Synthesis of Phenanthridine by Palladium Catalyzed Suzuki Coupling and Condensation Reaction

Jayanta K Ray* and Suvendu Dhara

Department of Chemistry, Indian Institute of Technology, Kharagpur 721302, India

jkray@chem.iitkgp.ac.in

Introduction

Transition metal catalyzed cross-coupling reactions such as Suzuki-Miyaura\(^1\), Heck\(^2\)\(^-\)\(^10\), Stille\(^11\), Hiyama,\(^12\) Negishi\(^13\), and Sonogashira reactions are likely to be the most powerful tool for the formation of C-C bonds for the past four decades. All these reactions have shown their widespread applicability ranging from academic area to research. Some of the reactions have also been applied in pharmaceuticals, agrochemicals, and fine material industries. The Suzuki-Miyaura cross coupling was remained the most attractive alternative for C-C bonds formation since its discovery in 1979. The wide range of applicability of this reaction is largely attributed to mild reaction conditions, broad range of functional group tolerance, easy access to organo-boron reagents, and their stability under air and moisture. Furthermore, boron compounds show low toxicity and easy to separate boron from the reaction mixtures.

Phenanthridine (3.1) is a nitrogen heterocycle that is the basis of DNA-binding fluorescent dyes through intercalation. Ethidium bromide and propidium iodide are the examples of such intercalating dyes. Phenanthridine is an isomeric compound of acridine (3.2) (Fig. 3.1).

![Fig. 3.1: Phenanthridine and acridine](image)

Phenanthridine was first discovered by Ame Pictet and H. J. Ankersmit in 1891 by pyrolysis of the condensed product of benzaldehyde and aniline. Earlier, phenanathridine and related
compounds were prepared using mainly Pictect-Hurbert and modified Morgan-Walls type of condensation reactions.

### 3.1.1 Bioactivity and natural occurrences

Phenanthridines and Benzo[c]phenanthridines are prevalent in a large number of natural and unnatural bioactive molecules exhibiting important pharmacological activities and applications, such as antibacterial, antiprotozoal, and anticancer agents. A well known member of this class of compound is ethidium (3.3), a common DNA intercalator and stain. Representative alkaloids of this kind with promising pharmacological potential are nitidine (3.4), chelerythrine (3.5), sanguinarine (3.6) (Fig. 3.2).

![Fig. 3.2: Some phenanthridiene and benzo[c]phenanthridine alkaloids.](image)

Because of great importance of these compounds in biology and medicine, shorter and high yielding synthetic methodologies are of great interest in synthetic organic chemistry as isolation from natural sources described is less than 1%.

In literature, various reports are there to construct these heterocycles. Among them, the Bischler-Napieralski cyclisation has been extensively used to synthesise phenanthridine derivatives. Wang et al. reported a cascade approach to 6-arylphenanthridine 3.10 from aromatic aldehyde 3.8, aniline 3.9 and benzenediazonium-2-carboxylate 3.7 (Scheme 3.1). The in situ generated benzyne from benzenediazonium-2-carboxylate 3.7 underwent a [4+2] cycloaddition reaction with the imine formed from aromatic amine and aldehyde to give dihydrophenanthridine. Finally, dehydrogenation in the reaction medium gave the 6-arylated phenanthridine 3.10 in quantitative yields.
Deiters *et al.* described a cyclotrimerization approach to build the phenanthridine moiety. Different transition metal complexes have been evaluated to catalyze the cyclotrimerization and the Ru-catalyst results the best. The Ru-catalyzed microwave assisted \([2+2+2]\) cyclotrimerization of diyne **3.11** afforded to dihydrophenanthridine **3.12**. Then CAN mediated deprotective aromatization ultimately gave the substituted phenanthridine **3.13** (Scheme 3.2).

In other way Yanada *et al.* constructed analogous benzo[\(c\)]phenanthridine *via* Lewis acid catalyzed tandem cyclization. The Lewis acid In(OTf)\(_3\) cyclizes *ortho*-alkynylbenzaldehydes **3.14** and *ortho*-alkynylanilines **3.15** to form the benzo[\(c\)]phenanthridine **3.16** in very good yields (Scheme 3.3). A series of other Lewis catalysts have been screened to effect the cyclization and In(OTf)\(_3\) was proved to be the best. The reaction goes *via* 6-*endo-dig* nucleophilic addition of carbonyl oxygen on the In(OTf)\(_3\) co-ordinated electrophilic *\(o\)*-alkynyl moiety to give the pyrilium cation intermediate. The intermediate pyrilium cation undergoes a Diels-Alder type cyclization with the *\(o\)*-alkynylaniline and followed by condensation to give the final product **3.16**.

**Scheme 3.1:** Cascade approach to phenanthridine

**Scheme 3.2:** Cyclotrimerisation towards phenanthridine
Scheme 3.3: Lewis acid catalysed Tandem cyclization

Annulation of acyloximes with aryne or alkyne has been adopted by Zhu and co-workers (Scheme 3.4). Among a series of palladium catalysts allyl-palladium complex (APC) along with a bulky phosphine ligand were the most promising catalytic system. The oxidative palladium insertion into the N-O bond of acyloxime 3.17 and cis-aminopalladation to the benzyne formed from the compound 3.18, followed by intramolecular C-H activation afforded the 6-phenylphenanthridine 3.19.

Scheme 3.4: APC–catalyzed synthesis of phenanthridine

Palladium catalyzed synthesis of phenanthridine has been accomplished by Pritchard and co-workers from imidoyl selenides. This was the first report of palladium insertion into the C-Se bond. The palladium insertion into the imidoyl selenides 3.20 followed by intramolecular cyclization and subsequent aromatization via the elimination of HSePh lead to the formation of substituted phenanthridines 3.21 (Scheme 3.5).
Scheme 3.5: Pd-catalysed synthesis of phenanthridine

A cascade reaction of \(N\)-acetylated biaryl 3.22 for the construction of phenanthridine ring has been described by Yao et al. The amide of biphenyl-2-amine undergoes a cascade annulations reaction initiated by Hendrickson reagents and subsequent Friedel-Crafts reaction to afford the 6-methyl phenanthridine 3.23 under mild reaction conditions (Scheme 3.6).

Scheme 3.6: Cascade synthesis of phenanthridine

Alternatively, Lautens group have synthesized phenanthridine by domino arylation, \(N\)-arylation protocol under Pd-catalysis. The Pd(OAc)\(_2\) catalyzed domino \(N\)-arylation of the silylimine 3.25 with aryl iodide 3.24 and followed by intramolecular C-H-activation produced the substituted phenanthridine 3.26 (Scheme 3.7).

Scheme 3.7: Convenient synthesis of phenanthridine

A very simple method of non-nucleophilic base 'BuOK mediate condensation between 2-methylbenzonitrile 3.28 and an arylaldehyde 3.27 has been demonstrated by Clement et al. Subsequently, resulting 6-amino-11,12-dihydrobenzo[c]phenanthridine 3.29 was converted to 11-substituted 6-aminobenzo[c]phenanthridine 3.30 via DDQ oxidation (Scheme 3.8).
Scheme 3.8: Synthesis of 6-aminobenzo[c]phenanthridine

An efficient method for the formation of [c]annulated isoquinoline has been developed by Pandey et al. via Pd-mediated sequential reactions. The Suzuki cross coupling between α-iodoenone 3.32 and protected aminoboronic acid 3.31, and subsequent condensation results in the [c]annulated isoquinoline derivatives 3.33 (Scheme 3.9).

Scheme 3.9: Sequential reaction towards the formation of [c]annulated isoquinoline

Dominguez et al. applied a two-step synthetic protocol towards the efficient synthesis of novel dibenzo[a,c]phenanathridine. Highly substituted novel dibenzo[a,c]phenanthridines 3.35 have been prepared from aryl ketone 3.34 via sequential reactions of Ritter-type heterocyclization and the classical two-step reductive amination/Bischler-Napieralski cyclization (Scheme 3.10).

Scheme 3.10: Synthesis of dibenzo[a,c]phenanthridine
In our continuous effort in finding the shorter and economic synthetic methods via palladium catalysis, we have achieved a synthesis of phenanthridines and its analogs in this chapter. Our aim was to find out one step method for the synthesis of phenanthidine. We envisioned that Suzuki coupling between 3.36 and 3.37 would be very effective for the construction of phenanathridine 3.38 in one-pot (Scheme 3.11).

![Scheme 3.11: Retrosynthesis of phenanthidine](image)

**Results and Discussions**

We report a one-pot strategy to achieve phenanthidine 3.38 and analogous derivatives 3.41 or 3.42 via Suzuki coupling of suitably substituted aromatic ortho-bromoaldehyde 3.39 or 3.40 and ortho-aminobenzenboronic acid 3.36 in quantitative to good yields (Scheme 3.12).

![Scheme 3.12: Synthesis of phenantridine and its analogues](image)

For the synthesis of phenanthidine analogs the starting aromatic o-bromoaldehydes 3.45 were synthesized by Vilsmeier-Haack reaction upon corresponding ketones 3.43 and followed by DDQ aromatization of o-bromoaldehyde 3.44 (Scheme 3.13).
Scheme 3.13: Synthesis of the aromatic o-bromoaldehyde

We have attempted the coupling step with 2-bromobenzaldehyde 3.37 and 2-aminobenzeneboronic acid 3.36. A variety of the palladium catalysts were tried in combination with ligand and different organic or inorganic bases as the catalytic system. The palladium (0) catalysts Pd(PPh$_3$)$_4$ and Pd$_2$(dba)$_3$ gave phenanathridines 41 to 60 %. Among the palladium(II) catalysts the Pd(OAc)$_2$ was the best catalyst with 95 % formation of phenanthidine 3.38. The inorganic base Cs$_2$CO$_3$ was proved to be superior to its other inorganic and organic analogues. When the reaction was carried out at 80 °C the reaction gave only 50 % of phenanathidine in the presence of Pd(PPh$_3$)$_2$Cl$_2$, Et$_3$N, and in DMF solvent. Increasing the reaction temperature to 90 °C afforded 82% of phenanathidine in the presence of Pd(OAc)$_2$, PPh$_3$ and K$_2$CO$_3$ catalytic system in DMF in 5 h. Changing the base to Cs$_2$CO$_3$ and solvent to DMA shorten the reaction time from 5 to 3 h with 95 % of yields. Further increase of reaction temperature and changing the solvent to DMSO has no effect on the reaction. So, the set of optimal reaction conditions were finalized to be Pd(OAc)$_2$ (5 mol %), PPh$_3$ (0.25 equiv.), Cs$_2$CO$_3$ (1.5 equiv.), in DMA (3 mL), at 90 °C, for 3 h (Table 3.1, entry 10).

Table 3.1: Catalyst Screening $^a$

| Entry | Catalyst | Ligand | Base | Solvent | T (h) | Temp (°C) | Yields (%)$^b$ |
|-------|----------|--------|------|---------|-------|-----------|----------------|
| 1     | Pd(PPh$_3$)$_2$Cl$_2$ | - | Et$_3$N | DMF | 5 | 80 | 50 |
| 2     | PdCl$_2$ | PPh$_3$ | Et$_3$N | DMF | 5 | 80 | 80 |
| 3     | Pd$_2$(dba)$_3$ | - | Et$_3$N | DMF | 5 | 80 | 41 |
Once we got the standard conditions for the cyclization procedure, we have generalized our methodology synthesizing various types of phenanthridine and analogous derivatives in excellent to good yields. The results are shown in the Table 3.2. Different substituted phenanthridines \(3.38a-f\) were synthesized from the corresponding 2-bromobenzaldehydes \(3.37a-f\) in good yields. The results in the Table 3.2 shows that this methodology is well tolerated both the electron-donation and electron with-drawing functionalities such as, nitro, methyl, methoxy group in the coupling partner \(3.7\).

**Table 3.2: Synthesis of phenanthridine derivatives**

| Entry | Substrate | Products | Yields (%) |
|-------|-----------|----------|------------|
| 1     | \(3.37a\) | \(3.38a\) | 95         |
c) Reaction Conditions and Reagents: 1 mmol of substrate 3.37a-f, 1.2 mmol of aminobenzeneboronic acid 3.36, Pd (OAc)$_2$ (5 mol%), PPh$_3$ (0.25 equiv.), Cs$_2$CO$_3$ (1.5 equiv.), DMA (3mL), 90 $^\circ$C, 3-5 h.

d) Isolated yields after purification

We have further extended the scope of our procedure to synthesize different higher analogues of phenanthridines. With the aforesaid optimal set of reaction conditions we have synthesized benzo[k]phenanthridines 3.41a-c and benzo[i]phenanthridine 3.42 from the corresponding bromonaphthaldehyde in good yields (Table 3.3). Here also different functionalities have been well tolerated.
Table 3.3: Synthesis of phenanthrine analogs

| Entry | Substrate | Product | Yields (%) |
|-------|-----------|---------|------------|
| 1     | 3.39a     | 3.41a   | 75         |
| 2     | 3.39b     | 3.41b   | 91         |
| 3     | 3.40      | 3.42    | 52         |
| 4     | 3.39b     | 3.41c   | 89         |

a) Reaction Conditions and Reagents: 1 mmol of substrate 3.39a-c or 3.40, 1.2 mmol of aminobenzeneboronic acid 3.36, Pd (OAc)$_2$ (5 mol%), PPh$_3$ (0.25 equiv.), Cs$_2$CO$_3$ (1.5 equiv.), DMA (3mL), 90 °C, 3-5 h.

b) Isolated yields.
The cyclization reaction was believed to follow the sequential steps of Suzuki coupling followed by condensation. The Suzuki coupling occurs first between the coupling partners to produce the intermediate I which then undergoes intramolecular cyclization to afford the phenanthridine II. In contrast, if the condensation is to be occurred first it would result the more stable trans-imine III from which intramolecular coupling is quite impossible as the two functional groups are far apart (Fig 3.3). Evidence in support of our proposal comes from that fact no imine was isolated during the reaction course.

![Plausible course of the reaction](image)

**Fig 3.3:** Plausible course of the reaction

### 3.6 Experiments and Results Section

#### 3.6.1 General procedure for the preparation of aromatic naphthaldehyde (3.45):

A mixture of 1 mmol of ortho-bromovinylaldehyde and 3 mmol of DDQ were taken in dry benzene in a 25 mL two necked round bottomed flask and refluxed for overnight. Completion of the reaction was confirmed TCL. After completion of the reaction the mixture was cool to room temperature and benzene was evaporated under reduced pressure. The crude product was purified the usual column chromatography using silica gel and mixture of petroleum ether and ethyl acetate as eluents.

#### 3.6.2 General procedure of Suzuki coupling for synthesis of phenanthridine (3.38):

*Ortho*-bromobenzaldehyde (50 mg, 0.273 mmol.), *ortho*-aminobenzeneboronic acid (53.5 mg, 1.2 equiv.), Pd (OAc)$_2$ (5 mol%), PPh$_3$ (0.25 equiv.), Cs$_2$CO$_3$ (133.5 mg, 1.5 equiv.) were taken in a two-necked round bottom flask in argon atmosphere. 3 mL of dry DMA was
added to the reaction mixture and degassed with nitrogen and heated at 90 °C temperature for 3 h. Completion of the reaction was monitored by TLC. The reaction mixture was cooled to rt and diluted with water. It was then extracted with ethyl acetate (50 mL × 3). Combined organic layer was washed with brine and dried over anhydrous Na₂SO₄. The solvent was evaporated under reduced pressure and crude product was purified by column chromatography using Silica gel and petroleum ether: ethyl acetate (5:1) as eluent.

**Spectral data of the representative Compounds:**

**Phenanthridine (3.38a):**

Yellow solid, mp: 102-104 °C (lit. 104-106 °C); Yields : 90 %; ¹H NMR (CDCl₃, 200 MHz): 9.18 (1H, s), 8.41 (2H, d, J = 8.0 Hz), 8.17 (1H, dd, J₁ = 1.2 Hz, J₂ = 8.0 Hz), 7.87 (1H, t, J = 7.0 Hz), 7.52-7.75 (4H, m); ¹³C NMR (CDCl₃, 50 MHz): 153.4, 144.1, 132.4, 131.0, 129.9, 128.7 (2C), 127.4, 127.1, 126.2, 124.0, 122.2, 121.7; Anal.Calcd for C₁₃H₉N: C: 87.12; H: 5.06; N: 7.82 %; Found: C: 87.00; H: 4.95; N: 7.72 %.

**2,3-dimethoxyphenanthridine (3.38c):**

Brown solid; mp: 127-129 °C Yield: 85 %; ¹H NMR (CDCl₃, 400 MHz): 9.17 (1H, s), 8.45 (1H, d , J = 7.6 Hz), 8.16 (1H, d, J = 8.0 Hz), 7.89 (1H, s), 7.63-7.71 (2H, m), 7.37 (1H, s), 4.15 (3H, s), 4.10 (3H, s); ¹³C NMR (CDCl₃, 100 MHz): 153.2, 152.0, 150.2, 139.5, 130.3, 130.0 128.5, 128.0, 126.8, 121.9, 114.3, 108.1, 102.1, 56.3; Anal.Calcd for C₁₅H₁₃NO₂: C: 75.30; H: 5.48; N: 5.85 %; Found : C: 75.25; H: 5.36; N: 5.72 %.

**1,2,3-trimethoxyphenanthridine (3.38d):**

Brown Sticky masss; Yield: 78 %; ¹H NMR (CDCl₃, 200 MHz): 9.34 (1H, dd, J₁ = 2.4 Hz, J₂ = 7.0 Hz), 9.14 (1H, s), 8.18 (1H, t, J = 7.0 Hz), 7.27-7.71 (2H, m), 7.27 (1H, s), 4.10 (9H, s); ¹³C NMR (CDCl₃, 50 MHz): 153.6, 152.6, 151.6, 146.6, 144.2, 130.0, 127.9, 127.4, 126.4, 124.3, 123.8, 121.8, 105.4, 61.5, 60.6, 56.3; Anal.Calcd for C₁₆H₁₅NO₃: C: 79.09; H: 5.23; N: 6.50 %; Found : C: 79.0; H: 5.15; N: 6.43 %; HRMS calcd for C₁₆H₁₆NO₃⁺ [M+ H⁺]: 270.1125; Found : 270.1125.
Conclusion

In conclusion a simple and efficient method for the synthesis of different substituted phenanthridine and its higher analogues benzo[κ] and benzo[ι] derivatives have been developed. Our synthetic strategy is a general one with tolerability to a variety of substituent and gave highly substituted phenanthridines in quite good yields from very cheap starting materials under mild reaction conditions. We anticipate that our methodology could be applicable to synthesize phenanthridine natural products of important medicinal value\textsuperscript{5,8,10,14-40}.

References

1. Suzuki, A., Organoboron compounds in new synthetic reactions. \textit{Pure and Applied Chemistry} 1985, 57 (12), 1749-1758.
2. Ray, D.; Ray, J. K., Novel Synthetic Approach Toward (±)-β-Cuparenone via Palladium-Catalyzed Tandem Heck Cyclization of 1-Bromo-5-methyl-1-aryl-hexa-1, 5-dien-3-ol Derivatives. \textit{Organic letters} 2007, 9 (2), 191-194.
3. Samanta, S.; Mohapatra, H.; Jana, R.; Ray, J. K., Pd (0) catalyzed intramolecular Heck reaction: a versatile route for the synthesis of 2-aryl substituted 5-, 6-, and 7-membered O-containing heterocycles. \textit{Tetrahedron Letters} 2008, 49 (50), 7153-7156.
4. Nandi, S.; Singha, R.; Samanta, S.; Ray, J. K., Synthesis of pentalongin and C (1)- and C (3)-substituted pentalonin using intramolecular Heck reaction. \textit{Tetrahedron Letters} 2012, 53 (21), 2659-2661.
5. Ray, D.; Nasima, Y.; Sajal, M. K.; Ray, P.; Urinda, S.; Anoop, A.; Ray, J. K., Palladium-Catalyzed Intramolecular Oxidative Heck Cyclization and Its Application toward a Synthesis of (±)-β-Cuparenone Derivatives Supported by Computational Studies. \textit{Synthesis} 2013, 45 (09), 1261-1269.
6. Dey, D.; Bhattacharya, T.; Majumdar, B.; Mandani, S.; Sharma, B.; Sarma, T. K., Carbon dot reduced palladium nanoparticles as active catalysts for carbon–carbon bond formation. \textit{Dalton Transactions} 2013, 42 (38), 13821-13825.
7. Yamamoto, Y., Synthesis of heterocycles via transition-metal-catalyzed hydroarylation of alkenes. \textit{Chemical Society Reviews} 2014, 43 (5), 1575-1600.
8. Ray, J. K.; Paul, S.; Ray, P.; Singha, R.; Rao, D. Y.; Nandi, S.; Anoop, A., Pd-catalyzed intramolecular sequential Heck cyclization and oxidation reactions: a facile pathway for the synthesis of substituted cycloheptenone evaluated using computational studies. \textit{New Journal of Chemistry} 2017, 41 (1), 278-284.
9. Ghosh, M.; Ray, J. K., Ten years advancement in the synthetic applications of 2-bromo-cyclohexenecarbaldehydes and 2-bromobenzaldehydes and derived substrates under palladium-catalyzed cross-coupling conditions. \textit{Tetrahedron} 2017, 73 (27), 3731-3799.
10. Ray, J. K.; Singha, R.; Ray, D.; Ray, P.; Rao, D. Y.; Anoop, A., Palladium-catalyzed expedient Heck annihilations in 1-bromo-1,5-dien-3-ols: Exceptional formation of fused bicycles. \textit{Tetrahedron Letters} 2019, 60 (13), 931-935.
11. Milstein, D.; Stille, J. K., Mechanism of reductive elimination. Reaction of alkylpalladium(II) complexes with tetraorganotin, organolithium, and Grignard reagents.
12. Nakao, Y.; Hiyama, T., Silicon-based cross-coupling reaction: an environmentally benign version. *Chemical Society Reviews* 2011, 40 (10), 4893-4901.

13. Negishi, E. -i., Magical Power of Transition Metals: Past, Present, and Future (Nobel Lecture). *Angewandte Chemie International Edition* 2011, 50 (30), 6738-6764.

14. Wang, C.-Y.; Ray, P.; Gong, Q.; Zhao, Y.; Li, J.; Lueking, A. D., Influence of gas packing and orientation on FTIR activity for CO chemisorption to the Cu paddlewheel. *Physical Chemistry Chemical Physics* 2015, 17 (40), 26766-26776.

15. Chaudhuri, S.; Maity, S.; Roy, M.; Ray, P.; Ray, J. K., A Vinyl Radical Cyclization Route to Hydroxycyclohexene Fused Carbocycles. *Asian Journal of Chemistry* 2016, 28 (1).

16. Ray, P., Interactions of nitrogen and hydrogen with various 1D and 3D carbon materials probed via in-situ vibrational spectroscopy. *Ph. D. Thesis* 2016.

17. Ray, P.; Gray, J. L.; Badding, J. V.; Lueking, A. D., High-Pressure Reactivity of Triptycene Probed by Raman Spectroscopy. *The Journal of Physical Chemistry B* 2016, 120 (42), 11035-11042.

18. Ray, P.; Xu, E.; Crespi, V. H.; Badding, J. V.; Lueking, A. D., In situ vibrational spectroscopy of adsorbed nitrogen in porous carbon materials. *Physical Chemistry Chemical Physics* 2018, 20 (22), 15411-15418.

19. Ray, P.; Gidley, D.; Badding, J. V.; Lueking, A. D., UV and chemical modifications of polymer of Intrinsic Microporosity 1 to develop vibrational spectroscopic probes of surface chemistry and porosity. *Microporous and Mesoporous Materials* 2019, 277, 29-35.

20. Ray, P. Calixarenes and Nanoparticles: Synthesis, Properties and Applications. Paris 11, 2013.

21. Singha, R.; Roy, S.; Nandi, S.; Ray, P.; Ray, J. K., Palladium-catalyzed one-pot Suzuki–Miyaura cross coupling followed by oxidative lactonization: a novel and efficient route for the one-pot synthesis of benzo[c]chromene-6-ones. *Tetrahedron Letters* 2013, 54 (7), 657-660.

22. André, E.; Boutonnet, B.; Charles, P.; Martini, C.; Aguiar-Hualde, J. M.; Latil, S.; Guérineau, V.; Hammad, K.; Ray, P.; Guillot, R.; Huc, V., A New, Simple and Versatile Strategy for the Synthesis of Short Segments of Zigzag-Type Carbon Nanotubes. *Chemistry* 2016, 22 (9), 3105-14.

23. Brahma, S.; Ray, P.; Singha, R.; Ray, J. K., Visible Colourimetric and Ratiometric Fluorescent Chemosensors for Cu (II) and Ni (II) Ions. *Asian Journal of Chemistry* 2016, 28 (5), 1035.

24. Ray, P.; Clément, M.; Martini, C.; Abdellah, I.; Beaunier, P.; Rodriguez-Lopez, J.-L.; Huc, V.; Remita, H.; Lampre, I., Stabilisation of small mono- and bimetallic gold–silver nanoparticles using calix[8]arene derivatives. *New Journal of Chemistry* 2018, 42 (17), 14128-14137.

25. Ghosh, A.; Sarkar, S.; Ghosh, S.; Ray, P.; Quadir, M.; Banerjee, S. K.; Banerjee, S., Abstract 1234: Zoledronic acid-induced suppression of invasive phenotypes of pancreatic cancer cells is mediated through downregulation of CYR61/CCN1. *Cancer Research* 2019, 79 (13 Supplement), 1234.

26. Ray, P.; Ferraro, M.; Haag, R.; Quadir, M., Dendritic Polyglycerol-Derived Nano-Architectures as Delivery Platforms of Gemcitabine for Pancreatic Cancer. *Macromol Biosci* 2019, 19 (7), e1900073.

27. Ray, P.; Alhalhooly, L.; Ghosh, A.; Choi, Y.; Banerjee, S.; Mallik, S.; Banerjee, S.; Quadir, M., Size-Transformable, Multifunctional Nanoparticles from Hyperbranched Polymers for Environment-Specific Therapeutic Delivery. *ACS Biomaterials Science & Engineering* 2019, 5 (3), 1354-1365.
28. Ray, P.; Confeld, M.; Borowicz, P.; Wang, T.; Mallik, S.; Quadir, M., PEG-b-poly (carbonate)-derived nanocarrier platform with pH-responsive properties for pancreatic cancer combination therapy. *Colloids and Surfaces B: Biointerfaces* 2019, 174, 126-135.

29. Ray, P.; Nair, G.; Ghosh, A.; Banerjee, S.; Golovko, M. Y.; Banerjee, S. K.; Reindl, K. M.; Mallik, S.; Quadir, M., Microenvironment-sensing, nanocarrier-mediated delivery of combination chemotherapy for pancreatic cancer. *Journal of Cell Communication and Signaling* 2019.

30. Abdullah, C. S.; Ray, P.; Alam, S.; Kale, N.; Aishwarya, R.; Morshed, M.; Dutta, D.; Hudziak, C.; Banerjee, S. K.; Mallik, S.; Banerjee, S.; Bhuiyan, M. S.; Quadir, M., Chemical Architecture of Block Copolymers Differentially Abrogate Cardiotoxicity and Maintain the Anticancer Efficacy of Doxorubicin. *Molecular Pharmaceutics* 2020, 17 (12), 4676-4690.

31. Clément, M.; Abdellah, I.; Ray, P.; Martini, C.; Coppel, Y.; Remita, H.; Lampre, I.; Huc, V., Synthesis and NMR study of trimethylphosphine gold(i)-appended calix[8]arenes as precursors of gold nanoparticles. *Inorganic Chemistry Frontiers* 2020.

32. Confeld, M. I.; Mamnoon, B.; Feng, L.; Jensen-Smith, H.; Ray, P.; Froberg, J.; Kim, J.; Hollingsworth, M. A.; Quadir, M.; Choi, Y.; Mallik, S., Targeting the tumor core: hypoxia-responsive nanoparticles for delivery of chemotherapy to pancreatic tumors. *Molecular Pharmaceutics* 2020.

33. Babak, K.; Torabi, M.; Foad, K.; Priyanka, R., Novel β-Cyclodextrin Functionalized Core-Shell Fe3O4 Magnetic Nanoparticles for the Removal of Toxic Metals from Water. 2021.

34. Brahma, S.; Ray, P.; Ray, J. K., Synthesis of azirines containing aldehyde functionality and their utilization as synthetic tools for five membered oxazoles and isoxazoles (vol 45, pg 311, 2008). *JOURNAL OF HETEROCYCLIC CHEMISTRY* 2021, 58 (6), 1388-1388.

35. Das, A.; Haque, I.; Ray, P.; Ghosh, A.; Dutta, D.; Quadir, M.; De, A.; Gunewardena, S.; Chatterjee, I.; Banerjee, S.; Weir, S.; Banerjee, S. K., CCN5 activation by free or encapsulated EGCG is required to render triple-negative breast cancer cell viability and tumor progression. *Pharmacol Res Perspect* 2021, 9 (2), e00753.

36. Ray, P., Polymer based drug delivery systems-benchtop to bedside transition. *Journal of Drugs Addiction & Therapeutics. SRC/IDAT-114* 2021, 3.

37. Ray, P., Curing Cancer with Nanotherapy Continues to be an Elusive Goal. *Journal of Immunological Sciences* 2021, 5 (2).

38. Ray, P.; Dutta, D.; Haque, I.; Nair, G.; Mohammed, J.; Parmer, M.; Kale, N.; Orr, M.; Jain, P.; Banerjee, S.; Reindl, K. M.; Mallik, S.; Kamhampati, S.; Banerjee, S. K.; Quadir, M., pH-Sensitive Nanodrug Carriers for Codelivery of ERK Inhibitor and Gemcitabine Enhance the Inhibition of Tumor Growth in Pancreatic Cancer. *Molecular Pharmaceutics* 2021, 18 (1), 87-100.

39. Ray, P.; Haideri, N.; Haque, I.; Mohammed, O.; Chakraborty, S.; Banerjee, S.; Quadir, M.; Brinker, A. E.; Banerjee, S. K., The Impact of Nanoparticles on the Immune System: A Gray Zone of Nanomedicine. *Journal of Immunological Sciences* 2021, 5 (1).

40. Ray, P.; Kale, N.; Quadir, M., New side chain design for pH-responsive block copolymers for drug delivery. *Colloids and Surfaces B: Biointerfaces* 2021, 200, 111563.