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Synthesis of indole based novel symmetrical nitroolefinic dendritic core through n-arylation route

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Synthesis of indole based novel symmetrical nitroolefinic dendritic core has been succeeded using *N*-arylation route followed by Henry reaction. Synthesized symmetrical 1,3,5-triindolyl benzene has been successfully synthesis of by N-arylation of indole, symmetrical 1,3,5-tri(3-formyl indolyl)benzene and 1,3,5-tris(3-((E)-2-nitrovinyl)-1H-indol-1-yl)benzene followed by Hendry reaction. These nitroolefinic cores have potential application in theoretical and medicinal chemistry and also used to prepare many new organic compounds of indole derivatives.

Keywords: Dendritic core, Henry reaction, Indole, N-arylation,Nitroolefin

Nitroolefin or nitroethylene are synthetic dendritic core and have been used in the research of a multiplicity of synthetic compounds of biological interest[1-5]. Antibiotics are chemicals often sourced from microorganisms. This is an imitation and not natural to execute or inhibit rival organs in the microenvironment, therefore the part of natural self-security is important. The nitrostyrene or Henry reaction is a traditional aldol type reaction of an aldehyde with nitroalkane[6]. The nucleophilic reaction treats with NaOH as a base catalyst and followed by working out of water for the elimination of an acidic proton is exist in the reaction[7]. The reaction produces a β-nitroalcohol structure in dendrimer core which undergo drying and results in the alternative nitroethylene derivative. The branched nitroolefin are members of the group of nitro alkenes, and their bioactivities have been reported[8]. β-nitroolefine is used in bulk for action aligned with microorganisms by Nazarova & Potemkin[9].In 1952, they have prepared 55 different compounds counting 20 new triarylnitroalkenes using the Henry reaction and experienced their antibacterial properties stirring the Gram positive bacterium, *Micrococcus pyogenes* var. *aureus*, and the Gram downbeat bacterium, *Escherichia coli*[9].The simple nitroolefine derivatives are obtained from aldehyde and nitromethane, with compounds having different substituent's on the aromatic ring by reaction using a variety of catalysts. Saigo *et al.*[10] have reported different nitroolefinic products effective against microorganism, but not against *E. coli*. Henry reaction on a range of heteroaromatic carbaldehydes[11-14] was also described recently under two different conditions[15,16]. A number of applications of microwaves and ultrasound-assisted reaction[17-21] have been reported earlier.

Indole derivatives are major class of *N*-heterocycles compounds and have notable applications in both biological and material chemistry. However, Indole moieties are very important bioactive molecules[22] which are mostly exists in variety of natural products[14,23] and synthetic organic compounds[24] which have conventional much thought during modern times due to their compound importance[25] and biological applications[26]. Many researchers were reported indole-based supramolecules utilized in various application fields such as theoretical, sensor[27], and biological applications[28]. Further, indole-based caged cyclphane[29] reported recently contains three-dimensional symmetrical aldehyde. The present investigation focuses on the synthesis of a three-dimensional symmetrical nitroolifinic dendritic core with indole moiety through N-arylation following Hendry reaction.

Experimental Section

Preparation of symmetrical 1,3,5-triindolyl benzene (2) by *N*-arylation of indole

To a combination of CuI (1.26 mmol), K_3PO_4 (6.00 mmol), trans-1,2-diamino cyclohexane (0.12 mmol) and indole (2.19 g 19.8 mmol) in toluene (150 mL)

were added along with 1,3,5-tribromobenzene (1) (2.1 g, 6.7 mmol) under nitrogen atmosphere. The reaction mixtures were refluxed at 110°C for 24 h. After completion of the reaction, the solvent was unconcerned under lowered pressure and the residue was removed with $CHCl_3$ (3 × 100 mL), washed with H_2O (2 × 100 mL), brine (150 mL) and dry over anhydrous Na_2SO_4. The solvent was detached and crude compound was purified by column chromatography on silica-gel using $CHCl_3$/Hexane (1:4, v/v) as eluent (solvent mixture) to give (2) as colourless solid. Yield 70%; mp: 222-225°C; ^{1}H NMR (300 MHz, $CDCl_3$, Fig. 1): δ 6.74 (d, 3H, *J* = 7.3 Hz); 7.18-7.30 (m, 6H); 7.42 (d, 3H, *J* = 7.3 Hz); 7.65 (s, 3H); 7.71 (d, 6H, *J* = 7.8 Hz): ^{13}C NMR (75 MHz, $CDCl_3$): δ 105.0, 110.5, 116.9, 121.1, 121.6, 123.1, 127.6, 129.7 (3C fussed ring), 135.6(3C-N fussed), 142.2 (3C-N); *m/z* (EI-MS) 423 (M^+). Elemental Anal. Calcd for $C_{30}H_{21}N_3$: C, 85.08; H, 5.00; N, 9.92. Found: C, 84.96; H, 5.18; N, 9.86.

Synthesis of symmetrical 1,3,5-tri(3-formyl indolyl)benzene (3)

To a stirred solution of dimethyl-formamide (19.9 mmol) at 0°C, added phosphorous oxychloride (5.0 mmol) drop wise under nitrogen atmosphere. Triindolyl benzene 2 (2.3 mmol) in dimethyl-formamide (5.9 mmol) was then added to the reaction at 0-10°C. After addition, the reaction mixture was permitted to reach 28°C and then stirred for further one hour at 35°C. Afterwards, the reaction was quenched by adding compressed ice (100 g) and secondary water (100 mL). Then the reaction mixture was treated thrice with NaOH solution (1 M). Then the mixture was excited after adding up one piece of NaOH solution and the reflex of the two portions was added later on with stirring. Subsequently, the stirred solution was reserved in refrigerator for overnight. In the reaction end, the precipitate obtained was collected by filtration and then dissolved in $CHCl_3$ (2 × 100 mL). Further, the dissolved product was washed with water and resulting product was allowed to remove water molecule by drying over Na_2SO_4, then the organic solution was filtered. The solvent was evaporated by keeping concentrated pressure. The residue was then chromatographed over SiO_2 using chloroform:methanol (99:1) as eluting solvent to give the corresponding trialdehyde 3 as white solid; Yield 64%; mp: 276-278°C; 1H NMR (300 MHz, $CDCl_3$, Fig. 2): δ 7.37-7.45 (m, 6H); 7.76 (d, 3H, J = 7.2 Hz); 8.06 (S, 3H); 8.36 (d, 3H, J = 7.2 Hz); 8.49 (s, 3H); 10.15 (s, 3H): ^{13}C NMR (75 MHz, $CDCl_3$): δ 110.5, 119.0, 119.9, 121.9, 123.4, 124.7, 125.3, 136.3, 138.5 (N- Ar-C fussed), 140.5 (N-C fussed), 184.6 (C=O); m/z (EI-MS) 507 (M^+). Elemental Anal. Calcd for $C_{33}H_{21}N_3O_3$: C, 78.09; H, 4.17; N, 8.28. Found: C, 77.96; H, 4.38; N, 8.15.

Synthesis of 1,3,5-tris(3-((E)-2-nitrovinyl)-1H-indol-1-yl) benzene (4)

To a stirred solution of 1,1',1"-(benzene-1,3,5-triyl)tris(1H-indole-3-carbalde, 0 mmol) was added at 0°C to room temperature. The reaction mixture was stirred at 0°C for 1 h. After completion of reaction, the mixture was added 5% dil HCl with ice water and yellow solid was filter out, in good yield (65%) as a colour solid.IR (KBr): 1643, 1579, 1583, 1327 cm^{-1}; ^{1}HNMR: δ 7.63 (d, 1H), 8.24(d, 1H), 7.17-8.43 (m, 54H); ^{13}C NMR: δ 106.70, 108.40, 114.01, 118.94, 119.44, 124.52, 125.15, 131.95, 132.37 (C-NO_2),142.71, 143.44 ppm; Chemical Formula: $C_{36}H_{24}N_6O_6$; Molecular Weight: 637; Anal. Calcd for: C, 67.92; H, 3.80; N, 13.20; Found: C, 67.90; H, 3.83; N, 13.21.

Results and Discussion

The preparation of an indole-based symmetrical nitroolifinic dendritic core is not much familiar. Consequently, we account herein the production of indole-based symmetrical dendritic core 4 through

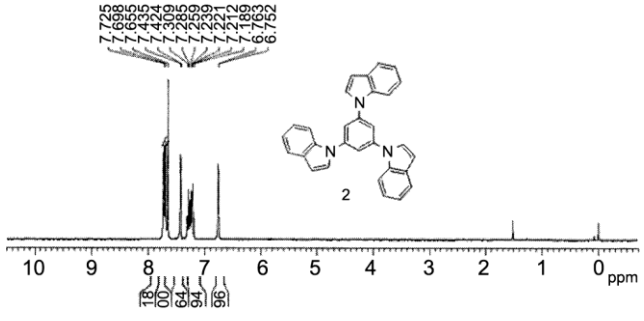


Fig. 1 —^{1}H NMR spectrum of 1,3,5-triindolyl benzene by *N*-arylation of indole (2)

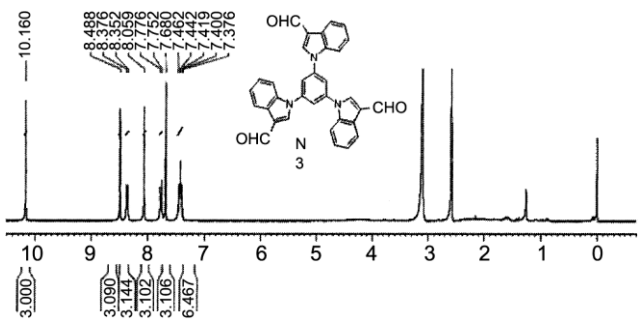
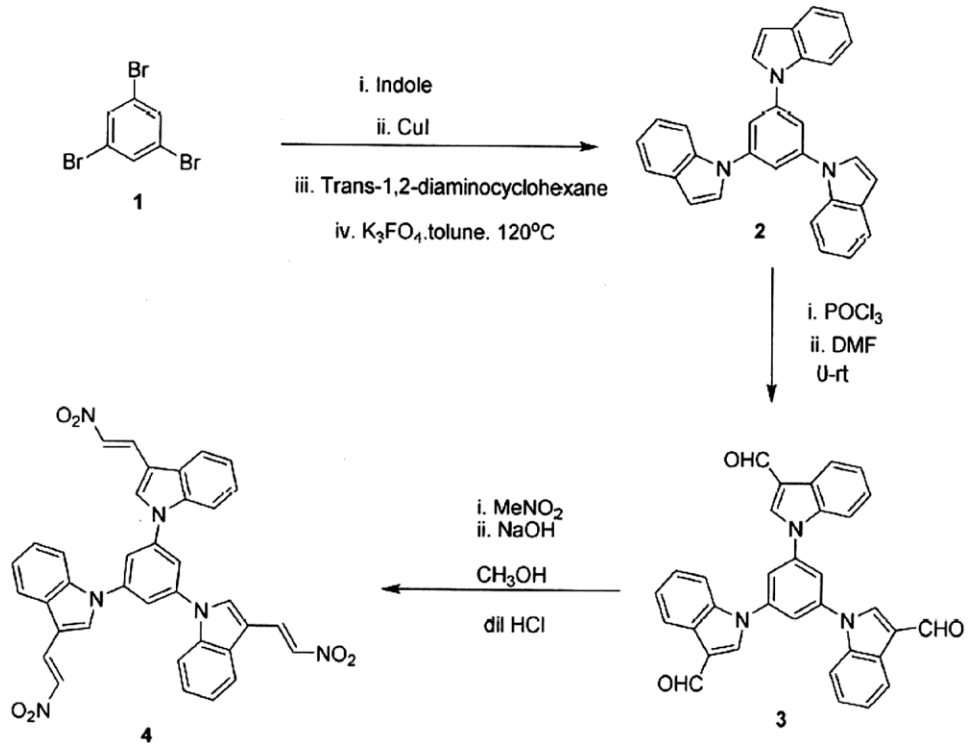


Fig. 2 — ^{1}H NMR spectrum of 1,3,5-tri(3-formyl indolyl)benzene (3)



Scheme 1 — Schematic representation of indole-based symmetrical nitroolifinic dendritic core synthesis

Henry reaction. Our research group The study started with the preparation of trinitroolefin from indole moiety with *N*-arylation and 1,3,5-tribromobenzene,trans-1,2-diaminocyclohexane in toluene at heating temperature for 36h produce regular 1,3,5-triindolyl benzene -3-carbaldehyde respectively[39]. The most favourable conditions were indole electrofile and nitromethane as reagents and a less amount of NaOH as a base; used in the reaction. In order to simplify this procedure, trinitroolefins were obtained from trialdehydes. The same procedure applied to prepare indole-3-carbaldehyde with 1,4-benzodioxan-6-carbaldehyde and the resulting preferred products formed after 5 h of the reaction. Conspicuously, the nitroalcohols were regularly transformed to the nitroolefin by drying out. The use of other base (CH_3ONa) was absolutely failed below the setting experienced. While mailed base catalyst the aldol summarizing, the olefin was obtain in suitable yield.

An efficient and scalable production of 1,3, 5-tris(3-((E)-2-nitrovinyl)-1H-indol-1-yl)benzene was investigated by examining the effects of flow conditions in the reaction of nitromethane (Scheme 1: step 4) with indole trialdehyde. Nitroolefin was synthesized from the corresponding trialdehyde under mild reaction conditions. The treatment of tribromo benzene with indole, CuI and Trans-1,2-diaminocycloheane under the K_3FO_4catalyst in as tolune solvent in reflux condition over a period of thirty six hours successfully provided the desired 1,3,5-tri(1H-indol-1-yl)benzene in 57% yield. Further Vilsmeier formylation of 1.0 eq. of triindolyl benzene 2 with 3.3 eq. of POCl3, 13.2 equiv. of DMF at 0°C for 3 h afforded the indole based trialdehyde 3 in 64% yield. The trialdehyde 3 further underwent Henry reaction with nitromethane and trialdehyde in presence NaOH and CH3OH as solvent for 5h, the reaction miture were quenched with dil HCl and filter out yellow crystalline solid according to Scheme 1 in 65% yield.

The compound 4 were characterized by IR, ^{1}H &^{13}C NMR spectroscopy, mass spectrometry (MS) and elemental analysis. The ^{1}H NMR spectrum of compound 4 showed a two doublet of doublet for olefin proton at δ 7.65 and 8.34. The aromatic protons peak appeared as multiplet in the region of δ 7.48-8.58 (Fig. 1).

Conclusion

In this study, we demonstrated synthesis of3D symmetrical novel nitroolifinic dendritic core with

indole moiety through N-arylation following Hendry reaction. The prepared indole-based symmetrical nitroolifinic dendritic core was confirmed with FTIR, NMR and EI-MS analysis. We recommended our methodology to synthesis of new nitroolefinic cored organic compounds. Further, preparation of other symmetrical dendritic core with nitrogen based N-heterocycles such as carbazole and pyrrole are being worked out in continuity with this work.

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