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SYNTHESIS AND CHARACTERISATION OF QUINOLINE FUNCTIONALISED IMIDAZOLIUM SALTS

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ABSTRACT
A series of quinoline based imidazolium salts were prepared and characterised as nucleophilic heterocyclic carbene (NHC) ligand precursors. The symmetrically saturated imidazolium salt prepared by ring closure of achiral tetradentate diquinolyl-diamine with triethyl orthoformate is a tridentate ligand and can function as pincer ligand while the two asymmetric imidazolium salts are bidentate and have different steric bulk which may have interesting implication in catalysis. The solubility of the symmetrical dihydroimidazolium salt was enhanced by replacing the counter ion tetraflouroborate with tetrakis (3,5-bis(triflouromethyl)phenyl)borate (Barf) and its structure confirmed by X- ray crystallography.

Keywords: Nucleophilic heterocyclic carbene (NHC), Imidazolium salt, ligand, ring closure. Barf

INTRODUCTION

The use of N- heterocyclic carbene (NHC) ligands is currently receiving much attention because of their wide applicability in coordination chemistry and catalysis. Monodentate NHC ligands have demonstrated remarkable activities in palladium-catalysed C-C coupling reactions. Recently, research efforts have also been devoted to the synthesis of polydentate ligands based on NHC. Specifically, the combination of pyridine and NHC functionalities attracts a considerable amount of interest ((Danopoulos *et al*. 2003). The ease of synthesis of imidazolium salts is one of the chief reasons for the popularity of NHCs. Other attractive features of imidazolium based NHCs are the wide variety of steric and asymmetric environments that are available through modification of the substituents on the nitrogen of the heterocycle. Furthermore, through the use of appropriate donor groups on the nitrogen substituents, it is possible to make multidentate NHC ligands. Such variability makes possible the synthesis of numerous ligands. Along these lines Cavell *et al.* (2005), Crabtree (2006) and Danopoulos *et al*. (2002) have reported wide variety of multidentate pyridyl functionalised ligands. Multidentate ligands especially those that can behave as a chelating ligand having both strong and weak donors (hemilabile ligands) are particularly important in catalysis. The weak hemilabile part of the ligand is capable of reversible dissociation from metal centre, thereby creating vacant coordinating sites during catalytic cycles and stabilising the metal centre by recoordinating when it is catalytically inactive. In addition to the works so far reported on pyridyl ligands, we envisioned the synthesis of an analogue of the quinoline framework. It was our hope that replacing the relatively small pyridine with large quinoline substituents will provide greater rigidity and hence stability to the complexes, though, the rigid structures also lead to steric crowding. The synthesis of a series of quinoline based imidazolium salts was successfully achieved and is hereby presented.

MATERIAL AND METHODS

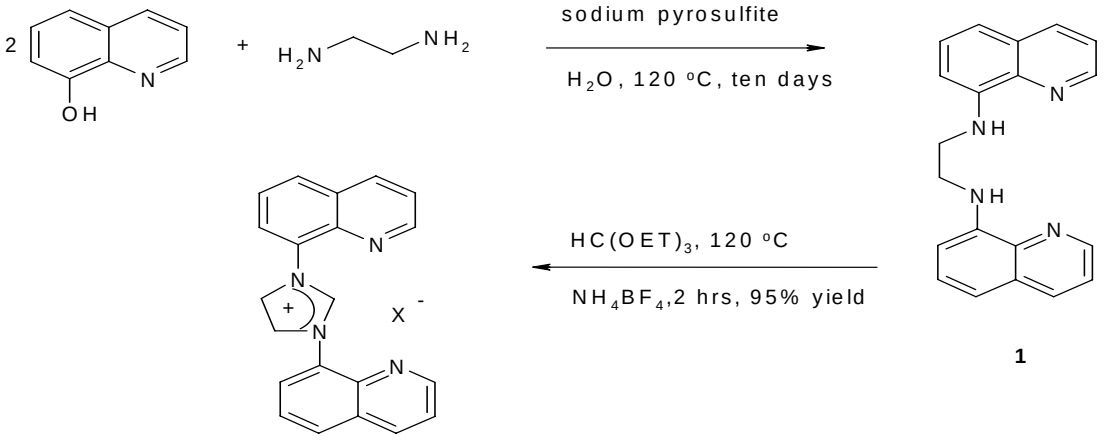
This research work was carried at Cardiff University, CF10 3AT, Wales, UK.

Unless otherwise stated all manipulations were carried out using standard Schlenk techniques under an atmosphere of dry argon or in an MBRAUN M72 glove box (N_2 atmosphere with 1ppm O_2 and H_2O). Glassware were dried overnight in an oven at 120^{o}C or flame dried prior to use. Tetrahydrofuran (THF), diethyl ether (Et_2O), and hexane were dried and freshly distilled before used. Dichloromethane (DCM), methanol (MeOH) and acetonitrile (MeCN) were dried over calcium hydride. All other anhydrous solvents were obtained by distillation from the appropriate drying agent under dinitrogen. Deoxygenation of solvents and reagents was carried out by freeze-thaw- degassing.

All NMR solvents were purchased from Aldrich and Goss, dried over 3Å molecular sieves and freeze-thaw degassed three times. All reagents were purchased from commercial sources and used without purification, unless otherwise stated.

All NMR data are quoted as δ in ppm. ^{1}H and ^{13}C spectra were recorded on a Bruker 400 MHz DPX Avance, unless otherwise stated, and referenced to TMS. Electrospray mass spectrometry (ESMS) was performed on a VG Fisons Platform II instrument by the department of Chemistry, Cardiff University. Micro analysis was performed by Warwick Analytical Service.

Preparation of Symmetrically saturated bis(1,3- quinoline) imidazolium salt



Scheme 1: Synthesis of quinoline functionalised dihydroimidazolium salt

Synthesis of N, N-Diquinolinethane -1, 2-diamine (1):

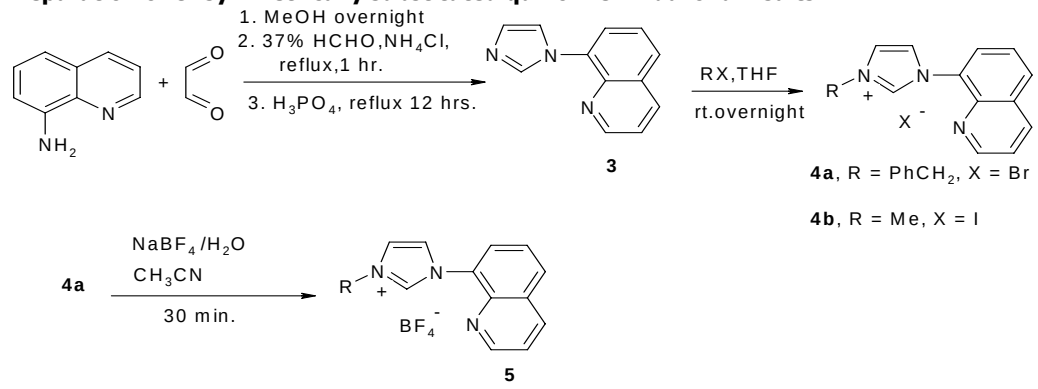
A mixture of 8-hydroxyquinoline (36.25 g, 0.25 mol), 1,2-diaminethane (9.75 g, 0.125 mol), sodium pyrosulfite (47.5 g , 0.25 mol) and water (250mL) was refluxed and stirred for ten days. The solution was made strongly alkaline, cooled and filtered. The solid product was extracted several times with hot 0.2N NaOH until removal of 8-quinolinolate was complete and the residue was recrystallised from ethanol to give the desired product as a light yellow solid (6.00g 16 %).^{1}H NMR ($CDCl_3$, 400MHz 298K): 8.6(m, 2H, J = 2.6 $H_{Z,}$ Quin-H),), 8.0(m, 2H, J = 6.8 $H_{Z,}$ Quin-H),), 7.3(m, 4H, J = 7.7 $H_{Z,}$ Quin-H), 7.0(m, 2H, J = 7.5 $H_{Z,}$ Quin-H), 6.7(m, 2H, J = 8.0 $H_{Z,}$ Quin-H), 6.35(b, 2H,CNH), 3.7(s,4H,NCH_2), ^{13}C NMR ($CDCl_3$ 72.5MHz R.T): 146.94, 144.68, 138.34, 136.01, 128.73, 127.77, 121.46, 114.23, 104.77(quin-C), 42.79(NCCN).

Synthesis of 1, 3-diquinolin-4, 5-dihydroimidazoluim tetraflouroborate (2):

N, N'-diquinolinethane-1, 2-diamine (0.3g 0.58mmol) and NH_4BF_4 (0.095g, 0.58mmol) in triethyl orthoformate were heated at 120°C for 2 hours. The precipitate which was isolated was washed several times with diethyl ether and recrystallised from $CHCl_3$/Diethyl ether to afford the desired product 0.3g (85%). Analytically Calculatedd for $C_{21}H_{17}N_4BF_4$: C, 61.19; H, 4.13; N, 13.60; F, 18.46%.

Found: C, 59.06; H, 4.01; N, 13.48; F, 19.04%. HRMS: Calculated for $C_{21}H_{17}N_4BF_4$: 325.1453. Found: 325.1437. ^{1}H NMR (DMSO-d_6, 400MHz R.T):11.40(s, 1H, NCHN), 9.20(m, 2H, J = 2.6 $H_{Z,}$ Quin-H), 8.70(m, 2H, J = 1.2 $H_{Z,}$ Quin-H), 8.20(m, 2H, J = 8.2 $H_{Z,}$ Quin-H), 8.10(m, 2H, J = 8.0 $H_{Z,}$ Quin-H), 7.90(m, 2H, J = 8.0 $H_{Z,}$ 7.8(m, 2H, J = 4.2 $H_{Z,}$ Quin-H), 4.95(s, 4H, NCH_2CH_2N). ^{13}C NMR (DMSO-d6, 72.5MHz R.T.): 158.91(NCN), 150.95(quin-C), 139.98(quin-C), 137.35(quin-C), 132.52(quin-C), 128.97(quin-C), 127.87(quin-C), 126.60(quin-C), 122.81(quin-C), 49.99(im-C).

Preparation of Unsymmetrically substituted quinoline imidazolium salts



Scheme 2: **Synthesis of unsymmetrically substituted quinoline imidazolium salts**

Synthesis of Imidazol-1-yl-quinoline (3):
8-aminoquinoline (2.27 g, 8.8 mmol) was mixed with 40% glyoxal (1.22 g, 8.8 mmol) in 30 mL MeOH and stirred overnight at room temperature to give a yellow mixture. NH_4Cl (0.94 g, 17,6 mmol) and 37% aq formaldehyde (1.42 g, 17.6 mmol) were then added to the mixture which was then diluted by further addition of 150 ml MeOH. This was refluxed for an hour and H_3PO_4 (1.6 mL.85 %) was slowly added to the mixture before heating to reflux for 12 hours. After removal of the solvent the dark residue was poured on to ice (100g) and neutralised with aqueous 40% KOH until pH 9. The resulting mixture was then extracted with diethyl ether (4 x 100 mL). The ethereal phase was then washed with water, brine and dried with Na_2SO_4. The solvent was then removed to give a light brown solid product, 0.19 g (10%). ^{1}H NMR ($CDCl_3$ 400 MHz 298K) : 8.90 (s, 1H, NCHN-H), 8.2 (m, 1H, J = 6.7 H_Z, quin-H), 8,05(s, 1H, CHHC), 7.8 (m,1H, J = 7.9 H_Z, quin-H), 7.6 (m, 1H, J = 1.3 H_Z, quin-H), 7.5 (m, 1H, J = 7.9 H_Z,), 7.4(m, 2H, J = 4.2 H_Z, quin-H), 7.2(s, IH, HCCH-H). ^{13}C NMR ($CDCl_3$ 100.61MHz 298K): 159.0, 140.5, 138.5, 136.0, 135.5, 128.5,127.0, 126.8, 125.0, 123.0, 122.5, 120.5.

Synthesis of 1-benzyl-3-quinolinimidazolium bromide (4a):
Benzyl bromide (1.41g, 8.25 mmol) was added to a solution 8-imidazol-1-yl-quinoline (0.70 g, 3.59 mmol) in 20 mL THF.The resulting mixture was allowed to stir overnight at room temperature. The resulting yellow/brown precipitate was filtered using filter stick and washed with fresh THF to afford a brown powder. This was then recrystallised from DCM/Hexane to give the desired imidazolium salt (light brown solid).^{1}H NMR($CDCL_3$:250MHz 298K):10.80(s, 1H, NCHN), 8.90(m,1H, J = 4.1 H_Z, Quin-H), 8.25(m, 1H, J = 8.7 H_Z, Quin-H), 8.00(m, 1H, J = 8.3 H_Z, Quin-H), 7.90(s, 1H, CHHC), 7.70(m, 1H, J = 5.7 H_Z, Quin-H), 7.60(m, 2H, J = 6.2 H_Z, Quin-H , CHHC), 7.50(broad 2H, Quin-H), 7.30(m, 3H, J = 7.3 H_Z, Ar-H), 5.85(s, 2H, CH_2). ^{13}C NMR ($CDCl_3$ 100MHz R.T): 152.07(NCN), 140.79, 137.30, 137.10,133.60, 131.40, 131.03, 129.86, 129.75, 129.70, 129.55, 126.90, 126.00, 124.72, 123.23, 121.95, 53.76(NCH2).

Synthesis of 1-methyl-3-quinolineimidazolium iodide (4b):
Methyl iodide (1g, 7mmol) was added to a solution of 8-imidazol-1-yl-quinoline (0.5g, 2.7mmol) in 20mL of THF. The resulting mixture was stirred at room temperature for 48 hrs. The resulting brown precipitate was filtered using filter stick and washed with further amount of THF to afford a brown powder. This was then recrystallised from DCM/Hexane to give the desired imidazolium salt (0.6g, 70%).Crystals suitable for X-ray were obtained by vapour diffusion of Et2O into the DCM solution of the compound. Analytically Calculated for $C_{13}H_{12}N_3I$: C, 46.30; H, 3.56; N, 12.47%. Found: C, 46.09; H, 3.60; N, 12.16%. ^{1}H NMR(DMSO-d6:250MHz R.T): 9.80(s, 1H, NCHN), 8.90(d, 1H, J = 1.7 H_Z, quin-H), 8.30(d, 2H, J = 1.6 H_Z, quin-H), 8.00(d,1H, J = 7.4 H_Z, quin-H), 7.80(s, 1H, CHHC), 7.70(d, 1H, J = 7.9 H_Z, quin-H), 7.50(m, 1H, J = 4.2 H_Z, quin-H), 7.40 (s, 1H, CHHC), 4.30(s, 3H, CH_3). ^{13}C NMR (DMSO-d6, 72.5MHz R.T.): 152.02(NCN), 140.62, 138.48, 136.95, 131.39, 130.69, 128.77, 126.38, 126.27, 124.41, 123.29, 123.06, 67.00(CH_3)

1-benzyl-3-quinolinimidazoliumtetraflouroborate (5): The counter ion bromide in **4a** was exchanged for tetraflouroborate ion by mixing one equivalent of 1-benzyl-3-quinolineimidazolium bromide (0.5g, 1.75 mmol) in acetonitrile with 1.5equivalent of $NaBF_4$(0.28g, 2.63mmol) in water. The acetonitrile was removed under reduced pressure and product was washed twice with water. The residue was then dissolved in DCM and the organic and aqueous layer separated. The DCM solution was dried over $MgSO_4$ and solution concentrated under reduced pressure. Addition of Et_2O precipitates out the product which was filtered and dried in vacuum to give the desired product as brown solid. Crystals suitable for X-ray crystallography were obtained by vapour diffusion of Et_2O into DCM solution of the product. Analytically Calculated for $C_{19}H_{16}N_3BF_4$: C, 61.29; H, 4.29; N, 11.27%. Found: C, 60.96; H, 4.31; N, 11.12%.^{1}H NMR ($CDCl_3$, 250MHz R.T.): 9.40(s, 1H, NCHN), 8.85(d, 1H, J = 4.2 H_Z, quin-H), 8.35(d, 1H, J = 7.5 H_Z, quin-H), 8.20(d, 1H, J = 8.4 H_Z, quin-H), 8.00(d, 1H, J = 8.3 H_Z, quin-H), 7.85(s, 1H, CHHC), 7.70(t, 1H, J = 4.2 H_Z, quin-H), 7,50(m, 3H, arom-H), 7.60(s, 1H, CHHC), 7.50(m, 3H, J = 7.0 H_Z, arom and quin-H), 5.50(s, 2H, CH_2). ^{13}C NMR ($CDCl_3$ 72.5MHz R.T): 150.70(NCN), 139.31, 135.92, 135.69, 131.97, 129.96, 129.68, 128.46, 128.41, 128.26, 128.16, 125.42, 124.21, 123.35, 121.85, 120.77, 52.68(NCH2).

RESULTS AND DISCUSSION
Prior to that the start of this work there was no reported synthesis of symmetrically substituted quinoline imidazolium salts and several attempts towards accessing this compound were not successful by the established procedure. However, Michon et al (2006) almost at the same time the synthesis of these quinoline based salts was achieved reported the synthesis of analogue chiral tetradentate diamine and chiral quinoline functionalised dihydroimidazolium salts. In their reaction they utilised Buchwald-Hartwig Palladium –catalysed amination involving 2.1 equivalents of 8-bromoquinoline, 3 equivalents of sodium t-butoxide, 5 mol% of $Pd_2(dba)_3$ and 10 mol% of rac-2,2′-bis(diphenylphosphino)-1,1′-binaphthalene (rac-BINAP) in toluene at 80 ^{o}C under argon affording the chiral amine in 90% . Ring cyclisation of the chiral diamine with triethylorthoformate solution at 135^{o}C afforded the desired dihydroimidazolium salts in 60-90% yield.

Previously this type of diamine was synthesised using a Bucherer reaction by refluxing 8-hydroxy quinoline, the desired diamine and sodium pyrosulfite in water for ten days (Jensen and Nielsen 1964), but the yield obtained via this method was low by almost 50% compared to that reported by Michon *et al.* (2006).

In this study, the diamine was prepared from the considerably cheaper 8-hydroxyquinoline material (Jensen and Nielsen 1964) and the achiral dihydroimidazolium **2** was prepared in 95% yield by reaction with triethyl orthoformate and ammonium tetraflouroborate salt at 120°C in 2 hours as depicted in (Scheme 1). Compound **1** was characterised by 1H and ^{13}C NMR spectroscopy while imidazolium salt **2a** was characterised by ^{1}H, ^{13}C NMR, mass spectroscopy and microanalysis. The salt is soluble only in high polar solvents such as DMSO or DMF. Of particular importance is the identification of CH unit between the N atoms which appeared at δ value of 11.4 which is higher than the figure reported by Michon *et al* 2006. The signal for the C2- carbon in ^{13}C NMR occurs at a δ of 159.21 which is typical of such group as reported by Michon *et al* 2006 (δ=161.90).

In order to carry out any further investigations with the salt there was a need to improve the solubility of the dihydroimidazolium salt. This was achieved by replacing the counter ion tetraflouroborate with tetrakis (3,5-bis(triflouromethyl)phenyl)borate (Barf) giving access to the imidazolium salt **2b** that is soluble in almost all organic solvents with the exception of petroleum ether and hexane. The characteristic features of **2b** as observed in the ^{1}H and ^{13}C NMR spectra did not change significantly in relation to what was observed in **2a**. Diffusion of hexane into the DCM solution of compound **2b** gave crystals suitable for X- ray crystallographic determination, figure 1.

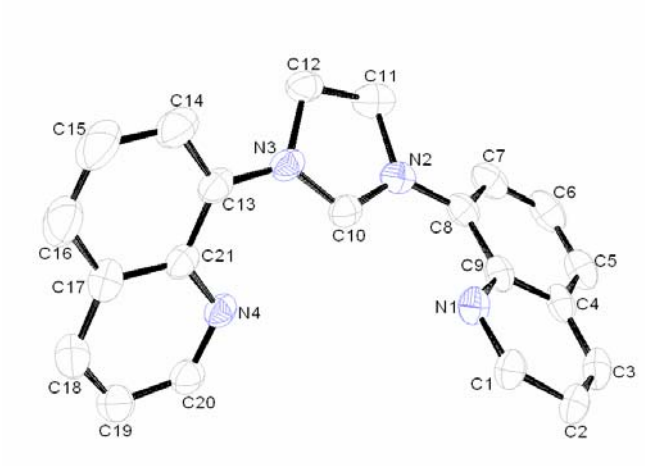


Figure 1: ORTEP projection of the cation of **2b.Barf**, excluding hydrogen atoms for clarity, showing labelling of atoms.

Selected bond lengths (Å) of **2b:** N2 -C8 =1.428, N2-C10 =1.315, N2- C11 = 1.481, N3- C10 = 1.316, N3-C12 =1.476, N3- C13 = 1.476, N4-C21 =1.369, C8- C9 =1.480; Selected bond angles (°) N2- C10 -N3 =113.4, N1-C9- C8 =119.9, N2 -C8- C7 =119.3, C10 -N2 -C8 =127.5, C10 -N3 -C13 =126.4 .

The N2-C10-N3 bond angle of 113.4° obtained is higher than that generally reported for imidazolium salts (108°) (Danopoulos *et al* 2002l and Cavell *et al* 2006), but there is no significant difference in bond lengths.

Unsymmetrical substituted Quinoline imidazolium salt

Two quinoline based imidazolium salts are herein reported. 8-imidazol-1-yl-quinoline was synthesised following the Zhang modified procedure for the synthesis of 1-arylimidazole (Zang *et al* 2003).The yield obtained is low (~ 20%) which is a known problem in the literature with most 1-aromatic substituted imidazoles.

The imidazolium salts were prepared following the standard N-alkylation using methyl iodide or benzyl bromide. The alkylation of the quinoline imidazole follows S_N2 behaviour and is difficult to achieve with nucleophile less reactive than a secondary alkyl bromide precluding access to desired bulky N-tert butyl, N- Mesityl and N-diisopropylphenyl (N-dipp) substituents on the resulting imidazolium salt via this route. The quinoline imidazole was reacted with either methyl iodide or benzyl bromide in THF overnight to give the desired imidazolium salts (**4a** and **4b**) as light brown solid in good yield. While imidazolium **4b** is stable towards air and moisture, compound **4a** is hygroscopic and the anion (bromide) was exchanged for tetraflouroborate anion to obtain compound **5**. The anion exchange was accomplished by mixing a solution of the halide salt in acetonitrile with a solution of an excess of sodium tetraflouroborate in water which on work gave the BF_4 salt in good yield. The imidazolium salts were fully characterised. The characteristic peak in the ^{1}H NMR is the C_2-H imidazolium proton appearing as singlet between 10.15-10.75ppm. In the ^{13}C NMR the C_2 appeared at a δ value of 150.70ppm. Quality crystals for X-ray crystallography were obtained for the BF_4 version of the imidazolium salt **5** by vapour diffusion of Et_2O into DCM solution. In the ^{1}H NMR spectra of the BF_4 salt ($CDCl_3$ solvent) the C_2-H imidazolium proton was observed to move upfield while only little of such change could be observed in ^{13}C NMR. The crystal structure for salt **5** is depicted in Figure 2.

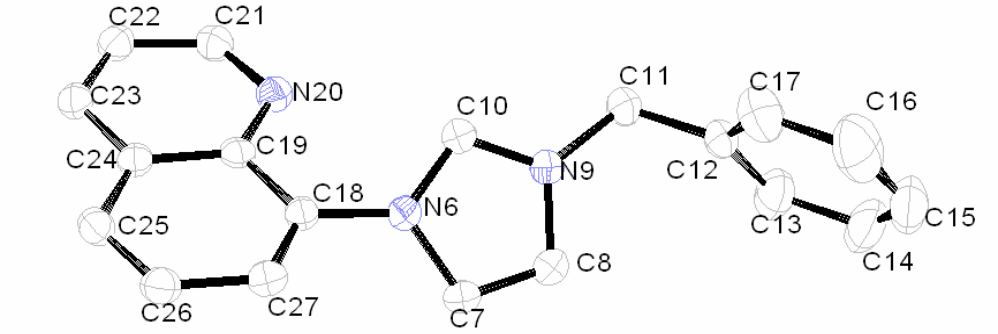


Figure 2: ORTEP projection of the cation of **5.BF_4** excluding hydrogen atoms for clarity showing atom labelling scheme.
Selected bond lengths (Å) of **5:** N6-C7 = 1.392(2); N6-C10 = 1.3405(19); N6-C18 = 1.441(19); C9-C10 = 1.324(2); N9-C11 = 1.4846(19); N9-C8 = 1.381(2); C7-C8 = 1.349(2); C12-C13 = 1.389(3); C19-N20 = 1.367(2); N20-C21 = 1.315(2); Selected bond angles (°);N6-C10-N9 108.38(14); C10-N6-C18 =127.40(13); N9-C11-C12 =111.31(14); C18-C19-N20 =119.85(14); N6-C18-C27 =118.31(14)

The quinoline and imidazolium rings make an angle of approximately 36.16° and both the nitrogen of the quinoline ring and imC_2-H are directed on the same sides of the molecules. The crystal structure of **5** reveals N6-C10-N9 bond angle of 108.38° and N6-C10, N9-C10 bond lengths of 1.3405(19) Å and 1.324(19) Å respectively which is within the expected values of imidazolium salts reported [Danopoulos *et al* 2002 and Cavell *et al* 2006]. Crystals suitable for X-ray chromatography were obtained for compound **4b** by diffusion of diethyl ether into the DCM solution of the compound. ^{1}H and ^{13}C NMR, MS, and micro analysis data correspond to the proposed structure.

CONCLUSION

A range of quinoline based imidazolium salts have been synthesised and characterised as precursors to the corresponding NHC ligands. A range of N-substituents give variable steric bulk to the imidazolium rings. The donor ability of dihydro imidazolium salt would be expected to be higher than that of unsaturated imidazolium salt due to the possibility of electron delocalisation and aromatic character in the later corresponding ligands.

REFERENCES

Arran A.D.T., Scott W., Danopoulos A.A., Graham E., and Michael B. H (2003). Functionalised and chelate heterocyclic carbene complexes of palladium; synthesis and structural studies. *Dalton Trans*, 699-708.

Crabtree R.H. (2006). Some chelating C-donor ligands in hydrogen transfer and related catalysis. *Jour.Organomet. Chem. 691*, 3146-3150.

Danopoulos. A. A., Scot W., Michael B. H. Thomas G. and Robert P.T. (2002). Synthesis and structural characterisation of stable pyridine and phosphine –functionalised N-heterocyclic carbenes. *Chem. Commun.*, 482-483.

David J. N., Cavell K. J., Brian W. S., Allan H. W., (2006). Methyl-palladium complexes of pyridine-bridged bis (nucleophilic heterocyclic carbene) ligands: Substituents effects on structure, stability and catalytic performance. *Inorganica Chimica Acta,* 359, 1855-1869.

Jensen K. A. and Nielsen P. H. (1964). Chelates derived from N, N-Bis- (8-quinolyl)-ethylenediamine and analogous compounds. *Acta Chem. Scand. 18*, 1-10.

Michon C., Ellern A., and Angelici R. J. (2006). Chiral tetradentate amine and tridentate aminocarbene ligands: Synthesis, reactivity and X-ray structural characterisations. *Inorganic Chimica Acta*, **359**, 4549-4556.

Zhang H., Liu J., Chen J., Zhao Y., Li L. (2003). Modified procedure for the synthesis of 1-arylimidazole. Synthesis No.17, 2661-2666.