A Fast and Highly Efficient Protocol for Synthesis of Pyrrolo[2,3-*d*]isoxazoles and a New Series of Novel Benzyl Bis-pyrrolo[2,3-*d*]isoxazoles Using Task-Specific Ionic Liquids as Catalyst and Green Solvent

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We report a mild, fast, highly efficient and eco-friendly protocol for the green synthesis of pyrrolo[2,3-*d*]isoxazoles and a new series of novel benzyl bis-pyrrolo[2,3-*d*]isoxazoles from nitro styrylisoxazoles in $SnCl_2$-ionic liquid by reductive cyclization. These reactions were performed at ambient temperature which resulted in good yields in short reaction time, without requiring any organic solvent and catalyst.

Key words task-specific ionic liquid; reductive cyclization; pyrrolo[2,3-*d*]isoxazole

Significant progress in green chemistry is being made in several key research areas, such as catalysis,[1] the design of safer chemicals, environmentally benign solvents[2] and the development of renewable feed stocks. Chemists are trained to design products and processes with an increased awareness of environmental impact. Outreach activities within the green chemistry community highlight the potential for chemistry to solve many of the global environmental challenges. In the recent years, ionic liquids have emerged as green solvents with desirable properties such as good solvating ability, wide liquidous range, tunable polarity, high thermal stability, negligible vapour pressure and ease of recyclability. These are referred to as designer solvents since they exhibit properties like hydrophilicity, hydrophobicity, Lewis acidity, viscosity and density. These can be altered by the fine tuning of parameters such as the choice of organic cation and the length of alkyl chain attached to an organic cation. These structural variations offer flexibility to the chemists to devise the most idealized solvent catering to the needs of any particular process. Due to the stabilization of charged intermediates by ionic liquids, they can promote unprecedented selectivities and enhanced reaction rates. Consequently, ionic liquids are being used as recyclable solvents for the immobilization of transition metal-based catalysts, Lewis acids and enzymes. During the past few years, a variety of room temperature ionic liquids have been demonstrated as efficient and practical alternatives to organic solvents for many important organic transformations.[3—9] Particularly, the use of [bmIm]OH as a novel and a recyclable reaction medium, as well as an efficient catalyst for Knoevenagel and Michael reactions has been reported in literature.[10—12] Similarly, 1-methyl imidazolium tetrafluoroborates has been exploited as an efficient Bronsted acid promoter ionic liquid in various organic transformations.[13—15] As a part of our study on environmentally friendly organic synthesis with isoxazoles,[16—19] avoiding organic solvent and toxic catalyst in reactions, we demonstrated the use of room temperature ionic liquids as efficient catalysts as well as reaction media for Knoevenagel and Michael reactions and also for conducting reductive cyclization.

Looking for a valuable procedure for the conversion of nitro styrylisoxazoles (**3**) to pyrrolo[2,3-*d*]isoxazoles (**4**), several approaches have been investigated. One method for pyrrole ring formation is by de-oxygenative cyclization of nitro styryl compounds using triethyl phosphite (TEP).[20—22] As the reaction requires heating of the nitro styrylisoxazole (**3**) in TEP at high temperature under N_2 atmosphere, the reaction results in cleavage of the isoxazole ring, which is unstable at higher temperature.[23] To overcome this problem, another method developed by Angelo Carotti[24] is employed, which involves the reductive cyclization of a nitro styryl compound using $SnCl_2$-*N*,*N*-dimethylformamide (DMF). However, we could not achieve the synthesis of the target compounds using this procedure, even though the reaction was performed with $SnCl_2$ in different solvents *i.e.*, DMF, dimethyl sulphoxide (DMSO), dioxane and tetrahydrofuran (THF) under a variety of reaction conditions. Thus, we decided to construct the pyrrolo[2,3-*d*]isoxazoles (**4**) by utilizing amino styrylisoxazoles rather than nitro styrylisoxazoles. Sharpless epoxidation of amino styrylisoxazoles resulted in title compounds in a one-pot synthesis.[25] However, this method requires Bu^{t}OOH, chiral (−) diethyl tartarate and $Ti(OR)_4$. The approach is not widely applicable due to the requirement of specific reagents and catalysts, which are not environmentally benign and is costlier. Hence, we thought of constructing the title compounds by adopting a greener approach utilizing ionic liquids. To our surprise, we could synthesize title compounds by reductive cyclization of nitro styrylisoxazoles (**3**) with $SnCl_2 \cdot 2H_2O$ in Bronsted acidic ionic liquid 1-methyl imidazolium tetrafluoroborate [(HMIm)BF_4] as a green solvent and catalyst, in which we initially failed by using $SnCl_2$-organic solvents. We report in this article, the application of task-specific ionic liquids [bmIm]OH and [HMIm]BF_4 as efficient catalysts as well as reaction media for the green synthesis of pyrrolo[2,3-*d*]isoxazoles and a new series of novel benzyl bis-pyrrolo[2,3-*d*]isoxazoles from readily available nitro styrylisoxazoles.

Results and Discussion

Knoevenagel condensation of 3,5-dimethyl-4-nitroisoxazole (**1**) with substituted benzaldehydes (**2**) in the presence of basic ionic liquid, 1-methyl-3-butylimidazolium hydroxide, [bmIm]OH, without any organic solvent and organic base at room temperature results in the rapid formation of 5-

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styrylisoxazoles (**3**) in 10—15 min with excellent yields (85—92%). The condensation of aromatic aldehydes with 3,5-dimethyl-4-nitroisoxazole (**1**), which is easily achieved by [bmIm]OH, did not proceed under the catalysis of other ionic liquids such as [bmIm]BF_4 and [bmIm]Br. This shows that [bmIm]OH is a task-specific ionic liquid in this transformation and the reaction is influenced by hydroxyl ion of the ionic liquid. The results revealed that ionic liquid [bmIm]OH plays the dual role of solvent as well as catalyst in this reaction. The ionic liquid, which was remaining in the reaction flask after being washed with ethyl acetate and dried at 80 °C under vacuum for 3—4 h was recycled in subsequent runs (four to five times). The structure of the products **3** were confirmed on the basis of IR, ^{1}H-NMR, ^{13}C-NMR and MS spectroscopy and finally by comparing with the authentic samples.[26] This reaction, when performed in the presence of ethanol in piperidine base as reported in literature,[26] requires 2—3 h refluxing and the yields are moderate (Entry 1—12, Table 1). The reaction of 3-methyl-4-nitro-5-styrylisoxazoles (**3**) with $SnCl_2 \cdot 2H_2O$ in the presence of a Bronsted acidic ionic liquid [HMIm]BF_4 at room temperature afforded the corresponding pyrrolo[2,3-*d*]isoxazoles (**4**) in excellent yields within 15 min (Entry 1—12, Table 2). $SnCl_2 \cdot 2H_2O$–[HMIm]BF_4 not only reduced the nitro group but efficiently catalyzed the subsequent cyclization (Chart 1).

In a typical experiment, 3-methyl-4-nitro-5-styrylisoxazole (**3**) (1 mmol) and $SnCl_2 \cdot 2H_2O$ (2 mmol) were taken in IL [(HMIm)BF_4] (5 ml). The reaction mixture was stirred at room temperature for 15 min. After the completion of the reaction (monitored by TLC), the reaction mixture was extracted with ethyl acetate. The evaporation of the solvent gave a crude product, which was purified by colum chromatography. The ionic liquid, left over in the reaction after being dried under vacuum was re-used for subsequent reactions. The product was identified as 3-methyl-5-phenyl-4*H*-pyrrolo[2,3-*d*]isoxazole **4** on the basis of spectral and analytical data. The reaction did not proceed in the absence of ionic liquid [HMIm]BF_4 as well as in the presence of [bmIm]Br and [bmIm]OH. This may be due to Bronsted acidic character of [HMIm]BF_4.

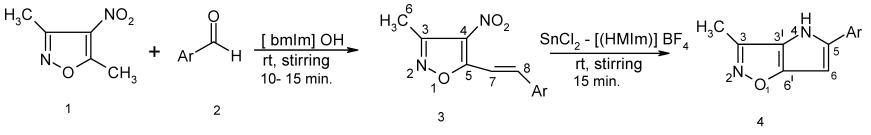
The applicability of this new procedure was assessed by subjecting substituted nitro styrylisoxazoles (**3**) to reductive cyclization under optimized conditions which afforded the corresponding pyrrolo[2,3-*d*]isoxazoles (**4**) (Ar=4-$CH_3C_6H_4$, 4-$CH_3OC_6H_4$, 4-ClC_6H_4, 2-ClC_6H_4, 2,4-$Cl_2C_6H_3$, 3,4-(O–CH_2–O)C_6H_3, 2-$CH_3C_6H_4$, 4-N$(CH_3)_2C_6H_4$, 2,6-$Cl_2C_6H_3$, 2-OHC_6H_4 and 3-CH_3O, 4-OHC_6H_3) in excellent yields (Entry 1—12, Table 2). The structure of the products **4** were estab-

Table 1. Ionic-Liquid Mediated Synthesis of 3-Methyl-4-nitro-5-styrylisoxazoles (**3**)

Entry	Ar	Reaction period		Yield (%)		mp (°C)	lit mp[21] (°C)
		In presence of ionic liquid [bmIm]OH (min)	In presence of solvent and base (h)	In presence of ionic liquid [bmIm]OH	In presence of solvent and base		
1	C_6H_5	10	2	85	50	151	153
2	4-$CH_3C_6H_4$	12	3	90	54	155	156
3	4-$CH_3OC_6H_4$	12	2	92	52	148	150
4	4-ClC_6H_4	15	2	85	55	162	166
5	2-ClC_6H_4	15	3	90	55	177	180
6	2,4-$Cl_2C_6H_3$	10	2	90	50	199	200
7	3,4-(OCH_2O)C_6H_3	12	2	85	55	138	140
8	2-$CH_3C_6H_4$	10	2	90	50	144	142
9	4-N$(CH_3)_2C_6H_4$	10	2	95	50	122	124
10	2,6-$Cl_2C_6H_3$	12	2	90	55	185	187
11	2-OHC_6H_4	15	2	85	50	230	228
12	3-CH_3O, 4-OHC_6H_3	10	2	85	52	171	173

Table 2. Synthesis of 3-Methyl-5-aryl-4*H*-pyrrolo[2,3-*d*]isoxazoles (**4**) in Ionic Liquid [HMIm]BF_4

Entry	Ar	Reaction period		Yield (%)		mp (°C)	lit mp[20] (°C)
		Green approach method (min) [HMIm]BF_4	Sharpless epoxidation method (h)	Green approach method (min) [HMIm]BF_4	Sharpless epoxidation method (h)		
1	C_6H_5	15	28	95	90	155—157	156—158
2	4-$CH_3C_6H_4$	15	26	95	90	144—146	143—145
3	4-$CH_3OC_6H_4$	15	26	95	90	130—131	128—131
4	4-ClC_6H_4	15	28	96	90	165—166	166—168
5	2-ClC_6H_4	15	26	95	90	160—162	159—162
6	2,4-$Cl_2C_6H_3$	15	28	98	90	170—172	171—175
7	3,4-(OCH_2O)C_6H_3	15	28	95	90	178—180	178—181
8	2-$CH_3C_6H_4$	15	26	95	90	168—171	167—170
9	4-N$(CH_3)_2C_6H_4$	15	28	98	90	180—182	180—184
10	2,6-$Cl_2C_6H_3$	15	28	98	90	195—197	196—199
11	2-OHC_6H_4	15	26	98	90	200—202	202—204
12	3-CH_3O, 4-OHC_6H_3	15	26	95	90	150—152	151—153



3,**4**. Ar= C_6H_5, 4-$CH_3C_6H_4$, 4-$CH_3OC_6H_4$, 4-ClC_6H_4, 2-ClC_6H_4, 2,4-$Cl_2C_6H_3$, 3,4-(O-CH_2-O)C_6H_3 , 2-$CH_3C_6H_4$, 4-$N(CH_3)_2C_6H_4$, 2,6-$Cl_2C_6H_3$, 2-OHC_6H_4, 3-CH_3O, 4-OHC_6H_3

Chart 1. Reductive Cyclization of Nitro Styrylisoxazoles (**3**) to Pyrrolo[2,3-*d*]isoxazoles (**4**)

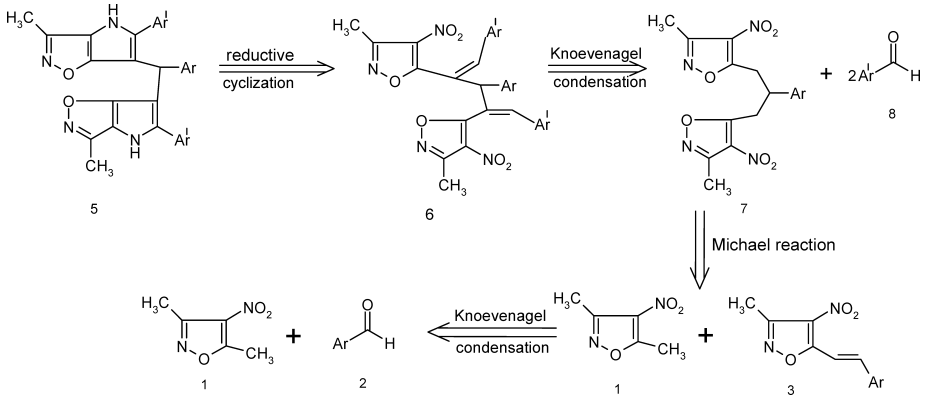


Chart 2. Retrosynthetic Analysis of Target Compound Benzyl Bis-pyrrolo[2,3-*d*]isoxazole (**5**)

lished by analytical and spectroscopic data and finally by comparing with authentic samples.[25)]

Contrary to our earlier method,[25)] the reaction time was effectively reduced from hours (26—28) to minutes (15) in the present approach. The product yield was improved from 90 to 98%. Moreover, the new process does not involve costly reagents, and is carried out under very mild experimental conditions. Further, the method is environmentally benign.

Having obtained favourable results with $SnCl_2$-ionic liquid for reductive cyclization, we then examined the synthesis of novel benzyl bis-pyrrolo[2,3-*d*]isoxazoles under similar conditions, once again with the same starting material *i.e.* nitro styrylisoxazole (**3**). Considering that, it is possible to run the Knoevenagel condensation and Michael addition in a domino fashion, we envisaged the possibility of building libraries of potentially pharmacologically active novel benzyl bis-pyrrolo[2,3-*d*]isoxazoles (**5**) from the commercially available materials **1** and **2**.

We proposed the following retro-synthetic analysis for the target compounds (Chart 2). This disconnection looked particularly attractive due to the commercial availability of 3,5-dimethyl-4-nitroisoxazole (**1**) and aromatic aldehydes (**2**) on the market. We reasoned that compound **5**, could be obtained from **6** by reductive cyclization. Significantly, compound **6**, precursor of **5**, could be achieved from **7** and **8** by Knoevenagel condensation. **7** could arise from **1** and **3** in a Michael type reaction, finally compound **3** could be obtained from commercially available materials **1** and **2** by a Knoevenagel condensation.

Our approach to the development of diversity-oriented synthesis of benzyl bis pyrrolo[2,3-*d*]isoxazoles (**5**) is based on the generation of building blocks that contain multiple functionalities which could be selectively reacted. In this context, compound **7** represents a class of poly functional

Table 3. Synthesis of 3-Methyl-5-[3-(3-methyl-4-nitro-5-isoxazolyl)-2-phenylpropyl]-4-nitroisoxazoles (**7**) in Ionic Liquid [bmIm]OH

Entry	Ar	mp (°C)	Yield (%)
1	C_6H_5	134	85
2	4-$CH_3C_6H_4$	140	90
3	3-CH_3O, 4-OHC_6H_3	167	92
4	4-$N(CH_3)_2C_6H_4$	103	88
5	2-OHC_6H_4	190	91
6	3,4-(OCH_2O)C_6H_3	114	95

scaffold which holds great potential for the generation of diversity. For example, in compound **7** two active methylene centers are available that can each be reacted independently either with aromatic aldehydes to give bis-nitrostyryl derivatives, which then subjected to reductive cyclization to afford benzyl bis-pyrrolo[2,3-*d*]isoxazoles or with aromatic ketones to give benzyl bis-isoxazolo[4,5-*b*]pyridine-*N*-oxides, or with chalcones to give Michael adducts which can be subsequently subjected to reductive cyclization to afford benzyl bis-isoxazolo[4,5-*b*]azepines. Compound **7** could easily be generated from commercially available marterials 3,5-dimethyl-4-nitroisoxazole (**1**) and an aromatic aldehyde (**2**) by Knoevenagel–Michael reaction either by domino fashion or by stepwise process. The synthetic approach for building the title compounds is as follows: 3-Methyl-4-nitro-5-styrylisoxazole (**3**) was reacted with 3,5-dimethyl-4-nitroisoxazole (**1**) in the presence of basic ionic liquid [bmIm]OH without any solvent and catalyst at room temperature for 15—30 min to afford Michael type adducts **7** in excellent yields (85—95%) (Entry 1—6, Table 3). This Michael type reaction, which is easily achieved by [bmIm]OH, did not proceed at all under the influence of other ionic liquids [bmIm]BF_4 or [bmIm]Br. This reaction once again demon-

Table 4. Synthesis of 3-Methyl-5-{(*Z*)-3-(3-methyl-4-nitro-5-isoxazolyl)-2,4-diphenyl-1-[(*Z*)-1-phenylmethylidene]-3-butenyl}-4-nitroisoxazoles (**6**) in Ionic Liquid [bmIm]OH

Entry	Ar	Ar′	mp (°C)	Yield (%)
1	C_6H_5	C_6H_5	166	90
2	C_6H_5	4-$CH_3C_6H_4$	170	88
3	C_6H_5	4-$CH_3OC_6H_4$	182	85
4	2-OHC_6H_4	2,4-$Cl_2C_6H_3$	242	92
5	4-$CH_3C_6H_4$	4-ClC_6H_4	190	91
6	3-CH_3O, 4-OHC_6H_3	2-ClC_6H_4	210	90
7	4-$(NCH_3)_2C_6H_4$	2-$CH_3C_6H_4$	198	88
8	3,4-$(OCH_2O)C_6H_3$	C_6H_5	154	90

Table 5. Synthesis of Novel 3-Methyl-[6-[(3-methyl-5-phenyl-4*H*-pyrrolo[2,3-*d*]isoxazole-6-yl)(phenyl)methyl]-5-phenyl-4*H*-pyrrolo[2,3-*d*]isoxazoles (**5**) in Ionic Liquid [HMIm]BF_4

Entry	Ar	Ar′	mp (°C)	Yield (%)
1	C_6H_5	C_6H_5	160	87
2	C_6H_5	4-$CH_3C_6H_4$	165	92
3	C_6H_5	4-$CH_3OC_6H_4$	170	90
4	2-OHC_6H_4	2,4-$Cl_2C_6H_3$	231	90
5	4-$CH_3C_6H_4$	4-ClC_6H_4	178	89
6	3-CH_3O, 4-OHC_6H_3	2-ClC_6H_4	191	91
7	4-$(NCH_3)_2C_6H_4$	2-$CH_3C_6H_4$	195	88
8	3,4-$(OCH_2O)C_6H_3$	C_6H_5	146	90

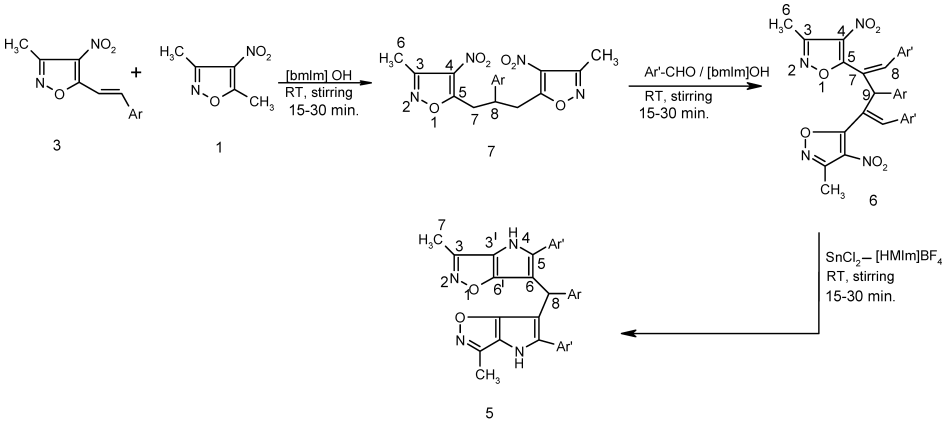
strates the specific role of the hydroxyl ion of this task-specific ionic liquid in this Michael reaction. The residual ionic liquid after being dried under vacuum was reused to subsequent runs. This Michael reaction, when conducted on nitro styrylisoxazoles (**3**) in the presence of either triethyl amine or piperidine base in ethanol resulted in approximately 50% product formation and reaction required nearly 2—4 h refluxing,[27] and the reaction resulted in formation of by products.[28] Hence, ionic liquid mediated Michael addition has a clear advantage over the conventional base catalyzed reaction with regard to reduction in reaction time, increasing the yields, without forming undesired side-products. Moreover, the process is environmentally benign. The present procedure catalyzed by ionic liquid provides an efficient and convenient protocol, without requirement of a conventional catalyst and organic solvent. Compounds **7** were subjected to Knoevenagel condensation reaction with various kinds of aromatic aldehydes in the presence of task-specific basic ionic liquid [bmIm]OH to afford the condensation products *viz.*; 3-methyl-5-{(*Z*)-3-(3-methyl-4-nitro-5-isoxazolyl)-2,4-diphenyl-1-[(*Z*)-1-phenylmethylidene]-3-butenyl}-4-nitroisoxazoles (**6**). The reaction was carried out at room temperature for 15 min without any solvent and catalyst. The products **6** were obtained in excellent yields (80—90%) without any undesired side products (Entry 1—8, Table 4). Similarly, this condensation did not proceed under the influence of other ionic liquids [bmIm]BF_4, or [bmIm]Br, indicating the specific role of [bmIm]OH as a catalyst and solvent. Finally, benzyl bis-nitro styrylisoxazoles (**6**) were converted to benzyl bis-pyrrolo[2,3-*d*]isoxazoles (**5**) by reductive cyclization on treatment with $SnCl_2 \cdot 2H_2O$–[HMIm]BF_4·$SnCl_2 \cdot 2H_2O$–[(HMIm)]BF_4 not only reduced the nitro group but efficiently catalyzed the subsequent cyclization. The reaction did not proceed in the absence of ionic liquid [HMIm]BF_4 as well as in presence of [bmIm]Br and [bmIm]OH (Chart 3).

In a typical experiment, benzyl bis-3-methyl-4-nitro-5-styrylisoxazole (**6**) (1 mmol) and $SnCl_2 \cdot 2H_2O$ (5 mmol) were taken in IL [(HMIm)BF_4] (5 ml). The reaction mixture was stirred at room temperature for 15 min. After the completion of the reaction (monitored by TLC), the reaction mixture was extracted with ethyl acetate. The evaporation of the solvent gave a crude product, which was purified by column chromatography. The ionic liquid left over in the reaction after being dried under vacuum was re-used for subsequent reactions. The product was identified as 3-methyl-6-[(3-methyl-5-phenyl-4*H*-pyrrolo[2,3-*d*]isoxazol-6-yl)phenylmethyl]-5-phenyl-4*H*-pyrrolo[2,3-*d*]isoxazole (**5**) on the basis of spectral and analytical data.

In order to study the scope of this methodology, several benzyl bis-nitro styrylisoxazoles (**6**) were tested under the similar conditions. We could succeed with reductive cyclization of these compounds with $SnCl_2 \cdot 2H_2O$–[HMIm]BF_4. The method has a general applicability and it is compatible with the reactivity of different functional groups. The products were obtained in excellent yields (80—90%) (Entry 1—8, Table 5). The structure of all the new products **5**—**7** were elucidated by spectroscopic (IR, ^{1}H-NMR, ^{13}C-NMR and MS) and micro analytical data.

Conclusion

The present procedure that uses task-specific basic ionic liquid [bmIm]OH provides a fast and highly efficient methodology for Knoevenagel condensation for the formation of compounds **3** and **6** and also for Michael type adducts **7**. The specificites and catalytic activity of [bmIm]OH for these reactions is established by the observation that the reaction did not proceed in the presence of other ionic liquids [bmIm]BF_4 and [bmIm]Br. This reaction catalyzed by task-specific basic ionic liquid [bmIm]OH, which is also acting as a solvent, provides an efficient and general methodology for Knoevenagel condensation and Michael addition. The significant improvements noticed in these reactions are: that a) they are fast, b) they are carried out under mild conditions, c) they produce high yields and d) they avoids hazardous organic solvents. We have developed a new protocol for synthesis of pyrrolo[2,3-*d*]isoxazoles and a new series of novel benzyl bis-pyrrolo[2,3-*d*]isoxazoles in $SnCl_2 \cdot 2H_2O$–[HMIm]BF_4 by reductive cyclization. This reaction did not proceed with other ionic liquids [bmIm]Br and [bmIm]OH. [HMIm]BF_4 which is a Bronsted acidic ionic liquid is task-specific in these reactions. These reactions were clean, and no by-products were detected under these conditions. There are several advantages in the use of ionic liquid for this transformation, which includes high conversion, short reaction time, avoidance of expensive reagents, and non-requirement of any additives or stringent reaction conditions. The reported procedure is mild, efficient, simple, user and environmentally friendly. To the best of our knowledge, this happens to be the first report to construct pyrrole ring by reductive cyclization of nitro styryl compounds with $SnCl_2 \cdot 2H_2O$–[HMIm]BF_4, in which the ionic liquid is playing the dual role of solvent as



3 1 7 6 5

5, 6, 7. Ar= C_6H_5, 4-$CH_3C_6H_4$, 3-CH_3O, 4-OHC_6H_3, 4-$N(CH_3)_2C_6H_4$, 2-OH C_6H_4, 3,4-$(OCH_2O)C_6H_3$

5, 6. Ar' = C_6H_5, 4-$CH_3C_6H_4$, 4-CH_3O C_6H_4, 2,4-$Cl_2C_6H_3$, 4-Cl C_6H_4, 2-Cl C_6H_4, 2-CH_3 C_6H_4

Chart 3. Synthesis of Benzyl Bis-pyrrolo[2,3-*d*]isoxazoles (**5**)

well as catalyst. Moreover, this work clearly demonstrates the potential of room temperature ionic liquids [bmIm]OH and [(HMIm)]BF_4 to act as an efficient and recyclable catalyst and green solvent and shows much promise for further applications.

Experimental

General The ionic liquids [bmIm]OH and [(HMIm)]BF_4 were prepared following the reported procedures.[29,30] All the melting points were determined on a Cintex melting point apparatus and are uncorrected. Analytical TLC was performed on Merck precoated 60 F254 silica gel plates. Visualization was done by exposing to iodine vapour. Column chromatography was conducted by using silica gel with benzene–ethyl acetate solvent systems as elute. IR spectra (KBr pellet) were recorded on a PerkinElmer BX series FT-IR spectrometer. ^{1}H-NMR spectra were recorded on a Varian Gemini 300 MHz spectrometer. Chemical shift values are given in ppm (δ) with tetramethyl silane as an internal standard. Mass spectral measurements were carried out by EI method on a Jeol JMC-300 spectrometer at 70 eV. Elemental analyses were performed on a Carlo Erba 106 and Perkin Elmer model 240 analyzers.

Typical Procedure. Ionic-Liquid Catalyzed Fast and Efficient Synthesis of 3-Methyl-4-nitro-5-styrylisoxazoles (3) 3,5-Dimethyl-4-nitroisoxazole **1** (1 mmol) and aromatic aldehyde **2** (1 mmol) were taken in IL [bmIm]OH (5 ml) and the reaction mixture was stirred at room temperature for 10—15 min. The reaction was monitored by TLC. After the completion of the reaction, the reaction mixture was extracted with ethyl acetate (3×10 ml). Evaporation of ethyl acetate gave crude product, which was purified by recrystallization from ethyl alcohol. The ionic liquid left over in the reaction was washed with ethyl acetate and dried at 80 °C under vacuum and was reused for conducting subsequent reactions (five times). This procedure was followed for all the reactions listed in Table 1.

Compound **3** (Entry 1, Table 1): Pale yellow solid; IR (KBr): 970 (s) cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 2.2 (s, 3H, CH_3), 6.8 (d, 1H, CH=CH, J=15 Hz), 7.0 (d, 1H, CH=CH, J=15 Hz), 7.3—7.9 (m, 5H, Ar-H); ^{13}C-NMR (75 MHz) δ: 11.41 (C-6), 109.27 (C-4), 109.87 (C-7), 115.20 (C-8), 127.35 (Ar-C), 127.81 (Ar-C), 128.52 (Ar-C), 129.01 (Ar-C), 129.09 (Ar-C), 130.65 (Ar-C), 156.28 (C-5), 158.85 (C-3). MS (EI) m/z: 230 [M]$^+$.

Compound **3** (Entry 2, Table 1): Pale yellow solid; IR (KBr): 989 (s) cm^{-1}; ^{1}H-NMR (300 MHz $CDCl_3$) δ: 2.4 (s, 3H, CH_3), 2.6 (s, 3H, CH_3), 6.9 (d, 1H, CH=CH, J=15 Hz), 7.1 (d, 1H, CH=CH, J=15 Hz), 7.6 (d, 2H, ArH, J=8.5 Hz), 7.8 (d, 2H, ArH, J=8.5 Hz); ^{13}C-NMR (75 MHz) δ: 11.50 (C-6), 21.40 (Ar-CH_3), 109.20 (C-4), 109.90 (C-7), 115.55 (C-8), 127.30 (Ar-C), 127.99 (Ar-C), 128.05 (Ar-C), 128.52 (Ar-C), 129.15 (Ar-C), 130.00 (Ar-C), 156.65 (C-5), 158.90 (C-3). MS (EI) m/z: 244 [M]$^+$.

Typical Procedure. Green Chemistry Approach to a Fast and Highly Efficient Synthesis of 3-Methyl-5-aryl-4*H*-pyrrolo[2,3-*d*]isoxazoles (4) 3-Methyl-4-nitro-5-styrylisoxazole **3** (1 mmol) and $SnCl_2 \cdot 2H_2O$ (2 mmol) were taken in IL [(HMim)BF_4] (5 ml), and the reaction mixture was stirred at room temperature for 15 min. The reaction was monitored by TLC. After the completion of the reaction, the reaction mixture was extracted with ethyl acetate (3×10 ml). Evaporation of ethyl acetate gave crude product, which was purified by silicagel column chromatography by eluting with benzene–ethyl acetate. The ionic liquid left over in the reaction was washed with ethyl acetate and dried at 80 °C under vacuum and was recycled for four consecutive runs. This procedure was followed for all the reaction listed in Table 2.

Compound **4** (Entry 1, Table 2): Brown solid; IR (KBr): 3250 (s), 1600, 980 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 2.52 (s, 3H, CH_3), 7.40—7.62 (m, 5H, Ar-H), 7.76 (s, 1H, C_6-H), 7.85 (s, 1H, NH, D_2O exchangeable). MS (EI) m/z: 198 [M]$^+$. ^{13}C-NMR (75 MHz) δ: 12.5 (C-7), 100.2 (C-3′), 110.4 (C-6), 128.5 (Ar-C), 129.4 (C-5), 130.2 (Ar-C), 132.8 (Ar-C), 136.3 (Ar-C), 143.2 (C-3), 152.4 (C-6′).

Compound **4** (Entry 2, Table 2): Brown solid; IR (KBr): 3300 (s), 1610, 975 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 2.42 (s, 3H, CH_3), 2.80 (s, 3H, CH_3), 7.29 (d, 2H, ArH, J=8 Hz), 7.50 (d, 2H, ArH, J=8 Hz), 7.81 (s, 1H, C_6-H), 7.93 (s, 1H, NH, D_2O exchangeable); MS (EI) m/z: 212 [M]$^+$. ^{13}C-NMR (75 MHz) δ: 11.3 (C-7), 21.1 (Ar-CH_3), 100.1 (C-3′), 112.6 (C-6), 127.3 (Ar-C), 128.5 (C-5), 130.0 (Ar-C), 133.1 (Ar-C), 137.8 (Ar-C), 145.5 (C-3), 156.0 (C-6′).

General Procedure for Synthesis of 3-Methyl-5-[3-(3-methyl-4-nitro-5-isoxazolyl)-2-phenyl propyl]-4-nitroisoxazoles (7) in Ionic Liquid (Entry 1, Table 3) 3-Methyl-4-nitro-5-styrylisoxazole **3** (Entry 1, Table 1) (1 mmol) and 3,5-dimethyl-4-nitroisoxazole **1** (1 mmol), were taken in a conical flask containing 5 ml [bmIm]OH and the mixture was shaken at ambient temperature for 15 min. The reaction mixture was extracted from the ionic liquid phase with ethyl acetate (3×10 ml). The organic layer was dried over anhydrous sodium sulphate and evaporated under reduced pressure. The residue was purified by petroleum ether to obtain the corresponding Michael adduct **7**. The ionic liquid left in the conical flask was further washed with ether, dried under vacuum at 90 °C for 2 h. To eliminate any water trapped from moisture and reused for subsequent reactions. After five runs, about 50% fresh ionic liquid was added to maintain consistent activity. This procedure was followed for all the reactions listed in Table 3. White solid; IR (KBr): 1575 (=N$^+$–O$^-$), 1610 (C=N), cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 2.4 (s, 6H, $2CH_3$), 3.5 (dd, 2H, J=14, 8 Hz, CH_2CH), 3.7 (dd, 2H, J=14, 8 Hz, CH_2CH), 4.0 (quintet, 1H, J=8 Hz, CH Ar), 6.7—7.2 (m, 5H, Ar-H). ^{13}C-NMR (75 MHz) δ: 11.10 (C-6), 33.37 (C-7), 41.05 (C-8), 109.87 (C-4), 125.10 (Ar-C), 126.87 (Ar-C), 127.35 (Ar-C), 127.81 (Ar-C), 130.05 (Ar-C), 130.88 (Ar-C), 155.20 (C-3), 156.80 (C-5). MS (EI) m/z: 372 [M]$^+$. *Anal.* Calcd for $C_{17}H_{16}N_4O_6$: C, 54.83; H, 4.30; N, 15.05. Found: C, 54.85; H, 4.35; N, 15.00%.

3-Methyl-5-[3-(3-methyl-4-nitro-5-isoxazolyl)-2-(4-methyl phenyl)propyl]-4-nitroisoxazole (Entry 2, Table 3) White solid; IR (KBr): 1570 (=N$^+$–O$^-$), 1625 (C=N), cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 2.4 (s, 6H, $2CH_3$), 2.5 (s, 3H, CH_3), 3.5 (dd, 2H, J=14, 8 Hz, CH_2CH), 3.7 (dd, 2H, J=14, 8 Hz, CH_2CH), 4.2 (quintet, 1H, J=8 Hz, CH Ar), 6.9—7.4 (m, 4H, Ar-H). ^{13}C-NMR (75 MHz) δ: 11.55 (C-6), 21.48 (Ar-CH_3), 33.50 (C-7), 41.55 (C-8), 110.05 (C-4), 126.10 (Ar-C), 127.00 (Ar-C), 127.55 (Ar-C), 128.00 (Ar-C), 131.77 (Ar-C), 133.50 (Ar-C), 156.05 (C-3),

158.02 (C-5). MS (EI) *m/z*: 386 $[M]^+$. *Anal.* Calcd for $C_{18}H_{18}N_4O_6$: C, 55.95; H, 4.66; N, 14.50. Found: C, 55.99; H, 4.62; N, 14.52%.

2-Methoxy-4-{2-(3-methyl-4-nitro-5-isoxazolyl)-1-[(3-methyl-4-nitro-5-isoxazolyl)methyl]ethyl}phenol (Entry 3, Table 3) White solid; IR (KBr): 1572 ($=N^+-O^-$), 1620 (C=N), cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 2.3 (s, 6H, $2CH_3$), 3.5 (dd, 2H, J=14, 8 Hz, CH_2CH), 3.7 (dd, 2H, J=14, 8 Hz, CH_2CH), 3.9 (s, 3H, OCH_3), 4.1 (quintet, 1H, J=8 Hz, CH Ar), 6.9—7.5 (m, 3H, Ar-H), 8.5 (br s, 1H, D_2O exchangeable) MS (EI) *m/z*: 418 $[M]^+$. *Anal.* Calcd for $C_{18}H_{18}N_4O_8$: C, 51.67; H, 4.30; N, 13.39. Found: C, 51.71; H, 4.26; N, 13.43%.

***N*,*N*-Dimethyl-*N*-(4-{2-(3-methyl-4-nitro-5-isoxazolyl)-1-[(3-methyl-4-nitro-5-isoxazolyl)methyl]ethyl}phenyl)amine (Entry 4, Table 3)** White solid; IR (KBr): 1575 ($=N^+-O^-$), 1615 (C=N), cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 2.3 (s, 6H, $2CH_3$), 3.2 (s, 6H, $2NCH_3$), 3.6 (dd, 2H, J=14, 8 Hz, CH_2CH), 3.8 (dd, 2H, J=14, 8 Hz, CH_2CH), 4.0 (quintet, 1H, J=8 Hz, CH Ar), 6.8—7.4 (m, 4H, Ar-H). MS (EI) *m/z*: 415 $[M]^+$. *Anal.* Calcd for $C_{19}H_{21}N_5O_6$: C, 54.93; H, 5.06; N, 16.86. Found: C, 54.90; H, 5.01; N, 16.88%.

2-{2-(3-Methyl-4-nitro-5-isoxazolyl)-1-[(3-methyl-4-nitro-5-isoxazolyl)methyl]ethyl}phenol (Entry 5, Table 3) White solid, mp; IR (KBr): 1565 ($=N^+-O^-$), 1613 (C=N), cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 2.2 (s, 6H, $2CH_3$), 3.5 (dd, 2H, J=14, 8 Hz, CH_2CH), 3.7 (dd, 2H, J=14, 8 Hz, CH_2CH), 4.0 (quintet, 1H, J=8 Hz, CH Ar), 7.0—7.5 (m, 4H, Ar-H), 9.5 (br s, 1H, OH, D_2O exchangeable). MS (EI) *m/z*: 388 $[M]^+$. *Anal.* Calcd for $C_{17}H_{16}N_4O_7$: C, 52.57; H, 4.12; N, 14.43. Found: C, 52.61; H, 4.09; N, 14.45%.

5-[2-(1,3-Benzodioxol-5-yl)-3-(3-methyl-4-nitro-5-isoxazolyl)propyl]-3-methyl-4-nitroisoxazole (Entry 6, Table 3) White solid; IR (KBr): 1570 ($=N^+-O^-$), 1620 (C=N), cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 2.2 (s, 6H, $2CH_3$), 3.5 (dd, 2H, J=14, 8 Hz, CH_2CH), 3.7 (dd, 2H, J=14, 8 Hz, CH_2CH), 4.1 (quintet, 1H, J=8 Hz, CH Ar), 5.0 (s, 2H, OCH_2O), 6.9—7.3 (m, 3H, Ar-H). MS (EI) *m/z*: 416 $[M]^+$. *Anal.* Calcd for $C_{18}H_{16}N_4O_8$: C, 51.92; H, 3.84; N, 13.46. Found: C, 51.90; H, 3.88; N, 13.50%.

General Procedure for Synthesis of 3-Methyl-5-{(*Z*)-3-(3-methyl-4-nitro-5-isoxazolyl)-2,4-diphenyl-1-[(*Z*)-1-phenylmethylidene]-3-butenyl}-4-nitroisoxazoles (6) in Ionic Liquid (Entry 1, Table 4) 3-Methyl-5-[3-(3-methyl-4-nitro-5-isoxazolyl]-2-phenyl propyl]-4-nitroisoxazoles **7** (1 mmol) and aromatic aldehyde (2 mmol) were taken in IL, [bmIm]OH (5 ml) and the reaction mixture was stirred at room temperature for 10—15 min. The reaction was monitored by TLC. After the completion of the reaction, the reaction mixture was extracted with ethyl acetate (3×10 ml). Evaporation of ethyl acetate gave crude product, which was purified by recrystallization from ethyl alcohol to give **6**. The IL left over in the reaction was washed with ethyl acetate and dried at 80 °C under vaccum and was further used for conducting the reaction once again. It has been used for subsequent runs of the reaction for five times. This procedure was followed for all the reactions listed in Table 4. IR (KBr): 978 (C=C), 1550 ($=N^+-O^-$), 1630 (C=N), cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 2.3 (s, 6H, $2CH_3$), 4.2 (s, 1H, benzylic H), 6.2 (s, 2H, 2=CH), 6.9—7.5 (m, 15H, ArH). ^{13}C-NMR (75 MHz) δ: 11.05 (C-6), 45.05 (C-9), 110.85 (C-4), 117.80 (C-7), 122.02 (C-8), 125.80 (Ar-C), 126.40 (Ar-C), 127.80 (Ar-C), 127.95 (Ar-C), 128.00 (Ar-C), 128.70 (Ar-C), 129.10 (Ar-C), 129.22 (Ar-C), 130.00 (Ar-C), 131.07 (Ar-C), 137.06 (Ar-C), 137.50 (Ar-C), 155.45 (C-3), 158.90 (C-5). MS (EI) *m/z*: 548 $[M]^+$. *Anal.* Calcd for $C_{31}H_{24}N_4O_6$: C, 67.88; H, 4.37; N, 10.21. Found: C, 67.85; H, 4.38; N, 10.20%.

3-Methyl-5-{(*Z*)-3-(3-methyl-4-nitro-5-isoxazolyl)-4-(4-methylphenyl)1-[(*Z*)-1-(4-methylphenyl)methylidene]-2-phenyl-3-butenyl}-4-nitroisoxazole (Entry 2, Table 4) IR (KBr): 980 (C=C),1570 (=N–O$^-$), 1625 (C=N), cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 2.3 (s, 6H, $2CH_3$), 2.5 (s, 6H, $2CH_3$), 4.2 (s, 1H, benzylic H), 6.1 (s, 2H, 2=CH), 6.8—7.4 (m, 13H, ArH). ^{13}C-NMR (75 MHz) δ: 11.40 (C-6), 21.75 (Ar-CH_3), 45.13 (C-9), 111.25 (C-4), 118.50 (C-7), 125.05 (C-8), 126.05 (Ar-C), 126.80 (Ar-C), 127.95 (Ar-C), 128.03 (Ar-C), 128.75 (Ar-C), 129.00 (Ar-C), 129.25 (Ar-C), 129.65 (Ar-C), 130.05 (Ar-C), 132.06 (Ar-C), 133.57 (Ar-C), 138.05 (Ar-C), 155.05 (C-3), 158.88 (C-5). MS (EI) *m/z*: 576 $[M]^+$. *Anal.* Calcd for $C_{33}H_{28}N_4O_6$: C, 68.75; H, 4.86; N, 9.72. Found: C, 68.77; H, 4.85; N, 9.70%.

5-{(*Z*)-4-(4-Methoxyphenyl)1-[(*Z*)-1-(4-methoxyphenyl)methylidene]-3-(3-methyl-4-nitro-5-isoxazolyl)-2-phenyl-3-butenyl}-4-nitroisoxazole (Entry 3, Table 4) IR (KBr): 960 (C=C),1525 ($=N^+-O^-$), 1622 (C=N), cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 2.3 (s, 6H, $2CH_3$), 3.8 (s, 6H, $2OCH_3$), 4.1 (s, 1H, benzylic H), 6.2 (s, 2H, 2=CH), 6.8—7.5 (m, 13H, ArH). MS (EI) *m/z*: 608 $[M]^+$. *Anal.* Calcd for $C_{33}H_{28}N_4O_8$: C, 65.13; H, 4.60; N, 9.21. Found: C, 65.10; H, 4.66; N, 9.25%.

2-[(*Z*)-3-(2,4-Dichlorophenyl)-1-[(*Z*)-2-(2,4-dichlorophenyl)-1-(3-methyl-4-nitro-5-isoxazolyl)-1-ethenyl]-2-(3-methyl-4-nitro-5-isoxazolyl)-2-propenyl]phenol (Entry 4, Table 4) IR (KBr): 980 (C=C),1575 ($=N^+-O^-$), 1630 (C=N), cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 2.2 (s, 6H, $2CH_3$), 4.3 (s, 1H, benzylic H), 6.2 (s, 2H, 2=CH), 6.8—7.5 (m, 10H, ArH), 9.5 (br s, 1H, OH, D_2O exchangeable). MS (EI) *m/z*: 700 $[M]^+$. *Anal.* Calcd for $C_{31}H_{20}N_4O_7Cl_4$: C, 53.14; H, 2.85; N, 8.00. Found: C, 53.10; H, 2.88; N, 8.05%.

5-[(*Z*)-4-(4-Chlorophenyl)-1-[(*Z*)-1-(4-chlorophenyl)methylidene]-3-(3-methyl-4-nitro-5-isoxazolyl)-2-(4-methylphenyl)3-butenyl]-3methyl-4-nitro-isoxazole (Entry 5, Table 4) IR (KBr): 975 (C=C), 1560 ($=N^+-O^-$), 1615 (C=N), cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 2.3 (s, 6H, $2CH_3$), 2.5 (s, 3H, CH_3), 4.1 (s, 1H, benzylic H), 6.2 (s, 2H, 2CH), 6.9—7.6 (m, 12H, ArH). MS (EI) *m/z*: 630 [M]. *Anal.* Calcd for $C_{32}H_{24}N_4O_6Cl_2$: C, 60.95; H, 3.80; N, 8.88. Found: C, 60.99; H, 3.81; N, 8.85%.

4-[(*Z*)-3-(2-(Chlorophenyl)-1-[(*E*)-2-(2-chlorophenyl)-1-(3-methyl-4-nitro-5-isoxazolyl)-1-ethenyl]-2-(3-methyl-4-nitro-5-isoxazolyl)-2-propenyl]-2-methoxyphenol (Entry 6, Table 4) IR (KBr): 975 (C=C), 1550 ($=N^+-O^-$), 1615 (C=N), cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 2.2 (s, 6H, $2CH_3$), 3.8 (s, 3H, OCH_3), 4.2 (s, 1H, benzylic H), 6.2 (s, 2H, 2=CH), 6.8—7.5 (m, 11H, ArH), 9.0 (br s, 1H, OH, D_2O exchangeable). MS (EI) *m/z*: 662 $[M]^+$. *Anal.* Calcd for $C_{32}H_{24}N_4O_8Cl_2$: C, 58.00; H, 3.62; N, 8.45. Found: C, 58.04; H, 3.66; N, 8.41%.

***N*,*N*-Dimethyl-N-{4-[(*Z*)-2-(3-methyl-4-nitro-5-isoxazolyl)-1-[(*Z*)-1-(3-methyl-4-nitro-5-isoxazolyl)-2-(2-methylphenyl)-1-ethenyl]-3-(2-methylphenyl)-2-propenyl]phenyl}amine (Entry 7, Table 4)** IR (KBr): 980 (C=C), 1575 ($=N^+-O^-$), 1630 (C=N), cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 2.3 (s, 6H, $2CH_3$), 2.5 (s, 6H, $2CH_3$), 3.2 (s, 6H, $N(CH_3)_2$), 4.0 (s, 1H, benzylic H), 6.2 (s, 2H, 2=CH), 6.8—7.5 (m, 12H, ArH). MS (EI) *m/z*: 619 $[M]^+$. *Anal.* Calcd for $C_{35}H_{33}N_5O_6$: C, 67.85; H, 5.33; N, 11.30. Found: C, 67.88; H, 5.35; N, 11.27%.

5-{(*Z*)-2-(1,3-Benzodioxol-5-yl)-3(3-methyl-4-nitro-5-isoxazolyl)-4-phenyl-1-[(*Z*)-1-phenylmethylidene]-3-butenyl}-3-methyl-4-nitro-isoxazole (Entry 8, Table 4) IR (KBr): 970 (C=C), 1550 ($=N^+-O^-$), 1620 (C=N), cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 2.3 (s, 6H, $2CH_3$), 4.3 (s, 1H, benzylic H), 5.0 (s, 2H, OCH_2O), 6.1 (s, 2H, 2=CH), 6.8—7.4 (m, 13H, ArH). MS (EI) *m/z*: 592 $[M]^+$. *Anal.* Calcd for $C_{32}H_{24}N_4O_8$: C, 64.86; H, 4.05; N, 9.45. Found: C, 64.85; H, 4.00; N, 9.40%.

General Procedure for Synthesis of 3-Methyl-6-[(3-methyl-5-phenyl-4*H*-pyrrolo[2,3-*d*]isoxazol-6-yl)(phenyl)methyl]-5-phenyl-4*H*-pyrrolo[2,3-*d*]isoxazoles (5) in Ionic Liquid (Entry 1, Table 5) A mixture of benzyl bis-nitro styrylisoxazoles **6** (1 mmol) and $SnCl_2 \cdot 2H_2O$ (5 mmol) were taken in IL [(HMIm)BF_4] (5 ml), and the reaction mixture was stirred at room temperature for 15—30 min. The termination of the reaction was monitored by TLC. The product was extracted with ethyl acetate (2×10 ml). Evaporation of ethyl acetate gave crude product, which was purified by a short column chromatography over silica gel (benzene–ethyl acetate) to provide the pure product, benzyl bis-pyrrolo[2,3-*d*]isoxazole as a pale yellow solid. The ionic liquid was dried under vacuum and reused for five reactions by adding some more $SnCl_2 \cdot 2H_2O$ with out any loss of efficiency. After five runs 50% of fresh IL and $SnCl_2 \cdot 2H_2O$ were added to it and this was used again. This procedure was followed for all the reactions listed in Table 5. Pale color solid, IR (KBr): 3300 (S), 1600, 970 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 2.3 (s, 6H, $2CH_3$), 4.6 (s, 1H, benzylic H), 7.2—7.8 (m, 15H, Ar-H), 8.1 (br s, 2H, pyrrole NH, D_2O exchangeable). MS (EI) *m/z*: 484 $[M]^+$. ^{13}C-NMR (75 MHz) δ: 11.01 (C-7), 40.05 (C-8), 105.20 (C-3′), 111.05 (C-6), 126.05 (Ar-C), 127.00 (Ar-C), 127.50 (Ar-C), 128.02 (Ar-C), 128.75 (Ar-C), 128.99 (Ar-C), 130.02 (C-5), 131.75 (Ar-C), 133.50 (Ar-C), 132.88 (Ar-C), 133.00 (Ar-C), 135.03 (Ar-C), 136.30 (Ar-C), 148.22 (C-3), 155.40 (C-6′). *Anal.* Calcd for $C_{31}H_{24}N_4O_2$: C, 76.85; H, 4.95; N, 11.57. Found: C, 76.88; H, 4.90; N, 11.58%.

3-Methyl-6-[(3-methyl-5-(4-methylphenyl)-4*H*-pyrrolo[2,3-*d*]isoxazol-6-yl)(phenyl)methyl]-5-(4-methylphenyl)-4*H*-pyrrolo[2,3-*d*]isoxazole (Entry 2, Table 5) Pale yellow solid, IR (KBr): 3250 (S), 1610, 980 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 2.2 (s, 6H, $2CH_3$), 2.5 (s, 6H, $2CH_3$), 4.8 (s, 1H, benzylic H), 6.8—7.6 (m, 13H, Ar-H), 8.5 (br s, 2H, pyrrole NH, D_2O exchangeable). ^{13}C-NMR (75 MHz) δ: 11.37 (C-7), 21.50 (Ar-CH_3), 41.85 (C-8), 105.55 (C-3′), 111.85 (C-6), 125.85 (Ar-C), 126.85 (Ar-C), 127.05 (Ar-C), 127.95 (Ar-C), 128.33 (Ar-C), 128.87 (Ar-C), 130.08 (C-5), 131.21 (Ar-C), 131.95 (Ar-C), 132.05 (Ar-C), 133.08 (Ar-C), 135.00 (Ar-C), 136.44 (Ar-C), 148.38 (C-3), 156.05 (C-6′). *Anal.* Calcd for $C_{31}H_{24}N_4O_2$: C, 76.85; H, 4.95; N, 11.57. Found: C, 76.88; H, 4.90; N, 11.58%. MS (EI) *m/z*: 512 $[M]^+$. *Anal.* Calcd for $C_{33}H_{28}N_4O_2$: C, 77.34; H, 5.46; N, 10.93. Found: C, 77.38; H, 5.40; N, 10.95%.

5-(4-Methoxyphenyl)-6-[(5-(4-methoxyphenyl)-3-methyl-4*H*-pyrrolo[2,3-*d*]isoxazol-6-yl)(phenyl)methyl]-3-methyl-4*H*-pyrrolo[2,3-*d*]isoxazole (Entry 3, Table 5) Pale yellow solid, IR (KBr): 3300 (S), 1620, 975 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 2.2 (s, 6H, $2CH_3$), 3.8 (s, 6H, $2OCH_3$), 4.0(s, 1H, benzylic H), 6.8—7.5 (m, 13H, Ar-H), 8.5 (br s, 2H, pyrrole NH, D_2O exchangeable). MS (EI) *m*/*z*: 544 $[M]^+$. *Anal.* Calcd for $C_{33}H_{28}N_4O_4$: C, 72.79; H, 5.14; N, 10.29. Found: C, 72.81; H, 5.15; N, 10.30%.

2-{Di-[5-(2,4-dichlorophenyl)-3-methyl-4*H*-pyrrolo[2,3-*d*]isoxazol-6-yl)methyl}phenol (Entry 4, Table 5) Pale yellow solid, IR (KBr): 3300 (S), 1625, 970 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 2.3 (s, 6H, $2CH_3$), 4.6(s, 1H, benzylic H), 6.8—7.5 (m, 10H, Ar-H), 8.5 (br s, 2H, pyrrole NH, D_2O exchangeable), 9.5 (br s, 1H, D_2O exchangeable) . MS (EI) *m*/*z*: 638 $[M]^+$. *Anal.* Calcd for $C_{31}H_{20}N_4O_3Cl_4$: C, 58.30; H, 3.13; N, 8.77. Found: C, 58.33; H, 3.10; N, 8.75%.

5-(4-Chlorophenyl)-6-[(5-(4-chlorophenyl)-3-methyl-4*H*-pyrrolo[2,3-*d*]isoxazol-6-yl]-4-methyl phenyl)methyl]-3-methyl-4*H*-pyrrolo[2,3-*d*]isoxazole (Entry 5, Table 5) Pale yellow solid, IR (KBr): 3235 (S), 1620, 975 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 2.2 (s, 6H, $2CH_3$), 2.5 (s, 3H, CH_3), 4.7 (s, 1H, benzylic H), 6.8—7.3 (m, 12H, Ar-H), 8.6 (br s, 2H, pyrrole NH, D_2O exchangeable). MS (EI) *m*/*z*: 566 $[M]^+$. *Anal.* Calcd for $C_{32}H_{24}N_4O_2Cl_2$: C, 67.84; H, 4.24; N, 9.89. Found: C, 67.70; H, 4.20; N, 9.87%.

4-{Di[5-(2-Chlorophenyl)-3-methyl-4*H*-pyrrolo[2,3-*d*]isoxazol-6-yl]methyl}-2-methoxyphenol (Entry 6, Table 5) Pale yellow solid, IR (KBr): 3300 (S), 1625, 970 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 2.2 (s, 6H, $2CH_3$), 3.8 (s, 3H, OCH_3), 4.6 (s, 1H, benzylic H), 6.8—7.5 (m, 12H, Ar-H), 8.8 (br s, 2H, pyrrole NH, D_2O exchangeable), 9.5 (br s, 1H, OH, D_2O exchangeable). MS (EI) *m*/*z*: 598 $[M]^+$. *Anal.* Calcd for $C_{32}H_{24}N_4O_4Cl_2$: C, 64.21; H, 4.01; N, 9.36. Found: C, 64.25; H, 4.05; N, 9.32%.

***N*-(4-{Di-[3-methyl-5-(2-methylphenyl)-4*H*-pyrrolo[2,3-*d*]isoxazol-6-yl]methyl}phenyl)-*N*,*N*-dimethylamine (Entry 7, Table 5)** Pale yellow solid, IR (KBr): 3335 (S), 1630, 980 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 2.2 (s, 6H, $2CH_3$), 2.5 (s, 6H, $2CH_3$), 3.2 (s, 6H, $N(CH_3)_2$), 4.8 (s, 1H, benzylic H), 6.8—7.6 (m, 12H, Ar-H), 8.6 (br s, 2H, pyrrole NH, D_2O exchangeable). MS (EI) *m*/*z*: 555 $[M]^+$. *Anal.* Calcd for $C_{35}H_{33}N_5O_2$: C, 75.67; H, 5.94; N, 12.61. Found: C, 75.65; H, 5.90; N, 12.65%.

6-[1,3-Benzodioxol-5-yl-(3-methyl-5-phenyl-4*H*-pyrrolo[2,3-*d*]isoxazol-6-yl)methyl]-3-methyl-5-phenyl-4*H*-pyrrolo[2,3-*d*]isoxazole (Entry 8, Table 5) Pale yellow color solid, IR (KBr): 3300 (S), 1620, 975 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 2.3 (s, 6H, $2CH_3$), 4.6 (s, 1H, benzylic H), 5.0 (s, 2H, OCH_2O), 6.8—7.3 (m, 13H, Ar-H), 8.5 (br s, 2H, pyrrole NH, D_2O exchangeable). MS (EI) *m*/*z*: 528 $[M]^+$. *Anal.* Calcd for $C_{32}H_{24}N_4O_4$: C, 72.72; H, 4.54; N, 10.60. Found: C, 72.70; H, 4.55; N, 10.63%.

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