



HIGHLY EFFICIENT SYNTHESIS OF ARYLDIPYRROMETHANES IN PRESENCE OF BRØNSTED ACIDIC IONIC LIQUIDS

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Abstract:

Highly efficient and selective synthesis of aryldipyrromethanes in presence of Brønsted acidic ionic liquids in dichloromethane is reported by the condensations of aromatic aldehydes with pyrrole (2 equivalents) at room temperature. The aryldipyrromethanes can be isolated directly from the reaction mixture in an essentially pure state by simple recrystallization with ethyl acetate and hexane. Time control seems to be essential to avoid significant formation of the tripyrromethane analogue and the reaction time is strongly dependent on the nature of the aromatic aldehyde. In this reaction the products were obtained in short reaction time and easy operation under mild conditions without using any strong acid.

Keywords: Brønsted acidic ionic liquids, dipyrromethane, pyrrole, carbonyl compound, catalysis.

1. Introduction:

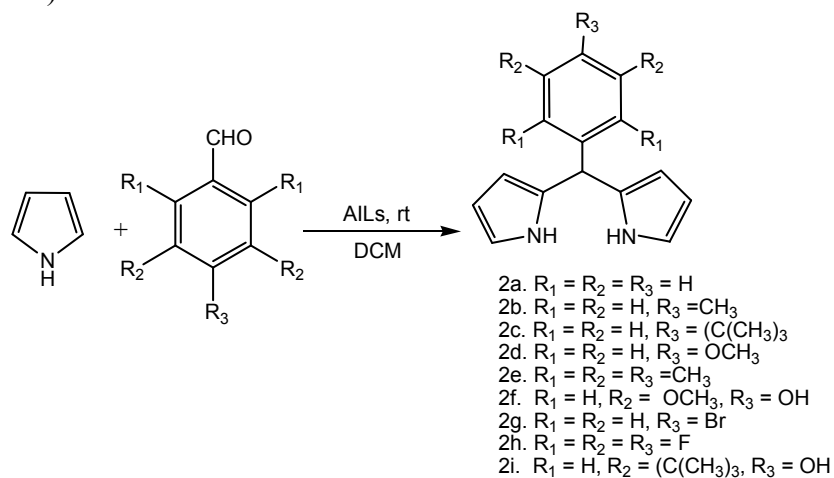
Dipyrromethanes have emerged as useful intermediates for the synthesis of porphyrins^{i-vii} and porphyrin-like macrocycles^{viii-xi}. The design and synthesis of anion receptors have become of increasing interest due to the important role of anions in many biological and chemical processes^{xii-xvi}. The synthesis of meso-substituted dipyrromethanes basically involve the acid-catalyzed condensation of aldehyde/ketone with pyrrole or its derivatives. Due to their great importance, many synthetic strategies have been developed. In 1994, Lindsay et al. for the first time reported the strong acid catalyzed synthesis of the meso-substituted dipyrromethanes from pyrrole and different aldehydes^{xvii}. Moreover, Sobral et al. proposed the synthesis of the dipyrromethanes using water and hydrochloric acid^{xviii}.

There are a number of methods available for the synthesis of meso-substituted dipyrromethanes, pyrrolidinium tetrafluoroborate^{xix}, cation exchange resins^{xx}, trifluoroacetic acid^{xxi}, BF₃-etherate^{xxii}, CF₃CHClBr/ Na₂ S₂O₄^{xxiii}. However, these methods require prolonged reaction time and exotic

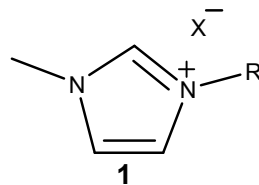
reaction condition. Generally, these methods involve excess of pyrrole and carbonyl compounds to give dipyrromethanes in low to moderate yields due to the formation of oligomeric product. Further, the purification of the dipyrromethanes from the reaction medium also becomes difficult. In addition to this, a direct synthesis of dipyrans from aldehydes and pyrroles gives a mixture of oligopyrromethanes which do not separate easily.^{xxiv} However, the use of excess and even stoichiometric amount of acids with organic solvents make such process environmental questionable.

In order to avoid the use of corrosive acid and minimize the amount of harmful organic solvents, the development of a new method for the synthesis of 5-aryl dipyrromethane catalysed by Brønsted acidic ionic liquids is desirable on the priority basis. The Brønsted acidic ionic liquids have gained special attention as a catalyst in organic synthesis because of many advantages such as their outstanding flexibility, non-volatility, noncorrosiveness, heat resistance, negligible vapour pressure, tunable polarity, operational simplicity and high reactivity with common organic solvents^{xxv,xxvi}.

Inspired by the early report^{xxvii,xxviii} and the critical role of AILs in organic synthesis provoked us to examine the catalytic scope of Brønsted acidic ionic liquids in the synthesis of dipyrromethane. Herein, authors report the high yield synthesis of dipyrromethanes (2) through the condensation of pyrrole and aryl aldehydes by making use of Brønsted acidic ionic liquids as catalysts (scheme 1).



Scheme 1: Synthesis of 5-aryldipyrromethanes



- | | |
|--|---|
| a. R = -CH ₂ CH ₂ CH ₂ SO ₃ H, X = CF ₃ COO | e. R = -CH ₂ COOH, X = CF ₃ COO |
| b. R = -CH ₂ CH ₂ CH ₂ SO ₃ H, X = CF ₃ SO ₃ | f. R = -CH ₂ COOH, X = CF ₃ SO ₃ |
| c. R = -CH ₂ CH ₂ CH ₂ SO ₃ H, X = CH ₃ SO ₃ | g. R = -CH ₂ COOH, X = CH ₃ SO ₃ |
| d. R = -CH ₂ CH ₂ CH ₂ SO ₃ H, X = HSO ₄ | h. R = -CH ₂ COOH, X = HSO ₄ |

Figure 1: Structures of different acidic ionic liquids (AILs)

2. Results and Discussion

Brønsted acidic ionic liquids, **1a-1h** (**Figure 1**) were synthesized by known procedure with minor modification^{xxix}. The identity of **1a-1h** were unambiguously confirmed by ¹H and ¹³C NMR Spectroscopy (See Supplementary data, **Figure S1-S12**).

The reaction of pyrrole with aryl aldehydes in the presence of Brønsted acidic ionic liquids in dichloromethane gave corresponding 5-aryl dipyrromethanes in good to excellent yields (**Table 1**). One equivalent (1 eq) of aryl aldehyde and two equivalents (2 eq.) of pyrrole were taken up in round bottom flask containing excess of Brønsted acidic ionic liquid or without any organic solvent. The reaction mixture was stirred at room temperature and the reaction progress was followed by TLC analysis (until complete disappearance of the aldehyde). After a certain time (**Table 1**), (semi-) solid product as precipitated was filtered off. The precipitate often sticks to the walls of the flask and the stirring bar might hamper the stirring. The crude product was washed with water and petroleum ether to achieve good yield of 5-aryldipyrromethane. Apart from the desired dipyrromethane some other unwanted linear byproducts (tripyrromethane and polypyrrole) were also observed. These are responsible for the low yields of 5-aryl dipyrromethane and purification of dipyrromethanes. In order to avoid the formation of side product the development of a new method for the synthesis of 5-aryldipyrromethanes catalyzed by Brønsted acidic ionic liquids in different organic solvents would be highly desirable. The reaction was performed in different Brønsted acidic ionic liquids and the best results were observed in the case of 1-methyl-3-(4-sulfopropyl)-imidazolium trifluoromethylacetate. The same reaction was examined using different solvents and the highest yield was obtained in dichloromethane (**Table 1**). The structures of all the 5-aryldipyrromethanes were confirmed by ¹H NMR and ¹³C NMR spectroscopic data (see supplementary data **Figure S12-S26**)

Table 1: Brønsted acidic ionic liquid catalyzed synthesis of dipyrromethane in organic solvents^a

Entry	Solvent	AILs ^b	Time (min)	Product (2)	Yield (%) ^c
1	-	1a	60	2a	80
2	CHCl ₃	1a	10	2a	89
3	CH ₂ Cl ₂	1a	10	2a	97
4	EtOAc	1a	20	2a	70
5	THF	1a	20	2a	80
6	C ₆ H ₆	1a	20	2a	75
7	Toluene	1a	20	2a	78
8	EtOH	1a	20	2a	80
9	Hexane	1a	25	2a	65

^aReaction conditions: arylaldehyde (10 mmol), pyrrole (20 mmol), catalyst (1 mmol), DCM (25 ml), ^bCatalyst was prepared by usual method. ^cIsolated yield.

The high yield formation of 5-aryldipyrromethane in the presence of 1-methyl-3-(4-sulfopropyl)-imidazolium trifluoromethylacetate Brønsted acidic ionic liquid prompted us to examine the yields of different 5-aryldipyrromethanes in dichloromethane (**Table 2**).

Table 2: Reaction of different aldehyde with pyrrole in DCM, catalyzed by 1-methyl-3-(4-sulfopropyl)-imidazolium trifluoromethylacetate^a

Entry	AILs ^b	Time (min)	Product (2)	Yield (%) ^c
1	1a	5	2a	97
2	1a	5	2b	95
3	1a	10	2c	93
4	1a	10	2d	91
5	1a	20	2e	85
6	1a	10	2f	93
7	1a	15	2g	91
8	1a	15	2h	80
9	1a	20	2i	85

^aReaction conditions: arylaldehyde (10 mmol), pyrrole (20 mmol), catalyst (1 mmol), DCM (25 ml), ^bCatalyst was prepared by usual method. ^cIsolated yield.

5-Aryl dipyrromethanes are formed in almost quantitative yields when pyrrole was react with various aldehydes in the presence of a catalytic amount of Brønsted acidic ionic liquids in dichloromethane. The electrophilic substitution reactions of pyrrole with aldehyde proceed smoothly at room temperature. The results summarized in (**Table 2**), clearly indicate the scope of the reaction as the reactions of aromatic aldehydes (**Entries 2a-2i**). A reaction of different substituted aromatic aldehydes with pyrrole in the presence of Brønsted acidic ionic liquid in dichloromethane gave the high yields of corresponding 5-Aryl dipyrromethanes. It is reported that aromatic aldehydes with strong electron withdrawing substituent on the ring require longer reaction time giving relatively low to moderate yields of the corresponding 5-aryl dipyrromethane (**Table 2 Entry 8**). Although the working action of Brønsted acidic ionic liquids, leading to 5-Aryl dipyrromethane in excellent yields, is not very clear at this stage, the preliminary experimental results dictate the excellent yield synthesis of 5-Aryl dipyrromethanes are quite acceptable.

Conclusions

The reported method gave a variety of 5-aryldipyrromethanes in high yields (80-97 %) as a result of the reactions of various aryl aldehydes with pyrrole in dichloromethane in the presence of a catalytic amount of 1-methyl-3-(4-sulfopropyl)-imidazolium trifluoromethylacetate. An improved yield of 5-Aryl dipyrromethanes compared to that reported previously with TFA and BF₃OEt₂ catalytic conditions were observed. To the best of our knowledge, the Brønsted AILs have been used for the first time as catalysts in 5-aryldipyrromethanes synthesis. It is quite reasonable to expect that the present work will enable the rapid development of the 5-aryldipyrromethanes, valuable in supramolecular chemistry and stimulate continued investigation of methods for one flask synthesis.

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