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Copper Nanoparticles in Ionic Liquid: An Easy and Efficient Catalyst for Selective Carba-Michael Addition Reaction

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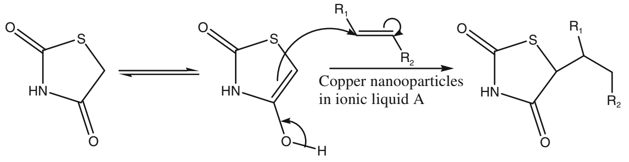
Abstract In this paper, we wish to report a novel synthesized copper nanoparticles in an ionic liquid employed as a catalyst for Michael addition between active methylene compound and α, β-unsaturated compounds to give corresponding compounds in excellent yield and in shorter reaction times.



Keywords Copper nanoparticles · Ionic liquid · Active methylene compounds · α, β—Unsatuated compounds

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1 Introduction

Recently, research has been directed towards the synthesis and application of metal nanoparticles in view of their unique properties compared to the bulk metals [1, 2]. Among various metal nanoparticles, copper and gold nanoparticles have received considerable attention because of their unusual properties and potential applications in diverse fields [3]. The various synthetic procedures for their synthesis include micro-emulsion [4], reverse micelles [5], reduction of aqueous copper salts [6], UV-light irradiation [7], physical vapor deposition [8] and impregnation methods [9, 10]. The core-shell particles are of great interest due to their potential applications in diverse fields including catalysis, drug delivery, photonics, sensors, etc. [11].

The classical Michael type reactions are certainly very importnat but need quite severe reaction conditions and thereby causing limitations [12] in their use in practice. However, these reactions require either basic or acidic catalysts [13], which seem to be detrimental to the desired synthesis. In order to overcome some of the disadvantages, a number of alternative procedures for the Michael addition have been reported over the past few years using $Yb(OTf)_3$, $InCl_3$, $CeCl_3 . 7H_2O$, $Bi(NO)_3$, $Bi(OTf)_3$, $Cu(OTf)_2$, $FeCl_3 \cdot 7H_2O/Co(OAc)_2$, $LiClO_4$ and boric acid [14–16]. Several heterogeneous catalysts, such as silica gels, copper nanoparticles, and $CeCl_3 \cdot 7H_2O/NaI$ system [17] have been reported. There is considerable interest in the use of ionic liquids as promising substitutes for volatile organic solvents.

Copper nanoparticles are highly efficient for the aza-Michael addition and thia-Michael addition reaction and they have been used in organic solvents which are very toxic in nature [18–21]. Copper nanoparticles are particularly attractive, being cheap (they can be prepared from $Cu(NO_3)_2$, are high yielding, need mild reaction conditions and are recyclable. Rothenberg and co-workers have recently reported the use of copper nanoparticles, which are less harmful to the environment than any other metals in Suzuki cross coupling reactions [20, 21]. Ionic liquids have been employed as reaction media for several organic reactions, namely alkylation [22], hydrogenation [23], oxidation [24–26]. Because of their tunable polarity and hydrophobicity, they can solvate various organic, inorganic, and polymeric compounds, and have been used as green solvents for liquid–liquid separations, extractions, and recycling in homogeneous catalysis.

Here, we used copper nanoparticles in an ionic liquid for selective carba-Michael addition i.e., C–C bond formation as well C–S and C–N bond formation. Ionic liquids are non-volatile and non-toxic in nature and known as green solvents [27].

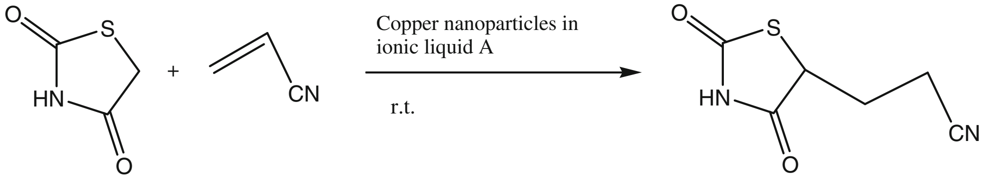
As per Table 1, the reaction yield and duration of time changes with the change of the catalyst. As every catalyst has different affinity with the reactants i.e., variation in the selectivity of products found. In Table 1, entry (1–3), there is lot of difference in the yields and duration of time. In entry 1–3, the yields are 65, 75 and 90% but this is not the only factor but also the duration of reaction also play an important role in this. By using copper nanoparticles in ionic liquid A the duration of reaction is very short in comparison with the reaction having no catalyst and copper nanoparticles alone. In entry 1 and 2 the duration of reactions is more and the yields are less with less selectivity.

Thiazolidine-2, 4-dione is a five member heterocyclic compound and it has three types of function groups, first is secondary amine (N–H), second is carbonyl (C=O) and third is active methylene group (CH_2). CH_2 present in thiazolidine-2, 4-dione is bonded with carbon of carbonyl and sulfur and both are electron withdrawing in nature that's why CH_2 becomes active methylene. In Michael addition i.e., between thiazolidine-2, 4-dione and α, β-unsaturated compound in mole ration of 1:1, double bond can react with secondary amine (N–H) and active methylene group (CH_2) but it reacts only with active methylene group not with N–H. But if the ratio is different means if α, β-unsaturated compound is more than thiazolidine-2, 4-dione than it can also reacts with N–H after the reaction with CH_2.

Ionic liquid is used for the stabilization of copper nanoparticles and also act as a green solvent as well ionic liquid can be recovered.

The ionic liquid used for Michael addition is only in entry 3 not in entry 1 and 2. Copper nanoparticles synthesized in the same manner. Here I am also incorporating the data for the reaction done in organic solvents. Amongst organic solvents methanol, ethanol and acetonitrile, acetonitrile is the best solvent for Michael addition as in entry 6-8 (Table 1). That's why we used acetonitrile with copper nanoparticles as in entry 9. But on comparing entry 2, entry 3 and entry 9, the catalyst used are copper nanoparticles, copper nanoparticles in ionic liquid A and copper nanoparticles in acetonitrile and we found that copper nanoparticles in ionic liquid A is best amongst these catalyst for Michael addition.

Table 1 Optimization of the catalyst for the Michael addition (Table 2, Entry 1)



Entry	Catalyst	Time (min)	Conversion (%)	Yield (%)
1	Blank	45	70	65
2	Copper nanoparticles	8	78	75
3	Copper nanoparticles in ionic liquid A	5	98	90
4	$InCl_3$	15	80	75
5	Phosphotungstic acid	20	75	70
6	Methanol	45	70	65
7	Acetonitrile	40	72	68
8	Ethanol	42	71	66
9	Copper nanoparticles in acetonitrile	20	85	78

As our ongoing research was on the catalytic applications of copper nanoparticles. The synthesized core-shell nanoparticles are well characterized by XRD and TEM techniques [28, 29] and employed as a recyclable catalyst for Carba-Michael addition of active methylene compound with α, β—unsatuated compounds selectively as in Scheme 1a as well as for hetero-Michael addition at room temperature as in Scheme 1b and c to produce the corresponding adducts in very high yields in short reaction time (Schemes).

2 Experimental

2.1 Reagents and Analysis

The chemicals were purchased from Sigma-Aldrich and Merck and used without purification. ^{1}H-NMR and ^{13}C-NMR (300 MHz.) spectrums were recorded on a Bruker Spectrospin 300 MHz spectrometer. MS spectrums were recorded on TOF-Mass spectrometer Model No. KC455. IR spectrums were recorded on Spectrum Bx2 IR.

2.2 Synthesis of Catalyst

2.2.1 Synthesis of Ionic Liquid A

In a 50 mL round bottom flask, 20 mmoL of 1-*H*-tetrazole-5-acetic acid and 25 mmoL of acrylonitrile in 50 mL of acetonitrile were stirred for 2 h. The extent of the reaction was monitored by TLC. On completion, the solvent and excess acrylonitrile were removed under reduced pressure. To 10 mmoL of the above compound in 25 mL of acetonitrile, 15 mmoL of bromobutane was added. The mixture was refluxed for 6 h and then the solvent and excess bromobutane were evaporated under reduced pressure to afford the ionic liquid **A** (yield 92%) (Fig. 1).

2.2.2 Synthesis of Copper Nanoparticles in Ionic Liquid A

In round bottom flask, 2 mL of the ionic liquid A and 10 mg of copper nitrate was treated with excess sodium borohydride solution. A black colored solution was obtained rapidly indicating the presence of Cu (0) particles. Stirring was continued for 6 h. One drop of the Cu nanoparticles dispersed in ionic liquid was taken carbon coated copper grid and analyzed by TEM. The remaining Cu nanoparticles dispersed in ionic liquid were taken in methanol (50 mL) and then centrifuged at 3,000 rpm for 10 min and the supernatant was decanted and the solid was analyzed by powder XRD technique [28, 29].

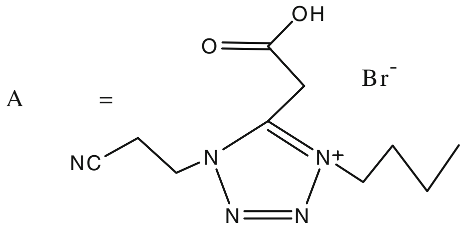


Fig. 1 Ionic liquid A

2.3 General Procedure for the Synthesis of Carba-Michael Addition Derivatives

In a typical experiment, the mixture of catalyst (0.005 g), thiazolidine-2, 4-dione (10 mmoL) and unsaturated compound (10 mmoL) in ionic liquid A (3 mL) were stirred at room temperature for the appropriate time. After completion of the reaction, as indicated by TLC, the product was extracted with ethyl acetate (3 × 10 mL). The combined organic extracts were concentrated in vacuum and the resulting product was purified by column chromatography on silica gel with ethyl acetate and *n*-hexane (2:8) as eluent to afford the pure product. The material left containing the catalyst was preserved for the next run. Structural characterizations of the products are based on their ^{1}H-NMR, ^{13}C-NMR, IR and mass analysis. The analysis of complete spectral and compositional data revealed the formation of Carba-Michael addition derivatives in 85-95% yield (Table 2). The above method also works equally for the other active methylene compounds see Table 1.

The same procedure followed for the hetero-Michael addition reaction between thiol/amines derivatives and α, β-unsaturated compounds. The analysis of complete spectral and compositional data revealed the formation of aza-Michal and thia-Michael addition derivatives in 85–95% yield (Table 3) and also confirmed by literature [30–33].

3 Results and Discussion

3.1 Catalytic activity of Copper Nanoparticles

To explore the potential activity of the synthesized Cu nanoparticles for the conjugate addition of a variety of α, β-unsaturated compounds such as methyl acrylate, acrylonitrile, 4-chlorostyrene, acrylates underwent 1, 4 addition with active methylene compounds like thiazolidine-2,4-dione in the presence of 5 mg Cu nanoparticles in ionic liquid at room temperature to give the corresponding compounds in high yields and in shorter duration and the results are summarized in Table 2. All the reactions were able to undergo the corresponding conjugate additions well within 5–30 min and the yields of the desired Michael

Table 2 Selective Carba-Michael addition of active methylene carbon with α, β—unsatuated compounds catalyzed by copper nanoparticles in ionic liquid A[a]

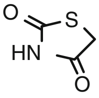
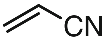
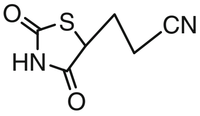
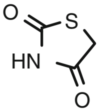
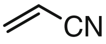
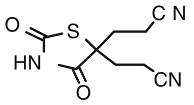
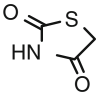
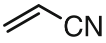
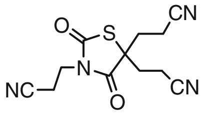
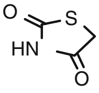
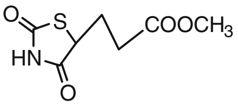
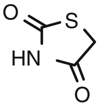
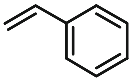
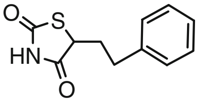
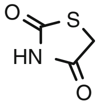
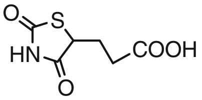
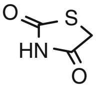
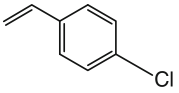
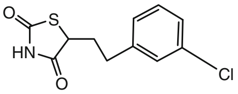
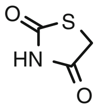
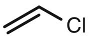
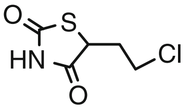
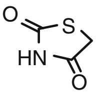
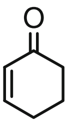
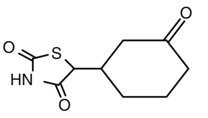
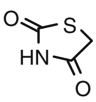
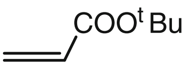
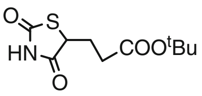
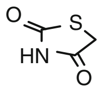
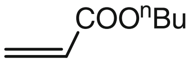
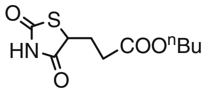
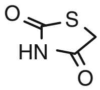
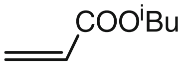
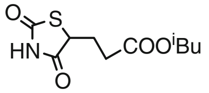
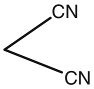
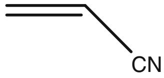
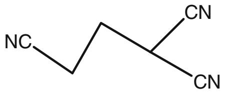
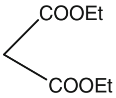
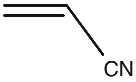
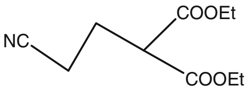
Entry[a]	Reactant[1]	Reactant[2]	Products	Time (minutes)	Yield (%)
1				5	90
2				9	85
3				15	82
4				7	85
5				9	82
6				10	85
7				10	92
8				8	96
9				15	90
10				12	82
11				9	88
12				10	85

Table 2 continued

Entry[a]	Reactant[1]	Reactant[2]	Products	Time (minutes)	Yield (%)
13				4	92
14				8	88

[a] All reactions were carried out using copper nanoparticles (0.005 g) in ionic liquid A, active methylene compound (10 mmoL), unsaturated compound (10 mmoL), r. t.

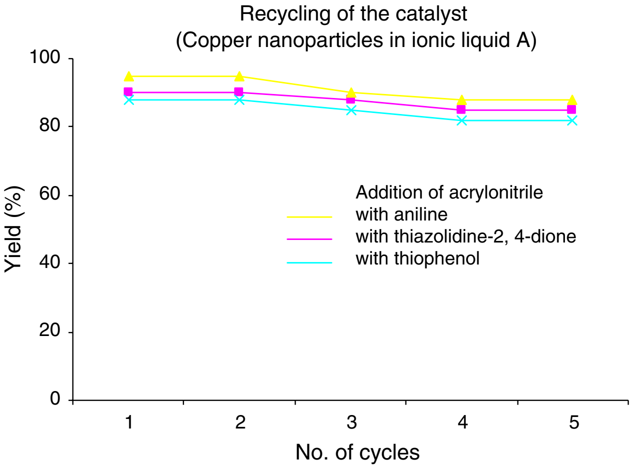


Fig. 2 Graph 1 recycling of the catalyst

adducts were good to excellent. Branched acrylates such as *iso*-butyl and *tert*-butyl acrylate required slightly longer reaction times than *n*-butyl acrylate.

Encouraged by the versatility and effectiveness of the catalyst for the Carba-Michael addition reaction, we attempted to study the hetero-Michael addition of unsaturated esters with thiols/amines (Scheme 1b and c). At room temperature, thiol/amines derivatives were introduced with alkenes to afford the corresponding Michael adducts in good yields and the results are presented in Table 3. In other words, this catalytic system also equally a good choice for the hetero-Michael addition between unsaturated compounds and thiols/amines.

We conduct the experiments for the addition reaction of thiazolidine–2, 4-dione, aniline and thiophenol individually with acrylonitrile for showing recycling

Scheme 1

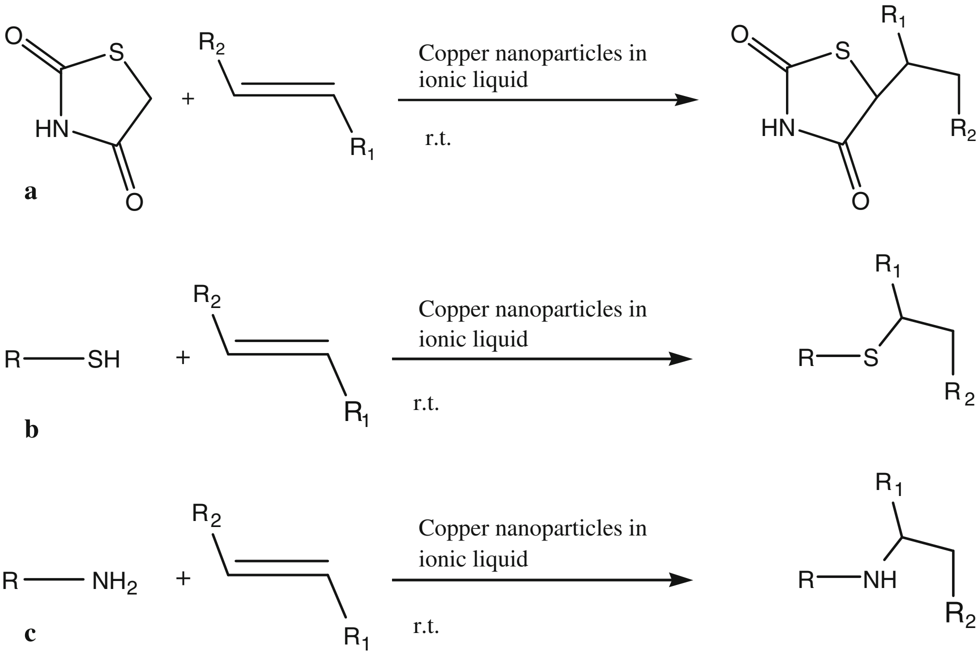
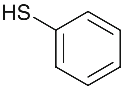
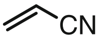
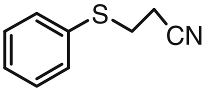
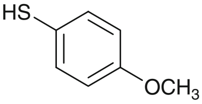
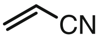
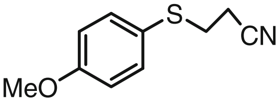
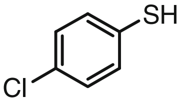
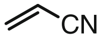
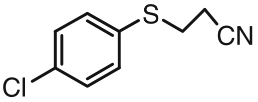
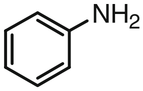
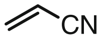
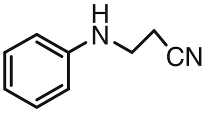
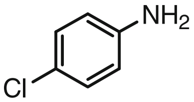
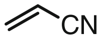
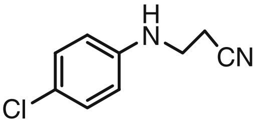
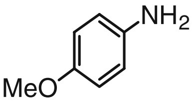
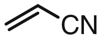
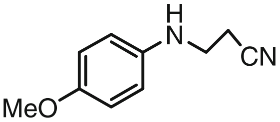


Table 3 Michael addition of thiols/amines with α, β—unsatuated compound catalyzed by copper nanoparticles in ionic liquid **A**[a]

S. No.	Reactant[1]	Reactant[2]	Product	Time (minutes)	Yield (%)
1				5	92
2				8	90
3				4	95
4				7	88
5				5	95
6				10	88

[a] All reactions were carried out in copper nanoparticles (0.005 g) in ionic liquid **A**, thiols/amines (10 mmoL), acrylonitrile (10 mmoL), r. t.

potential of catalyst for five cycles. We observed a gradual loss of activity of catalyst used in experiment with cycle (Fig. 2).

4 Conclusions

In summary, we have shown that the synthesized Cu nanoparticles in an ionic liquid A catalyzed Carba-Michael addition of active methylene compound with α, β-unsaturated compounds to give their corresponding compounds in high yields and in shorter reaction times. Extension of this method to thiols/amines afforded the corresponding Michael adducts in excellent yields. Our protocol avoids the use of expensive reagents, high temperatures and serves as an efficient method and also allows easy recyclability of the catalyst. It is remarkable that the reaction can be performed in ionic liquid which makes the procedure quite simple, more convenient and environmentally benign. Cu nanoparticles were well characterized by TEM and XRD techniques. Further catalytic applications of copper nanoparticles for addition reactions with complex structures of biological significance are currently under investigation.

5 Spectroscopic Data of Few Selected Compounds (Table 2)

(a) With Acrylonitrile (Entry 1)

IR (KBr): νmax (cm^{-1}) 3131, 1748, 1673, 2247. ^{1}H NMR (DMSO) δ 12.03 (s, NH, 1H), δ 4.37 (d, CH, 1H), δ 4.1(q, CH_2, 2H), δ 3.7(t, CH_2, 2H); ^{13}C NMR (DMSO) δ 171.77 (S-CO-NH), δ 174.03(S-CO-CH), δ 118 (CN), δ 40.32(CH), δ 39.23(CH_2), δ 34.08(CH_2); HRMS (M^{+}):: 170.0257

(b) With Methylacrylic Acid (Entry 4)

IR (KBr): νmax (cm^{-1}) 3433, 3128, 1749, 1735, 1695. ^{1}H NMR (DMSO) δ 9.06(s, O, 1H), δ 8.57(s, NH, 1H), δ 3.01 (d, CH, 1H), δ 2.57 (t, CH_2, 3H), δ 3.01 (q, CH, 1H), δ 1.83 (q, CH_3, 3H); ^{13}C NMR (DMSO) δ 145.89 (S-CO-NH), δ 168.86 (O-CO-CH_2), δ 175.01(COOH), δ 63.5 (CH), δ 40.03 (CH_2), δ 38.94 (CH), δ 18.47 (CH_3).

(c) With Styrene (Entry 5)

IR (KBr): νmax (cm^{-1}) 3133, 1738, 1654, 2900. ^{1}H NMR (DMSO) δ 11.6 (s, NH, 1H), δ 4.55 (d, CH, 1H), δ 4.35(q, CH_2, 2H), δ .41(q, CH_2, 2H), δ 7.1–7.5(m, aromatic, 5H); ^{13}C NMR (DMSO) δ 149.32(S-CO-NH), δ 174.21(S-CO-CH), δ 40.05(CH), δ 39.50(CH_2), δ 38.95(CH_2), 121.06–149.32(aromatic carbon); HRMS (M^{+}):: 170.0257.

(d) With Acrylic Acid (Entry 6)

IR (KBr): νmax (cm^{-1}) 3419, 3128, 1734, 1693, 1654. ^{1}H NMR (DMSO) δ 8.57 (s, OH, 1H), δ 7.7 (s, NH, 1H), δ 4.08 (d, CH, 1H), δ 3.72(q, CH_2, 2H), δ 3.56(q, CH_2, 2H); ^{13}C NMR (DMSO) δ 167.59(S-CO-NH), δ 174.35(O-CO-CH_2), δ 174.21(S-CO-CH), δ 40.08(CH), δ 39.77(CH_2), δ 38.95(CH_2).

(e) With Vinylchloride (Entry 8)

IR (KBr): νmax (cm^{-1}) 3413, 1747, 1693. ^{1}H NMR (DMSO) δ 9.24 (s, NH, 1H), δ 4.42 (d, CH, 1H), δ 3.20 (q, CH_2, 2H), δ 4.17 (t, CH_2, 2H); ^{13}C NMR (DMSO) δ 146.48 (S-CO-NH), δ 174.65 (S-CO-CH), δ 63.11 (CH), δ 39.79 (CH_2), δ 36.61(CH_2).

(f) With *n*-Butylacrylate (Entry 11)

IR (KBr): νmax (cm^{-1}) 3128, 1737, 1686, 1669. ^{1}H NMR (DMSO) δ 8.56 (s, NH, 1H), δ 4.30 (d, CH, 1H), δ 1.54–4.86 (m, CH_2, 10H), δ 1.36(q, CH_3, 3H); ^{13}C NMR (DMSO) δ 149.70(S-CO-NH), δ 174.27(O-CO-CH_2), δ 173.55 (O-CO-CH_3), δ 40.05(CH), δ 39.50(CH_2), δ 38.95(CH_2), δ 38.0–39.0 for 3 (CH_2), δ 36.10(CH_3).

(g) With t-Butylacrylate (Entry 12)

IR (KBr): νmax (cm^{-1}) 3132, 1737, 1690, 1654; ^{1}H NMR (DMSO) δ 10.46 (s, NH, 1H), δ 4.85 (d, CH, 1H), δ 4.17 (q, CH_2, 2H), δ 3.88(m, CH_2, 2H), δ 3.11(s, CH_3, 9H); ^{13}C NMR (DMSO) δ 149.80(S-CO-NH), δ 174.18(O-CO-CH_2), δ 173.49(O-CO-CH_3), δ 40.03(CH), δ 39.46(CH_2), δ 38.65(CH_2), δ 36.11(CH_3).

5.1 Spectroscopic Data of Ionic Liquid A

IR (KBr): νmax (cm^{-1}) 3398, 2962, 2361, 1749, 1635; ^{1}H NMR (DMSO) δ 9.39 (σ, OH, 1H), δ 4.7–5.6 (m, CH, 6H), δ 0.7–1.9 (m, CH, 10H); ^{13}C NMR 168.05 (CN), 166.75 (C=O), 146.92 (C=N), 145.37 (C–N), 30–65 (8 × C–H).

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