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Synthesis of dimeric pyridinium bromide under silica supported approach

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ABSTRACT
Synthesis of dimeric substituted ester derivative of pyridinium salt with flexible linker units under conventional/silica supported approach. Solid-phase approach is much superior to the conventional method due to nontoxic, solvent free, easy work up procedure, and lesser reaction period. Synthesized dimeric ester derivative of pyridinium salts is showed excellent catalytic response for the preparation of oxizinone derivatives under conventional/approach.

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KEYWORDS
Anion exchange; dimeric ester derivative; optimum concentration; oxazinone; solid phase

GRAPHICAL ABSTRACT

Introduction

Ionic liquids consist of an organic cation (pyridinium, pyrrolidinium, imidazolium) and inorganic or organic anions which shows ionic conductivity, high polarizing nature, non-volatility, higher chemical, and thermal stability.[1] Ionic liquids exhibit a number of biological applications such as an adhesive, antifouling reagent, antiseptic, biocide, and disinfectant.[2–5] Pyridinium containing amide-based poly (ionic liquids) are used to calculate the interaction and separation of CO_2 and methane gas by theoretical model.[6] Various concentration of anthracene-based dimeric substituted pyridinium chloride is acted as fluorescence sensing probe and showed significant response with $H_2PO_4^-$ ion.[7] Brønsted acid-surfactant mixed catalyst acted as a potential catalyst to enhance one-pot three components Mannich reaction (Br^-, HSO_4^-, $H_2PO_4^-$, Tos^-),

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various counter anions containing ionic liquids are used. Among these anions, the Tos^{-} ion showed better catalytic response than the others due to bulkier.[8] Multicomponent one-pot reaction has been attracted much interest in the area of synthetic organic chemistry to generate more derivatives in combinatorial drug discovery.[9,10] β-Amino carbonyl derivatives are prepared from one-pot multicomponent reaction which is catalyzed by acid–ionic polymer bearing imidazolium trifluoromethane sulfonate.[11] Didecyldimethyl ammonium cation with different organic anion are showed dual biological responses such as antimicrobial and sweetener.[12] Herein, we wish to report the synthesis of ester derivative of pyridinium salt under the conventional/greener approach and its catalytic application.

Results and discussion

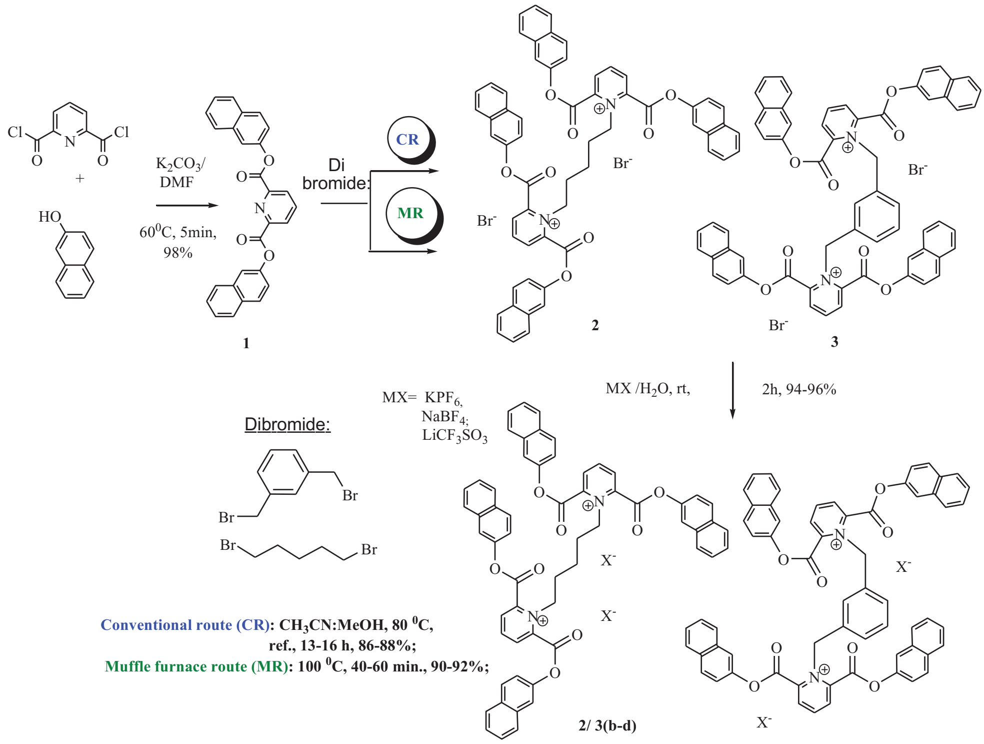
Synthesis of ester derivative pyridine **1** from pyridine 2, 6-dicarbonyl dichloride (1.0 equiv.; 1.47×10^{-2} mmol) and 2-naphthol (2.05 equiv.; 3.014×10^{-2} mmol) along with anhydrous K_2CO_3 (2.0 equiv.; 3.014×10^{-2} mmol) in the presence of 30 mL of dry DMF at 60 °C for 5 min. to give ester derivative pyridine **1** in 98% yield. *N*-alkylation is carried out by treating 2.05 equiv. of ester derivative pyridine **1** (2.673×10^{-3} mmol) and 1, 5-dibromopentane/*m*-xylenedibromide (1.00 equiv.; 1.304×10^{-3} mmol) in the presence of 20 mL dry CH_3CN under refluxing condition for 13–16 h to give *N*-alkylated substituted pyridinium bromide **2/3** in quantitative yield.

Same N-alkylation reaction is tried under solvent free silica supported reaction using Muffle furnace at 100 °C. Solid-phase silica-supported approach is much superior to conventional due to its lesser reaction period, higher yield, solvent-free, and environmental friendly approach. Solvent-free silica-supported reactions are nearly 15 times faster than the conventional method. *M*-Xylenedibromide reacts much faster than 1, 5-dibromopentane during *N*-alkylation reaction. In general, ionic liquids will show different physical and chemical properties based on counter anions. So anion exchange reaction is very important to study their various physical and chemical properties. Anion exchange reaction is carried out with different counter anion containing inorganic salts such as KPF_6, $NaBF_4$, and $LiCF_3SO_3$ in 20 mL of deionized water under room temperature with stirring for 2 h to give anion exchange products of **2/3(b–d)** in 80–94% of yield (Scheme 1).

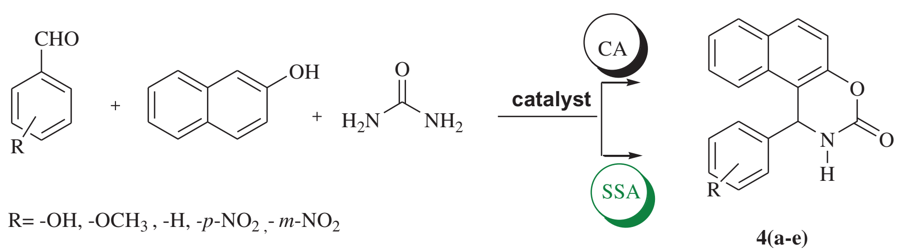
Catalytic activity

Flexible dimeric pyridinium salts are prepared from easily available starting materials under conventional and solid-phase solvent-free Muffle furnace method. One-pot multicomponent reaction is tried in the presence of various concentrations of our catalyst with/without solvent (Scheme 2).

Substituted dimeric pyridinium bromide **3** is showed excellent catalytic activity for the preparation of oxizinone derivative than the others. To optimize the catalyst concentration of *m*-xylene core moiety containing dimeric pyridinium bromide, the reactions are repeated with various concentrations such as 1.8135×10^{-2} mmol, 3.627×10^{-2} mmol, and 5.440×10^{-2} mmol for one-pot preparation of substituted



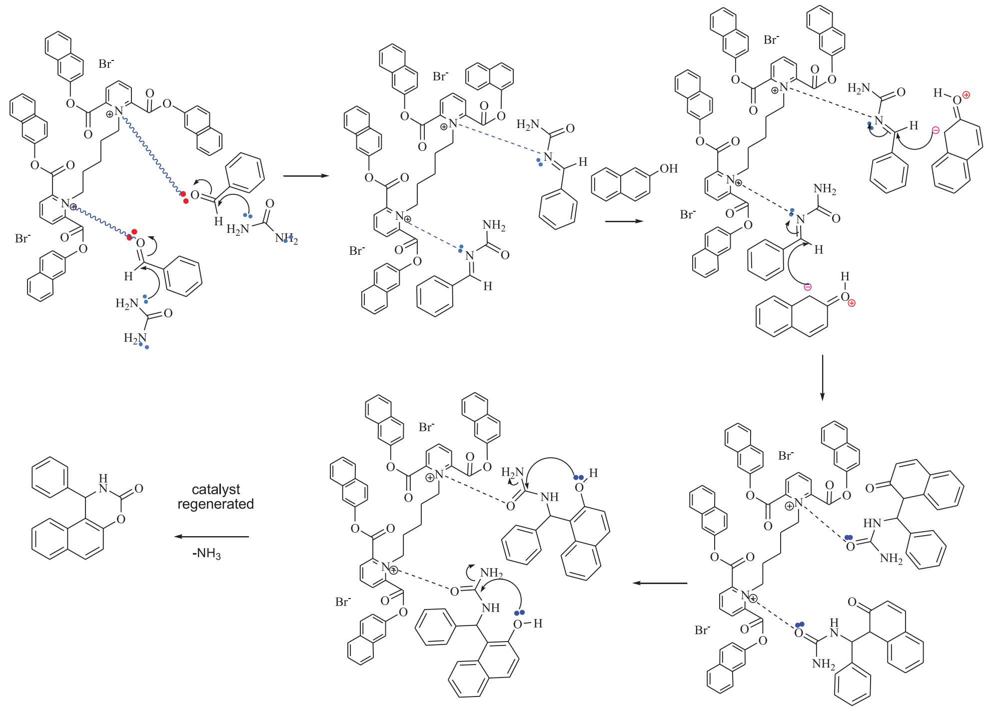
Scheme 1. Synthesis of substituted ester derivative of pyridinium salts under multiple approach.



Scheme 2. Synthesis of substituted oxazinone derivatives under multiple approach. Reagent and conditions: Conventional approach (CA): CH_3CN/ **3a**, ref, 03–120 min, 80–96%; Solid supported approach (SSA): Muffule furnace, 100 °C, 20–45 min., 84–98%

oxazinone derivatives. While increasing the catalyst concentration from 5.440×10^{-2} mmol into 7.254×10^{-2} mmol, there is no appreciable change in the percentage of yield and reaction time.

Plausible mechanism for preparation of oxazinone using flexible dimeric pyridinium bromide



Various substituted oxazinone derivatives are prepared under conventional/solid-phase approach; reactions are repeated with different concentrations. The results are summarized in Tables 1 and 2; $MgFe_2O_4$ and $SiO_2–SO_3H$ catalyst are used to prepare benzthioxazione under microwave-assisted solvent-free approach. Reaction time and percentage of yield are appreciable but expensive catalyst as well as base sensitive catalyst.[13] Oxazinone derivatives are prepared under 200 mg of Amberlite IRA-400 Cl catalyst which required more than 2 h for reaction completion.[14] Whereas only 60 mg of flexible/*m*-xylene bridged dimeric pyridinium salt under silica-supported approach required for just 20 min. for completion. Hence catalyst is potential due to its shorter reaction time, solvent-free higher yield, and environmental friendliness.

We have recycled upon fourth cycles and used for the preparation of 1, 2-dihydro-1-(4-hydroxyphenyl) naphtho [1, 2-e][1, 3]oxazin-3-one **4a** under same reaction condition; even after fourth cycles the product obtained was as observed in excellent to good yield which is shown in Table 3.

Conclusions

Dimeric ester derivative of pyridinium salts are prepared under conventional/silica-supported Muffle furnace reaction condition. Muffle furnace approach is nearly fifteen times faster than the conventional method. We have tried with various concentrations of our catalyst for the preparation of oxazine-3-one derivatives. Bromide counter anion containing dimeric ester derivative of pyridinium salts showed excellent catalytic

Table 1. Synthesis of 1, 2-dihydro-1-arylnaphtho [1, 2-e] [1, 3] oxazine-3-one derivatives assisted by various concentration of flexible dimeric pyridinium salts **2(a–d)**.

				Concentration of flexible pyridinium salts											
				1.8135×10^{-2} mmol				3.627×10^{-2} mmol				5.440×10^{-2} mmol			
				CA		SSA		CA		SSA		CA		SSA	
S. No	Catalyst		Derivative	T	Y	T	Y	T	Y	T	Y	T	Y	T	Y
1	Flexible dimeric pyridinium cation with	Br^- **2a**	**4a**	90	66	45	77	80	76	35	83	90	89	25	96
			4b	100	65	50	74	90	75	40	80	89	88	30	93
			4c	80	67	40	76	70	77	30	82	91	92	20	90
			4d	70	74	35	80	60	84	25	85	50	91	15	92
			4e	60	77	30	79	50	87	20	86	40	90	10	95
2		PF_6^- **2b**	**4a**	100	62	50	75	90	72	40	81	80	93	30	88
			4b	110	64	55	72	100	74	45	81	90	91	35	90
			4c	90	67	45	73	80	77	35	80	70	92	25	89
			4d	80	69	40	79	70	79	30	83	60	91	20	91
			4e	70	72	35	76	60	82	25	84	50	95	15	93
3		BF_4^- **2c**	**4a**	110	65	55	72	100	75	45	80	90	93	35	88
			4b	120	61	60	70	110	71	50	79	100	92	40	87
			4c	100	63	50	74	90	73	40	78	80	91	30	90
			4d	90	66	45	78	80	76	35	82	70	90	25	90
			4e	80	69	40	72	70	79	30	82	60	92	20	90
4		$CF_3SO_3^-$ **2d**	**4a**	115	75	53	70	105	85	43	79	95	89	33	85
			4b	125	57	63	69	115	67	53	78	105	92	43	88
			4c	105	59	52	70	95	69	42	79	85	90	32	87
			4d	95	64	47	76	85	74	37	81	75	95	27	86
			4e	85	67	43	71	75	77	33	80	65	92	23	90

TABLE 2. Synthesis of 1, 2-dihydro-1-arylnaphtho [1, 2-e] [1, 3] oxazine-3-one derivatives with low concentration of *m*-xylene bridged dimeric pyridinium salts **3(a–d)**.

				Concentration of flexible pyridinium salts											
				1.813×10^{-2} mmol				3.627×10^{-2} mmol				5.440×10^{-2} mmol			
				CA		SSA		CA		SSA		CA		SSA	
S. No	Catalyst		Derivative	T	Y	T	Y	T	Y	T	Y	T	Y	T	Y
1	*m*-xylene bridged dimeric pyridinium cation with	Br^- **3a**	**4a**	60	69	30	87	50	90	20	93	40	93	16	95
			4b	70	68	35	84	60	89	27	90	50	91	22	94
			4c	50	70	25	86	40	90	15	92	30	94	10	95
			4d	40	77	20	90	30	93	10	95	20	94	05	97
			4e	30	80	15	89	20	92	08	96	10	93	03	98
2		PF_6^- **3b**	**4a**	70	65	35	85	60	89	25	91	50	92	20	93
			4b	80	67	40	82	70	88	33	91	60	90	28	93
			4c	60	70	30	83	50	91	20	90	40	93	15	93
			4d	50	72	25	89	40	91	12	93	30	93	07	96
			4e	40	75	20	86	30	91	11	94	20	92	06	97
3		BF_4^- **3c**	**4a**	80	68	40	82	70	86	30	90	60	91	25	92
			4b	90	64	45	80	80	86	38	89	70	91	33	92
			4c	70	66	35	84	60	89	25	88	50	90	20	92
			4d	60	69	30	88	50	89	15	92	40	91	12	93
			4e	50	72	25	82	40	90	13	92	30	91	08	95
4		$CF_3SO_3^-$ **3d**	**4a**	85	78	45	80	75	84	35	89	65	90	30	90
			4b	95	60	50	79	85	87	43	88	75	89	38	91
			4c	75	62	40	80	65	87	30	89	55	91	25	91
			4d	65	67	35	86	55	88	20	91	45	90	15	92
			4e	55	71	30	81	45	89	15	90	35	89	10	94

Table 3. Study of catalyst re-useable efficiency up to fourth cycles.

		1st cycle				2nd cycle				3rd cycle				4th cycle			
		CA		SSA		CA		SSA		CA		SSA		CA		SSA	
S. No	Catalyst	T	Y	T	Y	T	Y	T	Y	T	Y	T	Y	T	Y	T	Y
1	**3a**	40	93	16	95	40	89	16	92	40	89	16	92	40	93	16	90
2	**3b**	50	92	20	93	50	88	20	90	50	88	20	90	50	92	20	89
3	**3c**	60	91	25	92	60	86	25	88	60	86	25	88	60	91	25	86
4	**3d**	65	90	08	90	65	86	08	88	65	86	08	88	65	90	08	86

T: Time in minutes; Y: percentage of yield.

response than the others; due to bigger size of anion which is away from cation so effective binding is possible. Hence, bromide counter anion containing dimeric ester derivative of pyridinium cation could perform as a better Lewis character. We have prepared two different linker units containing dimeric pyridinium salt. *m*-Xylene bridged dimeric pyridinium salts are showed excellent catalytic response than the flexible pentane moiety due to more flexibility which shows lesser Lewis character. We observed that 5.440×10^{-2} mmol concentration of *m*-xylene bridged dimeric pyridinium bromide **3a** is the optimum catalytic concentration for the preparation of oxazinone derivatives.

General experimental conditions

Preparation of bis (2-naphthyl) pyridine-2, 6-dicarboxylate 1: 3.0 g of pyridine-2, 6-dicarboyl dichloride (1.47×10^{-2} mmol; 1.0 equiv.) is mixed with 4.3 g of naphthalen-2-ol (3.014×10^{-2} mmol; 2.0 equiv.) and 4.1 g of K_2CO_3 dissolved (3.014×10^{-2} mmol; 2.0 equiv.) in the presence of 50 mL of *N, N*-dimethylformamide (DMF) at room temperature stirring for 5 min. to give compound **1** in quantitative yield. Yield: 3.4 g, (98%); Liquid; ^{1}H NMR: (400 MHz, DMSO-d_6) δ: 6.43–6.94 (m, 8H), 7.32 (s, 2H), 7.65–7.87 (m, 4H), 8.42–8.58 (m, 3H); ^{13}C NMR: (100 MHz, DMSO-d_6) δ: 117.8, 124.0, 126.6, 126.9, 128.2, 129.3, 131.1,134.9, 140.0, 147.9 and 156.5; MS (FAB): *m/z* 419.43; Anal. Calcd for: $C_{27}H_{17}NO_4$: C: 77.32: H: 4.09: N: 3.34; Found: C: 77.26: H: 3.94: N: 3.26.

General procedure for *N*-alkylation reaction: Bis (2-naphthyl) pyridine-2, 6-dicarboxylate 1 (2.328×10^{-3} mmol; 2.05 equiv.) is treated with 1, 5-dibromopentane/*m*-xylenedibromide (1.304×10^{-3} mmol; 1.0 equiv.) in the presence of 20 mL dry acetonitrile under refluxing condition for 13–16 h to give *N*-alkylated product of compound **2a/3a.**

Bis-2, 6-(dicarboyl) bis (naphthalene-2-yl naphthalene-3-yl dipyridinium 1, 5 (pentane) bromide **2a:** Yield: 1.27 g (86%); Liquid; ^{1}H NMR: (400 MHz, DMSO-d_6) δ: 2.50–2.58 (q, 2H), 2.80–2.92 (q, 4H), 4.40–4.48 (t, 4H), 6.22–6.75 (m, 16H), 7.12 (s, 4H), 7.23–7.37 (m, 8H), 7.40–8.64 (m, 6H); ^{13}C NMR: (100 MHz, DMSO-d_6) δ: 26.6, 31.7, 35.3, 117.8, 124.0, 126.6, 126.9, 128.2, 129.3, 131.1, 134.9, 140.0, 147.9 and 156.5; MS (FAB): *m/z* 1068.8; Anal. Calcd for: $C_{59}H_{44}Br_2N_2O_8$: C: 66.30: H: 4.15: N: 2.62; Found: C: 66.24: H: 4.08: N: 2.58

General procedure for anion exchange reaction was carried out from flexible dimeric pyridinium bromide **2a/3a** (2.65×10^{-4} mmol; 1.0 equiv.) is treated with various counter anion containing inorganic salt such as $NaBF_4$, K_4PF_6, and $LiCF_3SO_3$ (5.44×10^{-4} mmol; 2.05 equiv.) is dissolved in 20 mL of deionized water at room temperature with stirring for 2 h to give anion exchange product of compound **2/3(b–d)** in 90–97% yield. Metallic bromide and flexible dimeric pyridinium salts are soluble in water, so separation is not easier. Under these circumstance, Soxhlet extraction is used in for purification dry THF for 1 h refluxtion. Anion exchanged reaction is confirmed by aqueous $AgNO_3$ solution.

Bis-2, 6-(dicarboyl) bis (naphthalene-2-yl naphthalene-3-yl dipyridinium 1, 5 (pentane) hexafluorophosphate **2 b:** Yield: 0.28 g, (91%); Liquid; ^{1}H NMR: (400 MHz, DMSO-d$_6$) δ: 2.48–2.56 (q, 2H), 2.78–2.90 (q, 4H), 4.38–4.46 (t, 4H), 6.20–6.73 (m, 16H), 7.10 (s, 4H), 7.21–7.35 (m, 8H), 7.38–8.62 (m, 6H); ^{13}C NMR: (100 MHz, DMSO-d$_6$) δ: 26.4, 31.5, 35.1, 117.6, 123.8, 126.4, 126.7, 128.0, 129.1, 130.0, 134.7, 139.8, 147.7 and 156.3; MS (FAB): *m/z* 1198.92; Anal. Calcd for: $C_{59}H_{44}F_{12}N_2O_8P_2$: C: 59.11: H: 3.70: N: 2.34; Found: C: 59.05: H: 3.66: N: 2.28.

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