Novel betaines/mesoionic compounds via a simple and convenient MCR in aqueous micellar system: Synthesis of thiazolo[2,3-*a*]isoquinolin-4-ium derivatives

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Graphical abstract

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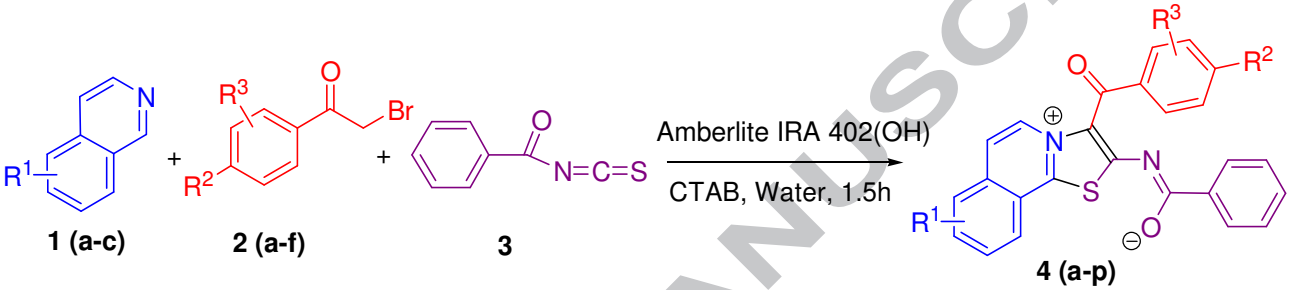

1 (a-c) 2 (a-f) 3 4 (a-p)

Novel betaines/mesoionic compounds via a simple and convenient MCR in aqueous micellar system: Synthesis of thiazolo[2,3-*a*]isoquinolin-4-ium derivatives

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Abstract: An inexpensive one-pot green methodology has been developed for the synthesis of thiazolo[2,3-*a*]isoquinolin-4-ium derivatives by the reaction of different derivatives of isoquinoline and 2-bromoacetophenone/ bromoacetonitrile with benzoyl isothiocyanate in aqueous micellar medium.

Keywords: Multicomponent reaction; 1,3-dipolar cycloaddition; thiazolo[2,3-*a*]isoquinolin-4-ium; benzoyl isothiocyanate; mesoionic; aqueous micellar system.

Mesoionic compounds (MICs) are mesomeric betaines in which both positive and negative charges are delocalized and have been known for more than a century.[1,2] MICs have always remained the centre of attraction to the chemists because of the bonding aspects associated with their unusual structure. These are also regarded as mesomeric heterocyclic betaines, strongly stabilized by π-electron delocalization and having large dipole moments.[3] Among the various synthetic approaches to mesoionic heterocycles, the 1,3 dipolar cycloaddition reactions were widely employed and most of those are concerned with the formation of münchnones (1,3-

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oxazolium-5-olates) and the newer isomünchnones (1,3-oxazolium-4-olates). Some research involving the mesoionic sydnones (1,2,3-oxadiazolium-5-olates), thiomünchnones (1,3-oxathiolium-5-olates), and thioisomünchnones (1,3-thiazolium-4-olates) have also appeared in the literature.[4] In recent years, the related fused ring system of thiazolo[2,3-*a*]isoquinolin-4-ium has received much attention, as the derivatives display various applications,[5] but surprisingly, work concerning the synthesis of this ring system exists scantily.[6] However, preparative methods involving cyclo-condensation reactions of 3,4-dihydroisoquinoline / 3,4-dihydroiso-thiocarbostyril or *N*-thioacylated phenyl ethylamine derivatives with α-mercapto-acids / esters,[7] β-mercaptoacid halides,[8] ethylene sulfide[9,10] or α-haloacids / acid halides[11-13] respectively have been reported for partially hydrogenated racemic compounds. Kroehnke and coworkers have prepared similar ring system by treatment of *N*-arylmethyl- and *N*-acylmethyl isoquinolinium salts with carbon disulfide and alkali.[14] An asymmetric synthesis of thiazolo[2,3-*a*]isoquinoline derivatives involving the reaction of 6,7-dimethoxy-3,4-dihydroisoquinoline and (−)-methyl thioglycolate also appeared in the literature.[15]

We felt that an eco- friendly, flexible and efficient synthetic protocol needed to be established for this type of compounds as the current trend in organic chemistry is to establish methods of ring formation from simple starting materials in fewer steps and using environmentally benign conditions. In this regard, water[16] is being preferred as solvent because it is abundant in nature, has virtually no cost, and is safest among all available solvents, thus leading to environmentally benign chemical processes.[17] But the solubility of organic compounds in water is very poor because of its hydrophobicity. Through the introduction of micelles[18] as the reaction media, which work both by solubilization due to hydrophobic effect and by counter ion binding due to

electrostatic forces, this problem of hydrophobicity has been minimized. The solubilization of water-insoluble reactants and products inside the micelles results not only in high concentration due to the small volume, but also in different orientations of the soluble molecules that influence the reaction mechanism, resulting in remarkable differences in reaction rate and selectivity than would be observed in a homogeneous system.[19] It has also been established that chemical reaction in aqueous micellar condition rather than in organic solvents results in better yield because the insolubility of the final product in water allows easy isolation of the compound in most of the cases. In continuation of our search in the area of 1,3-dipolar cycloaddition mostly exploiting this approach,[20] we herein report an efficient and environment-friendly methodology for the synthesis of 3-benzoyl-2-(benzoylamido)-thiazolo[2,3-*a*]isoquinolin-4-ium [**4a**] (Figure 1) employing an isoquinolinium ylide (generated *in situ* from isoquinoline and phenacyl bromide) and an activated dienophile (benzoyl isothiocyanate) in micellar solution at ambient temperature (Scheme 1).

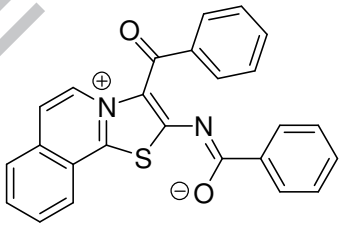
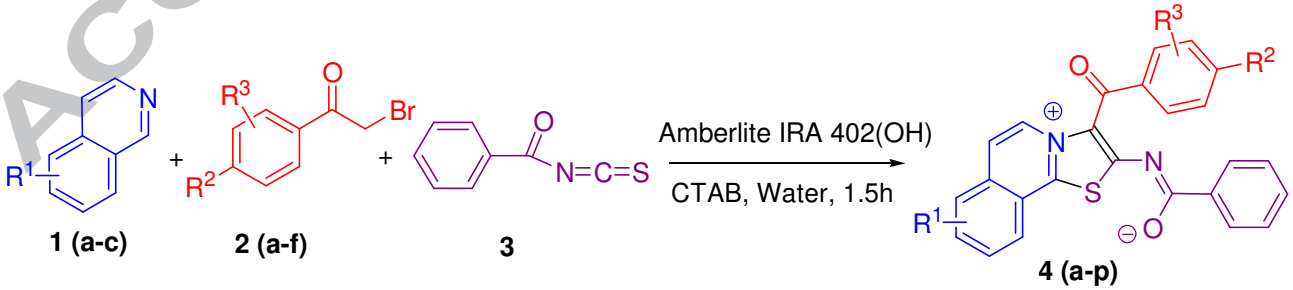


Figure 1. 3-benzoyl-2-(benzoylamido)-thiazolo[2,3-*a*]isoquinolin-4-ium [**4a**].



Scheme1. Synthesis of **4(a-p)** in aqueous micellar medium

At the outset, we chose isoquinoline (**1a**), phenacyl bromide (**2a**) and benzoyl isothiocyanate (**3**) as model reactants in presence of a base, Amberlite IRA 402(OH), for the synthesis of the thiazolo[2,3-*a*]isoquinolin-4-ium **4a**. These were reacted in water at room temperature for different time periods to evaluate the effect of various conditions. We also investigated the reactions systematically in aqueous solutions of cationic, anionic, and nonionic surfactants well above their critical micellar concentrations (CMC) in order to study the effect of surfactant solutions (Table-1).

The results revealed that reactions carried out without a surfactant were ineffective (Table 1, entry 1); no reaction occurred even after prolonged time period. Gratifyingly, adding the surfactant cetyl trimethyl ammonium bromide (CTAB: cmc value 0.92 mM) [21] to the system at a concentration of 40 mM furnished 20% (entry 2) of the desired product **4a** after 1.5 h of reaction. Raising the concentration of CTAB to 60 mM further enhanced the yield to 55% (entry 3), but the best result (yield 90%) was obtained when the concentration was raised to 80 mM (entry 4).

Table 1. Reaction monitored by using different surfactants

Entry[a]	Surfactant	Concentration[b] (mM)	Yield[c] of **4a**
1	None	-	NR[d]
2	CTAB	40	20
3	CTAB	60	55
4	CTAB	80	90
5	CTAB	90	90
6	CTAB	100	90
7	TTAB	50	40
8	TTAB	80	75
9	Triton X-114	80	55
10	SDS	80	50

[a]Reaction performed using **1a, 2a,** and **3** in water at room temperature for 1.5 h in presence of Amberlite IRA 402(OH)
[b]Concentrations of different surfactants (CTAB, SDS, TTAB and Triton-X).
[c]Yield of isolated product.
[d]No reaction.

No significant improvement in the yield was observed on further increase in the concentration to 90 mM (entry 5) or 100 mM (entry 6). We also used another surfactant tetradecyltrimethyl-ammonium bromide (TTAB: cmc value 3.8 mM) [22] at concentrations of 50 mM and 80 mM, but the yields that resulted were not satisfactory enough (40% for entry 7, 75% for entry 8). Use of the nonionic surfactant Triton X-114 (cmc 0.28 mM) [23] and the anionic surfactant sodium dodecylsulfate (SDS: cmc value 8.1 mM) [24] at 80 mM concentration also proved unsatisfactory, furnishing the product to the extent of 55% (Table 1, entry 9) and 50% (Table 1, entry 10).

Using CTAB, reactions were then performed in the presence of different bases like DBU, NEt_3, DABCO, DMAP, piperidine, K_2CO_3, and Amberlite IRA-402(OH) resin. The Amberlite IRA-402(OH) resin (Table 2, entries 1–8) was found to be the most effective base. It produced no side reaction, gave maximum yield of the product repeatedly even when reused, and was cost effective. But for other bases there were different side reactions and various colour formations which also affected in lowering the yield of the product.

Table 2. Reaction monitored by using different bases

Entry[a]	Base	Time (h)	Yield[b] of **4a**
1	DBU	4	65
2	NEt_3	4	70
3	DABCO	3	65
4	DMAP	3	60
5	Piperidine	9	70
6	K_2CO_3	5	50
7	Amberlite IRA-402(OH)	4	90
8	Amberlite IRA-402(OH)	1.5	90

[a]Reaction performed using **1a, 2a,** and **3** in water in presence of CTAB at room temperature.
[b]Yield refers to pure products after crystallization.

After work-up of the reaction, the resin was recovered by filtration and thoroughly washed with ethanol followed by alkaline water. It was then dried at 80 °C under reduced pressure for 2 h and

reused for subsequent runs. It was observed that after five-time use of the resin, there is a slight decrease in the yield (91–67%) of the fused quinolinium products (Figure 2). Though the mechanism is not yet established, the plausible pathway of the reaction is depicted in Scheme 2.

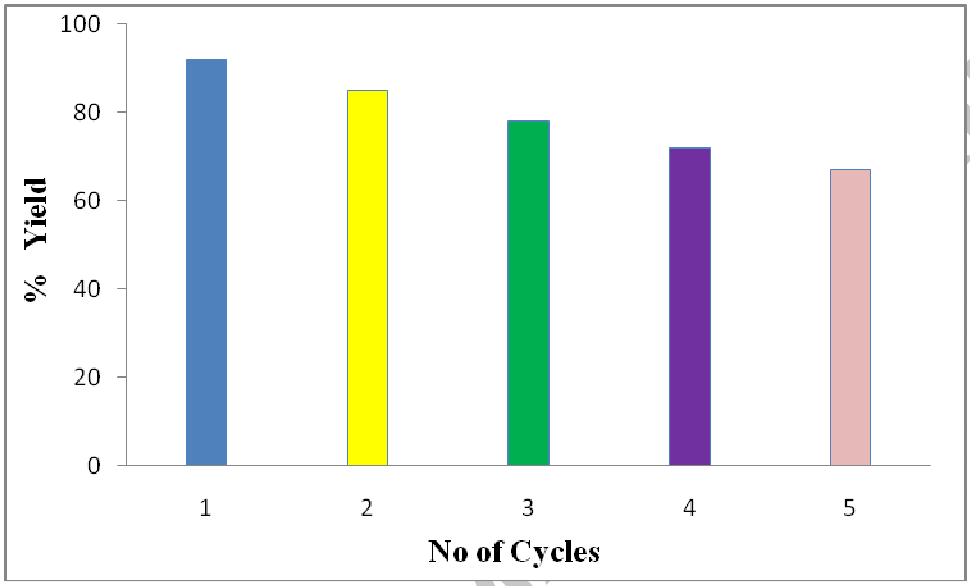
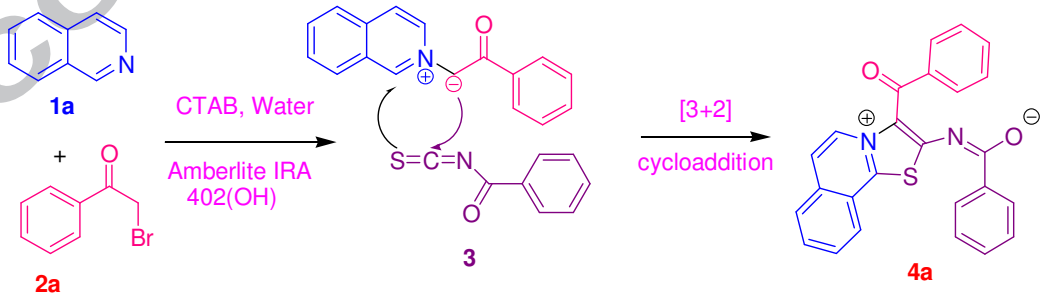


Figure 2. Reusability of the Amberlite IRA 402 (OH) resin. The reactions were performed with **1a** (1 mmol), **2a** (1 mmol) and **3** (1 mmol) successively using 350 mg Amberlite IRA 402 (OH) resin at room temperature for 1.5 h.

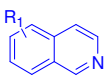
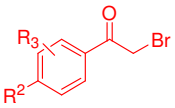
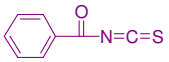
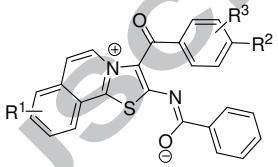
To establish the generality and scope of this green MCR, we employed different derivatives of isoquinoline and phenacyl bromide to carry out reactions with benzoyl isothiocyanate under the optimized condition. We extend the number of derivatives by replacing phenacyl bromide to bromo acetonitrile in two derivatives. The results are summarized in Table 3.



Scheme 2. Mechanistic pathway for Amberlite IRA 402 (OH) mediated 3-benzoyl 2(benzoylamido)-thiazolo[2,3-*a*]isoquinolin-4-ium [**4a**] formation.

The structures of compounds **4(a–r)** were deduced from their mass, ^{1}H NMR and ^{13}C NMR spectral data.[25] The mass spectra of these compounds displayed molecular ion peaks at the expected m/z values. Finally, the crystal structure of one of the products (**4i**) was conclusively proved through X-ray diffraction analysis (Figure 3).

Table 3: Synthesis of thiazolo[2,3-*a*]isoquinolin-4-ium derivatives

Entry[a]	N heterocycle	Phenacyl bromide	benzoyl isothiocyanate	Yield[b](%)
				
1	**1a** (R^1 = H)	**2a** (R^2=R^3= H)	**3**	**4a** (R^1=R^2=R^3=H)	85
2	**1a**	**2b** (R^2 = CH_3, R^3= H)	**3**	**4b** (R^1=R^3=H, R^2=CH_3)	90
3	**1a**	**2c** (R^2 = F, R^3= H)	**3**	**4c** (R^1=R^3=H, R^2=F)	87
4	**1a**	**2d** (R^2 = Cl, R^3= H)	**3**	**4d** (R^1=R^3=H, R^2=Cl)	91
5	**1a**	**2e** (R^2 = R^3= Cl)	**3**	**4e** (R^1=H, R^2= R^3= Cl)	90
6	**1a**	**2f** (R^2 = NO_2, R^3= H)	**3**	**4f** (R^1= R^3= H, R^2=NO_2)	82
7	**1b** (R^1 = 4-Br)	**2a**	**3**	**4g** (R^1=Br, R^2=R^3=H)	86
8	**1b**	**2b**	**3**	**4h** (R^1=Br, R^2=CH_3, R^3=H)	90
9	**1b**	**2c**	**3**	**4i** (R^1=Br, R^2= F, R^3=H)	83
10	**1b**	**2d**	**3**	**4j** (R^1=Br, R^2=Cl, R^3= H)	80
11	**1b**	**2e**	**3**	**4k** (R^1=Br, R^2=R^3=Cl)	90
12	**1b**	**2f** (R^2 = NO_2, R^3= H)	**3**	**4l** (R^1=Br, R^2=NO_2, R^3= H)	84
13	**1c** (R^1 = 5-Br)	**2a**	**3**	**4m** (R^1=Br, R^2=R^3=H)	85
14	**1c**	**2b**	**3**	**4n** (R^1=Br, R^2=CH_3, R^3=H)	87
15	**1c**	**2c**	**3**	**4o** (R^1=Br, R^2= F, R^3=H)	82
16	**1c**	**2d**	**3**	**4p** (R^1=Br, R^2=Cl, R^3= H)	86

17	**1a**	**2g**	**3**	**4q** (R^1=H)	85
18	**1b**	**2g**	**3**	**4r** (R^1=Br)	80

[a]Reaction condition: isoquinoline (1 mmol), phenacyl bromide (1 mmol), benzoyl isothiocyanate (1 mmol), CTAB (4 mmol) and water (50 ml), in air for 1.5 h at room temperature.
[b]Yield of isolated pure product.

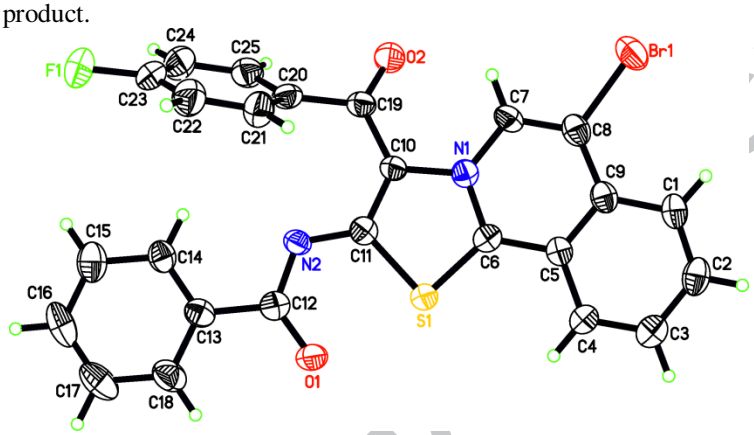


Figure 3. ORTEP diagram showing the molecular structure of **4i** at 30% probability level with atomic numbering scheme of the non-hydrogen atoms

In summary, we have demonstrated a simple, convenient, and efficient one step methodology for an environment friendly synthesis of thiazolo[2,3-*a*]isoquinolin-4-ium, a new group of mesoionic compounds. The notable features are moderate reaction conditions, greater selectivity, and operational simplicity that make it an attractive and useful process for the synthesis of newer heteroaromatics of various applications.

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Supplementary data

^{1}H and ^{13}CNMR spectra of all new compounds associated with this article can be found in the online version. Crystallographic data in CIF format are available free of charge via the Internet at CCDC 952393 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033; or deposit@ccdc.cam.ac.uk).

Reference

1. (a) Fischer, E.; Besthorn, E. Über die Hydrazinverbindungen. *Ann*, **1882**, *212*, 316-339. (b) IUPAC. *Compendium of Chemical Terminology* (*the 'Gold Book'*). 2nd ed. Compiled by McKnight AD, Wilkinson A. Oxford: Blackwell Scientific Publications **1997**.
2. (a) Schönberg, A. *J. Chem. Soc.* **1938,** 824-825.; (b) Baker, W.; Ollis, W.D. Mesoionic Compounds. *Quart. Rev*. **1957**, *11*, 15-29; (c) Ollis, W. D.; Ramsden, C. A. Mesoionic Compounds. *Adv. Heterocycl. Chem.* **1976**, *19*, 3-122.
3. De Athayde, P. F.; Miller, J.; Simas, A. M. *Synthesis* **2000**, *11*, 1565-1568.
4. (a) Potts, K. T. 1, 3-Dipolar Cycloaddition Chemistry; Padwa, A., Ed.; Wiley-Interscience: New York, NY, **1984**; Vol. 2, Chapter 8; (b) Padwa, A. 1, 3-Dipolar Cycloaddition Chemistry; Wiley-Interscience: New York, NY, **1984**; Vols. 1 and 2; (c) Gingrich, H. L.; Baum, J. S. The Chemistry of Heterocyclic Compounds, Oxazoles; Turchi, I. J., Ed.; Wiley:

New York, NY, **1986**; Vol. 45, p 731; (d) Schoffstall, A. M.; Padwa, A. Advances in Cycloaddition; (Ed.: D. P. Curran), Jai, Press Inc: Greenwich, CT, **1990**; Vol. 2, p 1.

5. Lee, S. K.; Kang, I. N.; Lee, J.C.; Shin, W. S.; So,W. W.; Moon S.J. *J. Poly. Sci. Part A: Poly. Chem.* **2011**, *49*, 3129–3137.
6. Shahrekipour , F.; Heydari , R.; Tahamipour , B.; Saravani, H.; Graiff, C. *Phosphorus, Sulfur, and Silicon*, **2014**, *189:2*, 263-273, DOI: 10.1080/10426507.2013.819866.
7. (a) Schneider, W.; Kammerer, E. *Arch. Pharm*. **1966**, *299*, 847–857; (b) Nair, M. D.; Malik, S. R.; Mehta, S. R. *Indian J. Chem*. **1967**, *5*, 221–223; (c) Menendez, J. C.; Delgado-Iribarren, A.; Sollhuber, M. M. *An. Real Acad. Farm*. **1987**, *53*, 238–248; (d) Menendez, J. C.; Sollhuber, M. M. *Heterocycles* **1990**, *31*, 2065–2071.
8. Wimmer, T. L.; Day, F. H.; Bradsher, C. K. *J. Org. Chem*. **1974**, *40*, 1198–1201.
9. Potekhim, A. A.; Sokolov, W. W.; Ogloblin, K. A.; Esacov, S. M. *Khim. Geterocycl. Soedin*. **1983**, *6*, 776–785.
10. Sokolov, W. W.; Salfetnikova, N.; Potekhin, A. A. *Zh. Org. Khim*. **1996**, *32*, 870–878.
11. Rozwadowska, M. D.; Sulima, A. *Tetrahedron* **2001**, *57*, 3499–3506.
12. Sheehan, S. M.; Beall, L. S.; Padwa, A. *Tetrahedron Lett.* **1998**, *39*, 4761–4764.
13. Padwa, A.; Beall, L. S.; Heidelbaugh, T. M.; Liu, B.; Sheehan, S. M. *J. Org. Chem.* **2000**, *65*, 2684–2695.
14. (a) Huisgen, R; Funke, F.; Scnaerer C. F.; Gotthardt, H.; and Brunn, E. *Tetrahedron Lett.* **1967**, 1809-1814; (b) Sato, S.; Ohta, R. *Bulletin of the Chem Soc of Japan.* **1967**, 4261; (c) Baldwin, E. J.; McDaniel, C. M.; Newton, M.; Paul, C. I. *Tetrahedron Lett.* **1966**, *35*, 4239-4241; (d) Kroehnke, F.; and Steuernagel, H. *Angew. Chem.* **1961**, *73*, 36; *Chem. Ber.* **1964**,

97, 1118-11126; (e) Sato, S. and Ohta, R. *Bulletin of the Chem Soc of Japan.* **1969**, 2054-2056.

15. Kagan, H. B. *Catalytic Asymmetric Synthesis*; 2nd ed.; Wiley-VCH, **2000**; *6C*, 329–356.
16. (a) Manabe, K. S.; Iimura, S.; Sun, X.-M.; Kobayashi, S. *J. Am. Chem. Soc.* **2002**, *124*, 11971-11978; (b) Li, C. J.; Chan, T. H. Organic Reactions in Aqueous Media; John Wiley: New York, **1997**; (c) Li, C.-J.; Chen, L. *Chem. Soc. Rev.* **2006**, *35*, 68-82.
17. (a) Anastas, P.; Warner, J. C. *Green Chemistry: Theory and Practice*; Oxford University Press: Oxford, **1998**; (b) Dallinger, D.; Kappe, C. O. *Chem. Rev.* **2007**, *107*, 2563-2591; (c) Polshettiwar, V.; Varma, R. S. *J. Org. Chem*. **2007**, *72*, 7420-7422.
18. Dwars, T.; Paetzold, E.; Oehme, G. *Angew. Chem., Int. Ed*. **2005**, *44,* 7174-7199.
19. Fendler, J. H.; Fendler, E. J. Catalysis in Micellar and Macromolecular Systems; Academic Press: New York, **1975**.
20. (a) Hazra, A.; Paira, P.; Sahu, K. B.; Naskar, S.; Saha, P.; Paira, R.; Mondal, S.; Maity, A.; Luger, P.; Weber, M.; Mondal, N. B.; Banerjee, S. *Tetrahedron Lett*. **2010**, *51*, 1585-1588; (b) Naskar, S.; Banerjee, M.; Hazra, A.; Mondal, S.; Maity, A.; Paira, R.; Sahu, K. B.; Saha, P.; Banerjee, S.; Mondal, N. B. *Tetrahedron Lett.* **2011**, *52*, 1527-1531; (c) Hazra, A.; Mondal, S.; Maity, A.; Naskar, S.; Saha, P.; Paira, R.; Sahu, K. B.; Paira, P.; Ghosh, S.; Sinha, C.; Samanta, A.; Banerjee, S.; Mondal, N. B. *Eur. J. Med. Chem*. **2011**, *46*, 2132-2140; (d) Mondal, S.; Maity, A.; Paira, R.; Banerjee, M.; Bharitkar, Y; Hazra, A.; Banerjee, S.; Mondal, N. B. *Tetrahedron Lett.* **2012,** *53*, 6288-6291;
21. Kalyanasundaram, K. *Photochemistry in Microheterogeneous Systems*; Academic Press: San Diego, **1987**.
22. Evans, D. F.; Allen, M.; Ninham, B. W.; Fouda, A. *J. Solution Chem*. **1984**, *13*, 87-101.

23. McCarroll, M.; Toerne, K.; Wandruszka, R. V. *Langmuir* **1998**, *14*, 2965-2969.

24. Israelachvili, *J. Intermolecular and Surface Forces*; Academic Press: San Diego, **1997**.

25. **General reaction procedure for the synthesis of thiazolo[2,3-*a*]isoquinolin-4-ium derivatives (4a–r).**

One mmol each of the isoquinolines (**1a**–**c**), phenacyl bromide (**2a**–**f**)/ bromoacetonitrile (**2g**), and benzoyl isothiocyanate (**3**) were taken in a 100 ml RB flask. Then water (50 ml), CTAB (4 mmol) and Amberlite-IRA-402 (OH) ion exchange resin (300mg) were added and the mixture was stirred continuously for 1.5 h at room temperature. After completion of the reaction (monitored by TLC), the solid was filtered off, washed thoroughly with water (until free from CTAB). Then the solid was dried, and dissolved in chloroform and again filtered to separate the Amberlite resin from solution. The compound was further purified by recrystallization from chloroform to yield the thiazolo[2,3-*a*]isoquinolin-4-ium derivatives (**4a–r**).

Spectral data of Compound **4a:** Yield: 85% ; ^{1}H-NMR (600 MHz, $CDCl_3$) δ 7.24 (m, 3H), 7.37 (m, 1H), 7.51 (m, 1H), 7.63 (m, 3H), 7.78 (d, 1H, *J* =7.2 Hz), 7.86 (m, 2H), 7.95 (m, 3H), 8.38 (d, 1H, *J* =7.8 Hz), 9.75 (d, 1H, *J* =6.6 Hz) ; ^{13}C-NMR (150 MHz, $CDCl_3$) δ 120.2 (CH), 120.5 (C) 125.0 (C), 125.7 (CH), 127.1 (CH), 127.7 (2xCH), 127.8 (CH), 128.1 (2xCH), 129.1 (2xCH), 129.7 (2xCH), 130.4 (CH), 131.2 (CH), 131.7 (CH), 132.2 (CH) 136.6 (C), 139.3 (C), 140.3 (C), 147.5 (C), 158.2 (C), 173.6(C), 187.4 (C); MS (ESI) *m/z*: 409 $[M+H]^+$, 408$[M]^+$.

Spectral data of Compound **4g**:

Yield: 85% ; ^{1}H-NMR (600 MHz, $CDCl_3$) δ 7.24 (m, 3H), 7.53 (m, 2H), 7.64 (m, 3H), 7.90 (m, 3H), 7.96 (m, 1H), 8.29 (d, 1H, *J* = 8.4 Hz), 8.38 (d, 1H, *J* = 8.4 Hz), 10.08 (s,1H); ^{13}C-

NMR (150 MHz, $CDCl_3$) δ 117.5 (C), 120.1 (C), 124.8 (C), 125.9 (CH), 127.6 (CH), 127.7 (CH), 127.9 (2xCH), 128.1 (2xCH), 128.1 (C), 129.2 (2xCH) 129.7 (2xCH), 131.2 (CH), 131.4 (CH), 131.9 (CH), 133.1 (CH), 136.4 (C), 140.0 (C) 146.5 (C), 158.0 (C), 173.7 (C), 187.2 (C); MS (ESI) *m/z*: 487 $[M+H]^+$, 489$[M+H+2]^+$.

Spectral data of Compound **4q**:

Yield: 82% ; ^{1}H-NMR (600 MHz, $CDCl_3$) δ 7.50 (m, 2H), 7.81 (d, 1H, *J* =7.8 Hz), 7.89 (m, 3H), 7.98 (m, 1H), 8.31 (m, 1H), 8.42 (m, 2H), 8.55 (d, 1H, *J* =7.2 Hz); ^{13}C-NMR (150 MHz, $CDCl_3$) δ 96.7 (C), 106.9 (C), 111.9 (C), 121.6 (CH), 124.1 (CH), 125.1 (C), 128.2 (2xCH), 129.5 (2xCH), 130.0 (C), 131.4 (CH), 131.8 (CH), 132.4 (CH), 136.1 (CH), 139.3 (CH), 145.8 (C), 159.3 (C), 175.0 (C); MS (ESI) *m/z*: 330 $[M+H]^+$, 352$[M+Na]^+$.

Spectral data of Compound **4r**:

Yield: 82% ; ^{1}H-NMR (600 MHz, $CDCl_3$) δ 7.50 (m, 2H), 7.73 (m, 1H), 7.87 (m, 1H), 8.10 (m, 1H), 8.27 (m, 2H), 8.40 (m, 2H), 8.61 (d, 1H, *J* =7.2 Hz); ^{13}C-NMR (150 MHz, $CDCl_3$) δ 105.4 (CH), 111.6 (C), 120.8 (CH), 123.4 (C), 124.3(CH), 124.9 (CH), 126.4 (C), 128.2 (CH), 128.2 (C), 129.5 (CH), 131.8 (CH), 132.0 (CH), 135.8 CH), 136.6 (CH), 137.3 (C), 140.9 (C), 145.1 (C), 159.5 (C), 175.3 (C); MS (ESI) *m/z*:408 $[M+H]^+$, 410 $[M+H+2]^+$.