dd, 2 H, J_1=13.3 Hz, J_2=2.8 Hz), 1.54-1.42 (m, 2 H), 1.31 (s, 12 H). ^{13}C NMR (DMSO-d6) δ (ppm): 181.7, 181.5, 146.6, 135.4, 134.9, 134.8, 133.9, 133.1, 113.0, 131.1, 128.3, 126.9, 124.2, 123.7, 56.4, 44.5, 41.4, 29.5, 24.0. IR: 3154 cm^{-1} (N-H stretching), 1675 (C=O stretching), 1589 cm^{-1} (C=C stretching), 1286 cm^{-1} (S=O stretching). HRMS (ESI+) calc'd for $C_{23}H_{27}N_2O_4S^+$ 427.1692, found 427.1210.

The protonated form of **51** can be washed with saturated $NaHCO_3$ solution to obtain compound sodium salt of **51** (mp: >250 ^{o}C). The ^{1}H NMR spectrum of the sodium salt of **51** was added in the appendices.

Anthraquinone-2-sulphonyl-TEMPO: Compound **51** (150 mg, 0.350 mmol) was added into water (20 ml). The reaction mixture was slightly basified with $NaHCO_3$. $Na_2WO_4.2H_2O$ (6.92mg, 21x10^{-3} mmol), EDTA(4.09 mg, 14x10^{-3} mmol) and 30% H_2O_2 (158.6 mg, 1.4 mmol) were added to the reaction mixture and stirred at room temperature. After 3 days, the reaction solution was extracted with CH_2Cl_2 and the organic phase separated. CH_2Cl_2 was evaporated to obtain **25** (77.20 mg, 50%, brown powder). m.p.: 231-233 ^{o}C. IR: 3300 cm^{-1} (N-H stretching), 1674 cm^{-1} (C=O stretching), 1587 cm^{-1} (C=C stretching), 1367 cm^{-1} (N-O$^{\cdot}$ stretching), 1285 cm^{-1} (S=O stretching); HRMS (ESI+) calc'd for $C_{23}H_{25}N_2O_5SNa^+$ 464.1367, found 464.1382.

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Anthraquinone-2-sulphonyl methylamine: The same procedure was applied with synthesis of **51**. m.p.: 188-190 ^{o}C. ^{1}H NMR ($CDCl_3$) δ (ppm): 8.78 (d, 1 H, J=1.8 Hz), 8.49 (d, 1 H, J=8.0 Hz), 8.38-8.33 (m, 2 H), 8.30-8.26 (m, 1 H), 7.90-7.84 (m, 2 H), 4.73-4.66 (m, 1 H), 2.77 (d, 3 H, J=5.3 Hz). ^{13}C NMR ($CDCl_3$) δ (ppm): 181.9, 181.7, 144.6, 135.8, 134.7, 134.1, 133.2, 132.0, 128.5, 127.6, 126.1, 29.4. IR: 3296 cm^{-1}(N-H stretching), 1671 cm^{-1} (C=O stretching), 1588 cm^{-1} (C=C stretching), 1286 cm^{-1} (S=O stretching).

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General Procedure for alcohol oxidation: Benzyl alcohol (32.4 mg, 0.300 mmol), ZnO (50.0 mg, 0.614 mmol), compound **4** (20.0 mg, 0.047 mmol), $AgNO_3$ (917.2 mg, 5.400 mmol) was added into 5 ml water. Stirred at room temperature under light (λ>350nm) for 1-18 hours (monitored with TLC, shown in **Figure 11**. After reaction was completed, organic compounds were extracted with CH_2Cl_2 from the reaction mixture. CH_2Cl_2 was separated, dried over $MgSO_4$, and volatiles were evaporated to get the aldehydes.

Benzaldehyde (15):[132] ^{1}H NMR ($CDCl_3$) δ (ppm): 10.04 (s, 1 H), 7.94-7.86 (m, 2 H), 7.68-7.61 (m, 1 H), 7.59-7.51 (m, 2 H).

4-Nitrobenzaldehyde (53):[132] ^{1}H NMR (CDC_3) δ (ppm): 10.16 (s, 1 H), 8.43-8.38 (m, 2 H), 8.10-8.06 (m, 2 H).

4-Methoxybenzaldehyde (54):[132] ^{1}H NMR (CDC_3) δ (ppm): 9.89 (s, 1 H), 7.87-7.82 (m, 2 H), 7.03-6.98 (m, 2 H), 3.89 (s, 3 H).

3-Pyridinecarboxaldehyde (55):[133] ^{1}H NMR (CDC_3) δ (ppm): 10.15 (s, 1 H), 9.11 (s, 1 H), 8.90-8.86 (m, 1 H), 8.26-8.20 (m, 1 H), 7.55 (dd, 1 H, J_1=7.8 Hz, J_2=4.8 Hz).

4-Pyridinecarboxaldehyde (56):[134] ^{1}H NMR (CDC_3) δ (ppm): 10.12 (s, 1 H), 8.94-8.90 (m, 2 H), 7.79-7.75 (m, 2 H).

4-Fluorobenzaldehyde (57):[132] ^{1}H NMR (CDC_3) δ (ppm): 9.98 (s, 1 H), 7.96-7.90 (m, 2 H), 7.26-7.20 (m, 2 H).

3-Fluorobenzaldehyde (58):[135] ^{1}H NMR (CDC_3) δ (ppm): 10.04 (d, 1 H, J=1.5), 7.85-7.53 (m, 4 H).

Cinnamaldehyde (59):[132] ^{1}H NMR (CDC_3) δ (ppm): 9.72 (d, 1 H, J=7.8 Hz), 7.62-7.43 (m, 6 H), 6.74 (dd, 1 H, J_1=7.8 Hz, J_2=16.1 Hz).

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APPENDICES

PART A: NMR SPECTRUMS

NMR spectra was recorded at 400 MHz Bruker NMR spectrometer with using $CDCl_3$ and DMSO-d_6.

Figure A1 ^{1}H NMR spectrum of **14**

Figure A2 ^{1}H NMR spectrum of **15**

Figure A3 ^{13}C NMR spectrum of **15**

Figure A4 ^{1}H NMR spectrum of **11**

Figure A5 ^{1}H NMR spectrum of **8**

Figure A6 ^{13}C NMR spectrum of **8**

Figure A7 COSY NMR spectrum of **8**

Figure A8 ^{13}C DEPT-90 NMR spectrum of **8**

Figure A9 ^{13}C DEPT-135 NMR spectrum of **8**

Figure A10 HSQC NMR spectrum of **8**

Figure A11 HMBC spectrum of **8**

Figure A12 ^{1}H NMR spectrum of **26**

Figure A13 ^{13}C NMR spectrum of **26**

Figure A14 ^{1}H NMR spectrum of **27**

Figure A15 ^{1}H NMR spectrum of **30**

Figure A16 ^{1}H NMR spectrum of **33**

Figure A17 ^{13}C NMR spectrum of **33**

Figure A18 ^{1}H NMR spectrum of **34**

Figure A19 ^{1}H NMR spectrum of **35**

Figure A20 ^{1}H NMR spectrum of 3**6**

Figure A21 ^{1}H NMR spectrum of **39**

Figure A22 COSY NMR spectrum of **39**

Figure A23 ^{1}H NMR spectrum of **40**

Figure A24 ^{1}H NMR spectrum of **45**

Figure A25 ^{1}H NMR spectrum of **48**

Figure A26 COSY NMR spectrum of **48**

Figure A27 ^{1}H NMR spectrum of **50**

Figure A28 ^{1}H NMR spectrum of the protonated form of **51**

Figure A29 ^{1}H NMR spectrum of the sodium salt of **51**

Figure A30 ^{13}C NMR spectrum of the protonated form of **51**

Figure A31 COSY NMR spectrum of the protonated form of **51**

Figure A32 ^{13}C DEPT-90 NMR spectrum of the protonated form of **51**

Figure A33 ^{13}C DEPT-135 NMR spectrum of the protonated form of **51**

Figure A34 HSQC NMR spectrum of the protonated form of **51**

Figure A35 HMBC NMR spectrum of the protonated form of **51**

Figure A36 ^{1}H NMR spectrum of **52**

Figure A37 ^{13}C NMR spectrum of **52**

PART B: IR SPECTRUMS

IR spectra were recorded at ATR-IR spectrometer.

Figure A38 IR spectrum of **14**

Figure A39 IR spectrum of **15**

Figure A40 IR spectrum of **5**

Figure A41 IR spectrum of **11**

Figure A42 IR spectrum of **8**

Figure A43 IR spectrum of **4**

Figure A44 IR spectrum of **26**

Figure A45 IR spectrum of **30**

Figure A46 IR spectrum of **33**

Figure A47 IR spectrum of **34**

Figure A48 IR spectrum of **36**

Figure A49 IR spectrum of **39**

Figure A50 IR spectrum of **40**

Figure A51 IR spectrum of **48**

Figure A52 IR spectrum of **50**

Figure A53 IR spectrum of **51**

Figure A54 IR spectrum of **25**

Figure A55 IR spectrum of **52**