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Synthesis of solid state fluorescent quino[2,3-*b*]carbazoles via copper(II) triflate-catalyzed heteroannulation: application to detection of TNT

K.S. Prakash, Rajagopal Nagarajan *

School of Chemistry, University of Hyderabad, Hyderabad 500046, India

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ABSTRACT

New analogues of solid state fluorescent quino[2,3-*b*]carbazoles have been synthesized from heteroannulation of quinoline alkynylaldehyde and indole. Their preliminary photophysical properties are studied and application as chemosensory material for detection of trinitrotoluene is explored.

1. Introduction

Carbazole nucleus forms a basic skeleton of various alkaloids and they are found to have a wide range of biological activities. Among these, heteroaryl-annulated carbazoles are one of the attractive class of compounds due to their biological activities.[1] Their biological significance and synthetic importance have been extensively reviewed by Knölker et al.[1a] Pyrido[4,3-*b*]carbazole (ellipticine, olivacine and their derivatives) and quinolino[4,3-*b*]carbazole alkaloids (calothrixin A and its *N*-deoxy derivative, calothrixin B) are naturally occurring important biologically active molecules.[1a] Furthermore, staurosporine-inspired metallo-pyridocarbazole scaffolds are useful in designing selective inhibitors for various kinases of human kinome,[2a] GSK3,[2b–e] Pim1,[2d–f] MSK1,[2d] PAK1[2g] and also in the binding of ATP.[2h]

Carbazole-based compounds are being used in the field of organic electronics. For example, carbazole-based donor-acceptor compounds (1,2-dicyano-*trans*-1,2-bis-4-(carbazolyl)phenylethylene, 1,2-dicyano-*trans*-1,2-bis-4-(3,6-di-*tert*-butylcarbazolyl)phenyl ethylene),[3a] hole-transport molecule to afford highly efficient Organic Light Emitting Diodes (OLEDs),[3c] organic field-effect transistors,[3d] host materials for triplet emitters in OLEDs,[3e,f] high-performance organic semiconductors are suitable for organic thin-film transistor applications and organic solar cells (OSCs).[3b]

The applications of fluorescent scaffolds have been extensively reviewed in literature,[4a–k] e.g., intracellular pH indicators,[4b] sensors for reactive oxygen and nitrogen species,[4c] metal sensors,[4d–h] detection of nitric oxide (NO) in living systems[5] and hydrogen peroxide (H_2O_2) inside living cells,[6] as well as chemosensor for detection of high explosives[7a–o] (commonly, 2,4,6-trinitrotoluene (TNT), 1,3,5-trinitro-1,3,5-triazinane (RDX) and pentaerythritol tetranitrate (PETN)).

Now a days, considerable effort has been paid to the development of fluorescence-sensors;[8] especially in the detection of nitroaromatics. Swager group showed that pentiptycene-derived conjugated polymer is an excellent fluorescent chemosensor for the detection of nitroaromatics.[7i] Most recently, Ajayaghosh et al. demonstrated the attogram level detection of TNT,[7g] and Pradeep group has reported a simple and reliable strategy for detection of TNT and Hg^{2+} at sub-zeptomole level.[7m]

Over the past few years, there are amazing findings in the annulations involving phenylacetylenes bearing a carbonyl group or an imino group in the *ortho* position are explored, and this protocol is being used as an extremely rapid and powerful approach for the synthesis of carbocyclic and heterocyclic compounds.[9a–m] However, to the best of our knowledge synthesis of solid state fluorescent quinocarbazoles is not reported. We envisioned that quino[2,3-*b*]carbazoles would be obtained by cyclization of indole and

* Corresponding author. Tel.: +91 40 23134831; fax: +91 40 23012460; e-mail addresses: rnsc@uohyd.ernet.in, naga_indole@yahoo.co.in (R. Nagarajan).

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quinoline alkynylaldehyde.[11c] Interestingly, *N*-protected quino[2,3-*b*]carbazoles show bright green emission in liquid and red emission in solid state (Fig. 2). While adding trace amount of nitrobenzene, sensing was observed by naked eye. With this view point, we studied fluorescent sensing in various nitroaromatics and TNT. Herein, we report the first solid state fluorescent quino[2,3-*b*]carbazoles synthesized from copper(II) triflate-catalyzed heteroannulation and their sensing response to TNT.

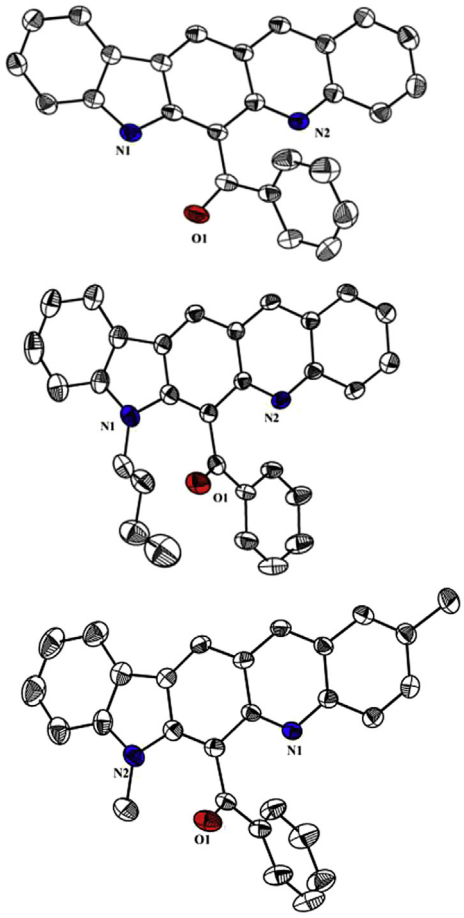


Fig. 1. ORTEP diagrams of **3a**, **3e** and **3l**. Hydrogen atoms are omitted for clarity.

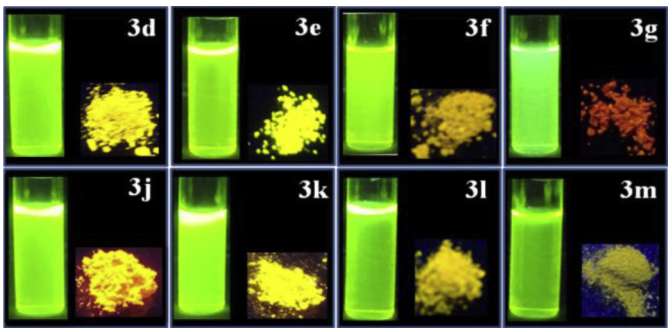


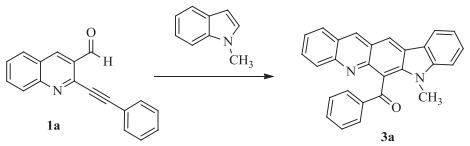
Fig. 2. Photographs of quinocarbazoles in solution state ($CHCl_3$) and solid-state irradiated with UV light (365 nm).

2. Results and discussion

At the outset, we investigated the model reaction of *N*-methyl indole with 2-(2-phenylethynyl)quinoline-3-carbaldehyde using metal catalysts and solvents. The results are summarized in optimization Table 1.

While using $Cu(OTf)_2$ (5 mol %) and 1,2-dichloroethane as solvent, the expected quinocarbazole (QC) is formed only in 35% yield

Table 1
Optimization of reaction conditions[a]



Entry	Catalyst	Solvent	Time (h)/temp (°C)	Yield[b] (%)
1	$Cu(OTf)_2$	DCE	10/80	35
2	CuBr	DCE	10/80	30
3	CuCl	DCE	10/80	20
4	CuI	DCE	10/80	35
5	$Cu(OTf)_2$	DCM	10/80	30
6	$Cu(OTf)_2$	THF	10/80	20
7	$Cu(OTf)_2$	Dioxane	10/80	25
8	$Cu(OTf)_2$	Toluene	12/100	35
9	$Cu(OTf)_2$	DMF	12/120	51
10	**$Cu(OTf)_2$**	**DMA**	**6/120**	**63**
11	$Cu(OTf)_2$	DMA	6/120	60
12	CuI	DMA	6/120	53
13	$Cu(OTf)_2$	CH_3CN	12/80	40
14	—	DMA	24/120	NR
15	$CuCl_2$	DMA	10/120	25

[a] Reaction conditions: **1a** (0.5 mmol), *N*-methyl indole (0.5 mmol) and solvent 5.0 mL. Catalyst 5 mol %.
[b] Isolated yields. [NR] No reaction. Optimized reaction condition is in bold.

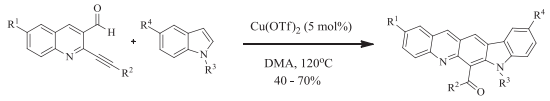
(Table 1, entry 1). Other copper catalysts CuCl, CuBr, CuI and $CuCl_2$ did not improve the yield of the product (Table 1, entries 2–4 and entry 15). Screening various metal catalysts also gave only inferior results ($La(OTf)_3$, $Sc(OTf)_3$, $Yb(OTf)_3$). However, we also screened other solvents. Gratifyingly, when DMA (as solvent) and 5 mol % of copper(II) triflate were employed, the yield of expected product was significantly enhanced to 63% after 6 h heating at 120 °C (Table 1, entry 10). Reaction did not occur in absence of catalyst. By using the above mentioned optimized reaction conditions, the substrate scope of the heteroannulation and the optical properties of the products were studied (Table 2). The yield was decreased, when unprotected indoles were used as substrate (**3a**, **3b**, **3h** and **3i**). No reaction occurred, when reaction occurred between *N*-sulfonylindole and **1a**. The structures of compounds **3a**, **3e** and **3l** were also unambiguously confirmed by single-crystal X-ray diffraction analysis (Fig. 1).[10]

Based on the literature,[11] the mechanism for formation of products is explained in Scheme 1. As depicted in Scheme 1, copper(II) triflate activates the triple bond and then 6-*endo*-dig cyclization leads to the formation of indol-3-yl-pyrano[4,3-*b*]quinoline (**I**). Subsequent electrocyclization and followed by aromatization deliver quino[2,3-*b*]carbazoles (Scheme 1).

It is noteworthy that all *N*-protected QCs show intense fluorescence in liquid as well as in solid states. The photographs of QCs are shown in Fig. 2. These compounds emit light in red region in solid state and green region in liquid state (Fig. 5). It is observed that, unprotected derivatives of QCs (**3a**, **3c**, **3h** and **3i**) did fluoresce, neither in solution nor in the solid state.

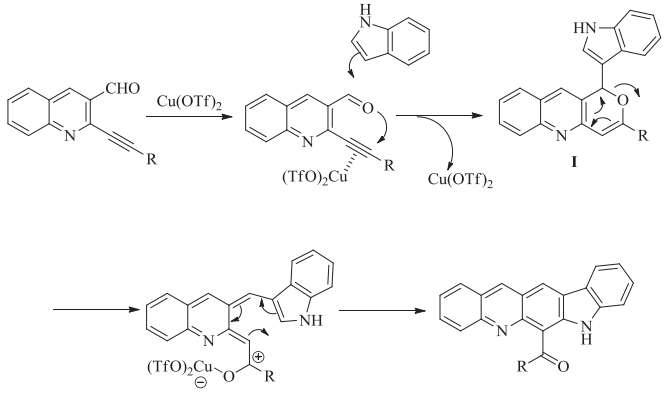
Fluorescence behaviour is explained from the crystal packing. We expected that fluorescence of unprotected QCs is quenched by hydrogen bonding interaction between free –*NH* and carbonyl oxygen. As we expected, strong inter and intramolecular hydrogen bonding are observed in **3a**. The H(1)–O(1) distance is 2.202(2) Å (intermolecular), 2.458(2) Å (intramolecular) (Fig. 3a). Such strong

Table 2
Heteroannulation of various indoles with quinoline alkynylaldehyde[a] and optical properties of QCs



Entry	Substrate	Product	Yield (%)/time (h)	λ_{abs} (nm)		λ_{em} (nm)	
				Liquid	Solid	Liquid	Solid
1[b]	R^1=H, R^2=Ph, R^3=H, R^4=H	**3a**	42/8	—	—	—	—
2	R^1=H, R^2=Ph, R^3=CH_3, R^4=H	**3b**	63/6	384	355	530	626
3[b]	R^1=H, R^2=Ph, R^3=H, R^4=Br	**3c**	40/8	—	—	—	—
4	R^1=H, R^2=Ph, R^3=C_2H_5, R^4=H	**3d**	62/6	382	358	531	600
5	R^1=H, R^2=Ph, R^3=C_4H_9, R^4=H	**3e**	60/6	384	324	518	630
6	R^1=H, R^2=Ph, R^3=C_6H_{13}, R^4=H	**3f**	61/6	384	333	531	590
7	R^1=H, R^2=Ph, R^3=Bn, R^4=H	**3g**	58/6	383	313	519	611
8[b]	R^1=H, R^2=*p*-tolyl, R^3=H, R^4=H	**3h**	43/6	—	—	—	—
9[b]	R^1=H, R^2=*p*-tolyl, R^3=H, R^4=Br	**3i**	41/6	—	—	—	—
10	R^1=H, R^2=*p*-tolyl, R^3=CH_3, R^4=H	**3j**	64/6	384	333	533	600
11	R^1=H, R^2=*p*-tolyl, R^3=Bn, R^4=H	**3k**	62/6	382	323	532	590
12	R^1=CH_3, R^2=Ph, R^3=CH_3 R^4=H	**3l**	68/5	384	318	527	600
13	R^1=OCH_3, R^2=Ph, R^3=CH_3, R^4=H	**3m**	70/5	384	321	527	544

[a] Unless otherwise noted, all the reactions were carried out in DMA as a solvent at 120 °C in presence of $Cu(OTf)_2$ (5 mol %). Isolated yields.
[b] No fluorescence was observed.



Scheme 1. Possible mechanism for the formation of quino[2,3-*b*]carbazoles.

intermolecular hydrogen bonding was not possible in *N*-protected QCs. It is known that, emissive nature in the solid state of the protected derivatives is more related to the lack of effective π-stacking rather than intermolecular hydrogen bonding.[12] In crystal structure for an unprotected derivative (**3a**), the molecules are effectively π-stacked along the crystallographic *b* axis. But, in crystal structures **3e** and **3l**, only isolated pairs of π-stacked molecules can be found.[13]

Surprisingly, fluorescent QCs showed significant quenching of fluorescence in the presence of nitrobenzene; this interesting result led us to an investigation on the efficiency of sensing for TNT. We have thus extended our work on sensing of fluorescence using such nitroaromatic explosives.

We studied TNT sensing and the results are given in Fig. 4. Quenching of fluorescence was observed from other nitroaromatics (2,6-dinitrotoluene, 1,3-dinitrobenzene, 1-chloro-2,4-dinitrobenzene, nitrobenzene) in 10 μM level, while doing fluorescence titration of compound **3b** in CH_3CN. Upon addition of incremental amount of 10 μM solution of TNT, fluorescence sensing was observed (Fig. 4). Visual changes of colour is also observed (Fig. 6), when TNT is spotted in quinocarbazole coated Whatman filter paper (See Supplementary data, Page S7).

No sensing was observed with nitromethane. The fluorescence intensity of **3b** decreases linearly with increasing concentration of nitroaromatic compounds. Visual sensing of nitrocompound also

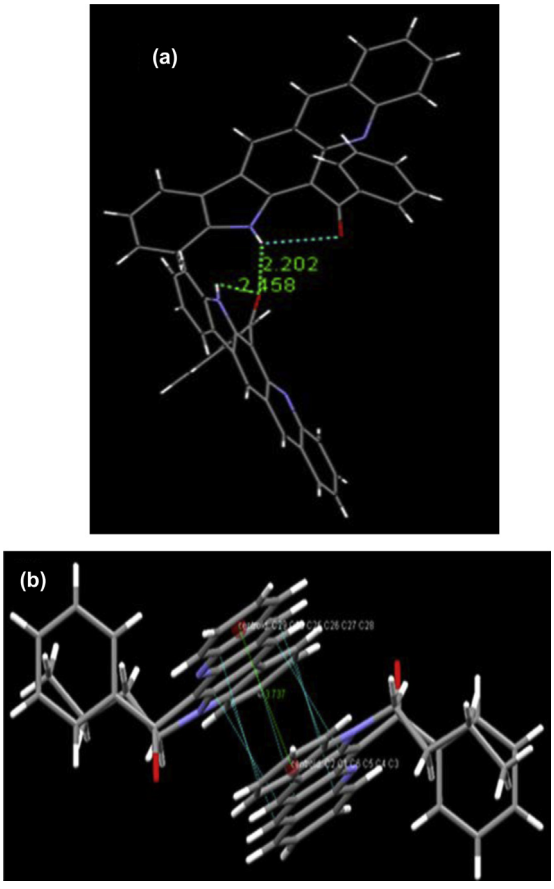


Fig. 3. a. Perspective view of strong inter- (H(1)–O(1)=2.202(2) Å) and intramolecular hydrogen bonding interaction ((H(1)–O(1)=2.458(2) Å)) in **3a**. b. Centroid-to-centroid distance (c1, c2, c3, c4, c5, c6 to c25, c26, c27, c28, c29=3.737 Å) in **3e** is shown.[13]

observed. There is clear colour change while addition of DNT (10 mM) in quinocarbazole (**3b**). After addition of nitrocompound, fluorescent behaviour of QC was fully disappeared (Fig. 6). We expect that there is an occurance of electron transfer between **3b** and electron deficient nitroaromatics by formation of a π-donor–acceptor (D–A) complex.

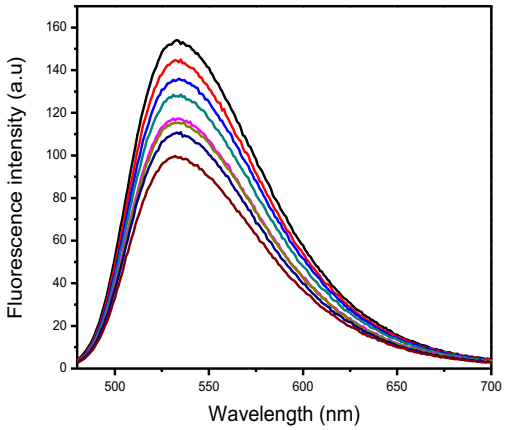


Fig. 4. Emission spectral change (λ_{ex}=384 nm) of **3b** with titration of 10 μM solution of TNT in CH_3CN (showing variation of emission intensity).

3. Conclusion

In summary, we have reported herein the synthesis of a family of quino[2,3-*b*]carbazoles and the study of their photochemical behaviour in solution and in the solid state. These are very interesting molecules, which have more stokes shift in solid phase than liquid phase. Their fluorescent nature has been utilized for the sensing of TNT. From the crystal packing, inter and intramolecular hydrogen bonding for unprotected derivative (**3a**) were observed. It is noteworthy that all compounds are linear, highly conjugated and have binding sites. Moreover, the pyridine nitrogen, carbonyl oxygen and free −*NH* are arranged in linear fashion. From this arrangement, these molecules can find a new application in the field of chemical biology as well as organic material. Further studies into the scope and applications of this heteroannulation are currently pursued in our laboratory and will be reported as events materialize.

4. Experimental section

4.1. General information

^1H and ^{13}C NMR spectra were recorded at 400 and 100 MHz, respectively, or at 500 and 125 MHz, respectively. Chemical shifts were calculated in parts per million downfield from TMS (δ=0) for ^1H NMR, and relative to the central $CDCl_3$ resonance (δ=77.0) and DMSO-d_6 (δ=39.51) for ^{13}C NMR. Data are presented as follows: chemical shift, multiplicity (br=broad signal, bs=broad singlet, s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet), coupling constant in Hertz (Hz) and integration. HRMS (ESI) was carried out at School of Chemistry, University of Hyderabad. UV–vis spectra were performed in a conventional quartz cell on UV–vis-NIR spectrophotometer (UV-3600). Fluorescence spectra were recorded in a conventional quartz cell at 25 °C on spectrofluorometer. X-ray diffraction measurements were carried out at 298 K on an automated diffractometer using graphite-monochromated Mo-Kα (l=0.71073 Å) radiation with CAD4 software or the X-ray intensity data were measured at 298 K on an instrument equipped with a graphite monochromator and a Mo-Kα fine-focus sealed tube (l=0.71073 Å). Melting points were measured in open capillary tubes and are uncorrected. All the obtained products were purified by column chromatography using silica gel (100–200 mesh). All reaction solvents used were of GR grade and used without drying unless mentioned. All other commercial reagents were used as received. Quinoline alkynylaldehydes were prepared according to methods already reported in the literature.[9b]

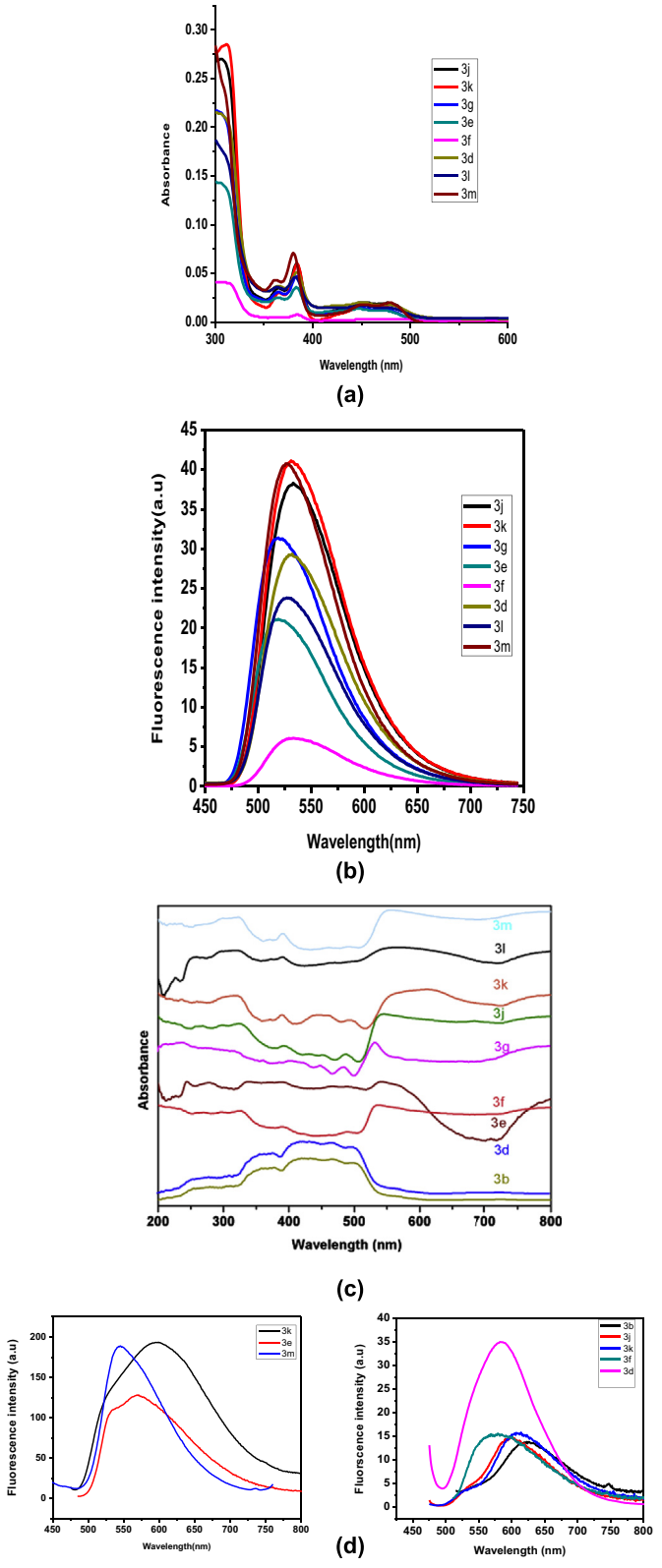


Fig. 5. Absorption and emission spectra of quinocarbazoles. (a) Absorption spectra of QCs in CH_3CN. (b) Emission spectra of QCs in CH_3CN. (c) Absorption spectra of QCs (solid state). (d) Emission spectra of QCs (solid state).

4.2. General procedure for synthesis of quino[2,3-*b*]carbazoles

An oven-dried 10-mL round-bottomed flask equipped with a Teflon-coated magnetic stirring bar was charged with 0.5 mmol

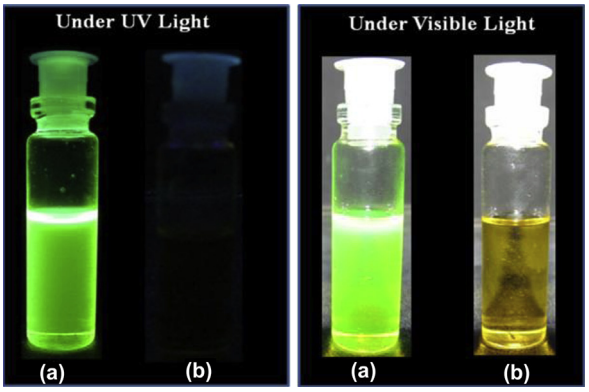


Fig. 6. Visual sensing of quino[2,3-*b*]carbazole (**3b**). a 10 mM solution of quino[2,3-*b*] carbazole (**3b**). b 10 mM solution of quino[2,3-*b*]carbazole (**3b**)+10 mM solution of 2,6-dinitrotoluene (DNT).

2-(2-phenylethynyl)quinoline-3-carbaldehyde (**1a**) 5 mol % of $Cu(OTf)_2$, and 5 mL DMA. To this 0.5 mmol of *N*-methyl indole (**2a**) was added. Then the reaction mixture was stirred at 120 °C until the complete consumption of starting materials as monitored by TLC. Then, solvent was removed under reduced pressure. The crude reaction mixture was then poured over water and extracted with EtOAc (3×20 mL). The organic layer was dried with anhydrous Na_2SO_4 and the solvent was removed. The residue was purified by column chromatography using silica gel with hexanes/ethyl acetate mixture (eluent: 5% ethyl acetate in hexanes) to afford the product **3b**; the product **3b** was eluted as fluorescent solid. Yield: 63%. The same procedure was followed for the synthesis of other quino[2,3-*b*]carbazoles (**3a**–**m**).

*4.2.1. (7H-Indolo[3,2-b]acridin-6-yl)(phenyl)methanone (**3a**).* Yield: 42%; R_f=0.35 in 90% hexanes/10% EtOAc; mp 274–276 °C; IR (KBr): 3395, 2955, 2910, 2850, 1655, 1594, 1468, 1400, 1250, 1100, 805 cm^{-1}; ^1H NMR (400 MHz, TMS, $CDCl_3$): 10.21 (s, 1H), 8.98 (s, 1H), 8.86 (s, 1H), 8.25 (d, *J*=8.0 Hz, 1H), 8.02 (d, *J*=8.4 Hz, 1H), 7.71 (m, 2H), 7.60–7.66 (m, 1H), 7.52–7.58 (m, 3H), 7.46–7.49 (m, 2H), 7.35–7.41 (m, 3H); ^{13}C NMR (100 MHz, TMS, $CDCl_3$): 198.8, 147.9, 146.4, 146.2, 142.9, 142.4, 136.7, 131.1, 130.2, 129.3, 129.2, 129.0, 128.1, 127.9, 127.5, 124.8, 124.7, 124.4, 122.3, 121.8, 121.4, 121.0, 111.6, 111.1 (Aromatic C); HRMS (ESI-MS) calcd for $C_{26}H_{16}N_2O$; 373.1341 (M+H), found: 373.1341.

*4.2.2. (7-Methyl-7H-indolo[3,2-b]acridin-6-yl)(phenyl)methanone (**3b**).* Yield: 63%; R_f=0.45 in 90% hexanes/10% EtOAc; mp 252–254 °C; IR (KBr): 3400, 2945, 2890, 2750, 1559, 1500, 1400, 1250, 1128, 790 cm^{-1}; ^1H NMR (500 MHz, TMS, $CDCl_3$): 8.94 (s, 1H), 8.76 (s, 1H), 8.27 (d, *J*=7.5 Hz, 1H), 7.97–8.00 (m, 3H), 7.92 (d, *J*=9.0 Hz, 1H), 7.54–7.67 (m, 3H), 7.43 (t, *J*=8.0 Hz, 2H), 7.30–7.35 (m, 2H), 7.24–7.27 (m, 1H), 3.66 (s, 3H); ^{13}C NMR (125 MHz, TMS, $CDCl_3$): 199.3, 148.6, 147.2, 145.0, 141.2, 140.0, 135.8, 133.0, 130.0, 129.6, 129.55, 128.8, 128.6, 128.5, 127.9, 127.6, 124.7, 124.4, 122.1, 121.1, 120.0, 119.3, 115.2, 108.4, (Aromatic C), 31.9 (Aliphatic C); HRMS (ESI-MS) calcd for $C_{27}H_{18}N_2O$; 387.1497 (M+H) found: 387.1497.

*4.2.3. (10-Bromo-7H-indolo[3,2-b]acridin-6-yl)(phenyl)methanone (**3c**).* Yield: 40%; R_f=0.35 in 90% hexanes/10% EtOAc; mp 262–264 °C; IR (KBr): 3380, 2955, 2870, 2690, 1555, 1490, 1256, 790 cm^{-1}; ^1H NMR (500 MHz, TMS, $CDCl_3$): 10.16 (s, 1H), 8.98 (s, 1H), 8.82 (s, 1H), 8.36 (s, 1H), 8.03 (d, *J*=8.5 Hz, 1H), 7.72 (d, *J*=8.0 Hz, 2H), 7.66 (t, *J*=6.5 Hz, 2H), 7.53–7.58 (m, 2H), 7.49 (t, *J*=7.5 Hz, 1H), 7.35–7.40 (m, 3H); ^{13}C NMR (125 MHz, TMS, $CDCl_3$): 198.7, 148.2, 146.3, 145.9, 142.0, 141.6, 136.9, 131.6, 131.3, 130.5, 129.3, 129.2, 127.9, 127.6, 126.9, 125.0, 124.7, 124.3, 124.2, 121.8, 113.6, 112.5, 112.0 (Aromatic C); HRMS (ESI-MS) calcd for $C_{26}H_{15}BrN_2O$; 451.0466 (M+H), found: 451.0464 (M+H), 453.0466 (M+2).

*4.2.4. (7-Ethyl-7H-indolo[3,2-b]acridin-6-yl)(phenyl)methanone (**3d**).* Yield: 62%; R_f=0.42 in 90% hexanes/10% EtOAc; mp 258–260 °C; IR (KBr): 3742, 2958, 2915, 2860, 1660, 1594, 1468, 1101, 1019, 805 cm^{-1}; ^1H NMR (500 MHz, TMS, $CDCl_3$): 8.96 (s, 1H), 8.78 (s, 1H), 8.27 (d, *J*=8.0 Hz, 1H), 7.93–8.00 (m, 4H), 7.53–7.63 (m, 3H), 7.40–7.44 (m, 3H), 7.32–7.36 (m, 2H), 4.21 (q, *J*=7.0 Hz, 2H), 1.20 (t, *J*=7.0 Hz, 3H); ^{13}C NMR (125 MHz, TMS, $CDCl_3$): 199.3, 148.6, 147.2, 144.1, 139.9, 139.4, 135.7, 133.1, 129.9, 129.6, 129.57, 128.6, 128.5, 127.9, 127.8, 124.8, 124.4, 122.5, 121.1, 121.0, 120.1, 119.2, 115.0, 108.7 (Aromatic C), 39.6, 13.2 (Aliphatic C); HRMS (ESI-MS) calcd for $C_{28}H_{20}N_2O$; 401.1654 (M+H), found: 401.1654.

*4.2.5. (7-Butyl-7H-indolo[3,2-b]acridin-6-yl)(phenyl)methanone (**3e**).* Yield: 60%; R_f=0.48 in 90% hexanes/10% EtOAc; mp 230–232 °C; IR (KBr): 3739, 2988, 2900, 2880, 1657, 1590, 1448, 1090, 1030, 810 cm^{-1}; ^1H NMR (400 MHz, TMS, $CDCl_3$): 8.95 (s, 1H), 8.77 (s, 1H), 8.26 (d, *J*=7.6 Hz, 1H), 7.93–7.99 (m, 4H), 7.53–7.64 (m, 3H), 7.39–7.43 (m, 3H), 7.30–7.34 (m, 2H), 4.10 (t, *J*=8.0 Hz, 2H), 1.53 (br, 2H), 1.18 (sextet, *J*=7.2 Hz, 2H), 0.74 (t, *J*=7.2 Hz, 3H); ^{13}C NMR (100 MHz, TMS, $CDCl_3$): 199.1, 148.6, 147.2, 144.5, 140.1, 139.2, 135.7, 133.1, 130.0, 129.6, 128.6, 128.5, 127.9, 124.7, 124.4, 122.3, 121.1, 121.0, 120.0, 119.1, 115.0, 108.8 (Aromatic C), 44.7, 30.5, 20.0, 13.6 (Aliphatic C); HRMS (ESI-MS) calcd for $C_{30}H_{24}N_2O$; 429.1967 (M+H), found: 429.1967.

*4.2.6. (7-Hexyl-7H-indolo[3,2-b]acridin-6-yl)(phenyl)methanone (**3f**).* Yield: 61%; R_f=0.50 in 90% hexanes/10% EtOAc; mp 224–226 °C; IR (KBr): 3749, 2955, 2900, 2850, 1647, 1490, 1448, 1110, 816 cm^{-1}; ^1H NMR (500 MHz, TMS, $CDCl_3$): 8.94 (s, 1H), 8.75 (s, 1H), 8.24 (d, *J*=7.5 Hz, 1H), 7.90–7.98 (m, 4H), 7.50–7.61 (m, 3H), 7.36–7.42 (m, 3H), 7.29–7.31 (m, 2H), 4.07 (t, *J*=8.5 Hz, 2H), 1.50 (br, 2H), 1.09–1.17 (m, 4H), 1.01–1.05 (m, 2H), 0.80 (t, *J*=7.5 Hz, 3H); ^{13}C NMR (125 MHz, TMS, $CDCl_3$): 199.0, 148.6, 147.3, 144.5, 140.1, 139.2, 135.7, 133.0, 130.0, 129.6, 129.55, 128.6, 128.5, 127.9, 127.8, 124.8, 124.4, 122.3, 121.0, 120.0, 119.1, 115.0, 108.8 (Aromatic C), 44.9, 31.3, 28.4, 26.3, 22.5, 14.0 (Aliphatic C); HRMS (ESI-MS) calcd for $C_{32}H_{28}N_2O$; 457.2280 (M+H), found: 457.2280.

*4.2.7. (7-Benzyl-7H-indolo[3,2-b]acridin-6-yl)(phenyl)methanone (**3g**).* Yield: 58%; R_f=0.48 in 90% hexanes/10% EtOAc; mp 252–254 °C; IR (KBr): 2998, 2920, 2840, 1656, 1580, 1438, 1080, 1040, 800 cm^{-1}; ^1H NMR (400 MHz, TMS, $CDCl_3$): 8.97 (s, 1H), 8.83 (s, 1H), 8.31 (d, *J*=7.2 Hz, 1H), 8.00 (d, *J*=8.4 Hz, 1H), 7.86 (d, *J*=8.8 Hz, 1H), 7.60–7.64 (m, 3H), 7.53 (t, *J*=7.6 Hz, 1H), 7.44 (t, *J*=7.2 Hz, 1H), 7.31–7.38 (m, 2H), 7.25 (s, 1H), 7.15 (t, *J*=7.6 Hz, 2H), 6.96–6.97 (m, 3H), 6.79–6.81 (m, 2H), 5.48 (s, 2H); ^{13}C NMR (100 MHz, TMS, $CDCl_3$): 198.9, 148.5, 147.3, 145.1, 140.4, 139.2, 136.4, 135.7, 132.4, 129.7, 129.6, 128.8, 128.3, 128.0, 127.8, 127.1, 126.1, 124.8, 124.5, 122.3, 121.2, 121.1, 120.5, 119.4, 115.8, 109.3 (Aromatic C), 48.1 (Aliphatic C); HRMS (ESI-MS) calcd for $C_{33}H_{22}N_2O$; 463.1810 (M+H), found: 463.1810.

*4.2.8. (7H-Indolo[3,2-b]acridin-6-yl)(p-tolyl)methanone (**3h**).* Yield: 43%; R_f=0.38 in 90% hexanes/10% EtOAc; mp 276–278 °C; IR (KBr): 3023, 2998, 2920, 2890, 1647, 1690, 1548, 1160, 1032, 805 cm^{-1}; ^1H NMR (500 MHz, TMS, $CDCl_3$): 10.10 (br s, 1H), 8.96 (s, 1H), 8.81 (s, 1H), 8.22 (d, *J*=8.0 Hz, 1H), 8.02–8.03 (m, 4H), 7.66–7.67 (m, 1H), 7.54 (t, *J*=7.0 Hz, 1H), 7.45–7.47 (m, 2H), 7.34 (t, *J*=7.0 Hz, 1H), 7.18 (d, *J*=8.0 Hz, 2H), 2.45 (s, 3H); ^{13}C NMR (125 MHz, TMS, $CDCl_3$): 198.3, 148.0, 146.3, 145.7, 144.4, 143.1, 142.1, 138.9, 136.6, 130.3, 130.1, 129.8, 129.2, 128.9, 128.3, 127.9, 124.7, 123.7, 122.3, 121.8, 121.4,

120.8, 112.2, 111.1 (Aromatic C), 21.7 (Aliphatic C); HRMS (ESI-MS) calcd for $C_{27}H_{18}N_2O$; 387.1497 (M+H), found: 387.1497.

*4.2.9. (10-Bromo-7H-indolo[3,2-b]acridin-6-yl)(p-tolyl)methanone (**3i**).* Yield: 41%; R_f=0.36 in 90% hexanes/10% EtOAc; mp 282–284 °C; IR (KBr): 3740, 3005, 2950, 2850, 1627, 1490, 1348, 1080, 1035, 820 cm^{-1}; ^1H NMR (500 MHz, TMS, $CDCl_3$): 9.93 (s, 1H), 8.99 (s, 1H), 8.81 (s, 1H), 8.35 (s, 1H), 8.04 (d, *J*=8.5 Hz, 1H), 7.65–7.68 (m, 5H), 7.48–7.51 (m, 1H), 7.33 (d, *J*=8.0 Hz, 1H), 7.18 (d, *J*=8.0 Hz, 2H), 2.45 (s, 3H); ^{13}C NMR (125 MHz, TMS, $CDCl_3$): 198.1, 148.3, 146.3, 145.4, 142.4, 141.6, 138.7, 136.9, 131.5, 130.5, 130.2, 129.9, 129.2, 128.4, 128.0, 126.8, 125.0, 124.8, 124.3, 124.2, 121.8, 113.4, 112.7, 112.4 (Aromatic C), 21.7 (aliphatic C); HRMS (ESI-MS) calcd for $C_{27}H_{17}BrN_2O$; 465.0602 (M+H), found: 465.0602 (M+H), 467.0585 (M+2).

*4.2.10. (7-Methyl-7H-indolo[3,2-b]acridin-6-yl)(p-tolyl)methanone (**3j**).* Yield: 64%; R_f=0.48 in 90% hexanes/10% EtOAc; mp 258–260 °C; IR (KBr): 3739, 2958, 2905, 2860, 1657, 1540, 1468, 1060, 1020, 810 cm^{-1}; ^1H NMR (500 MHz, TMS, $CDCl_3$): 8.89 (s, 1H), 8.71 (s, 1H), 8.21 (d, *J*=7.5 Hz, 1H), 7.92 (m, 2H), 7.83 (d, *J*=8.0 Hz, 2H), 7.53–7.57 (m, 2H), 7.38 (t, *J*=8.0 Hz, 1H), 7.24–7.30 (m, 2H), 7.18 (d, *J*=8.0 Hz, 2H), 3.62 (s, 3H), 2.37 (s, 3H); ^{13}C NMR (125 MHz, TMS, $CDCl_3$): 198.9, 148.6, 147.1, 145.0, 143.9, 141.0, 137.6, 135.8, 130.1, 129.6, 129.5, 129.3, 128.6, 127.9, 127.6, 124.8, 124.4, 122.1, 121.2, 121.1, 120.0, 119.2, 115.5, 108.4 (Aromatic C), 31.8, 21.7 (Aliphatic C); HRMS (ESI-MS) calcd for $C_{28}H_{20}N_2O$; 401.1654 (M+H), found: 401.1654.

*4.2.11. (7-Benzyl-7H-indolo[3,2-b]acridin-6-yl)(p-tolyl)methanone (**3k**).* Yield: 62%; R_f=0.45 in 90% hexanes/10% EtOAc; mp 262–264 °C; IR (KBr): 3735, 2991, 2900, 2480, 1647, 1690, 1458, 1090, 1030, 816 cm^{-1}; ^1H NMR (400 MHz, TMS, $CDCl_3$): 8.87 (s, 1H), 8.74 (s, 1H), 8.24 (d, *J*=6.8 Hz, 1H), 7.90 (d, *J*=8.0 Hz, 1H), 7.85 (d, *J*=8.8 Hz, 1H), 7.50–7.52 (m, 2H), 7.30–7.37 (m, 4H), 7.16 (d, *J*=7.6 Hz, 1H), 6.87–6.94 (m, 5H), 6.79 (m, 2H), 5.40 (s, 2H), 2.24 (s, 3H); ^{13}C NMR (100 MHz, TMS, $CDCl_3$): 198.6, 148.6, 147.2, 145.0, 143.3, 140.3, 136.7, 136.6, 135.7, 129.9, 129.7, 129.6, 128.8, 128.76, 128.3, 127.9, 127.8, 126.8, 126.1, 124.8, 124.5, 122.3, 121.2, 121.1, 120.4, 119.2, 116.1, 109.3 (Aromatic C), 48.1, 21.6 (Aliphatic C); HRMS (ESI-MS) calcd for $C_{34}H_{24}N_2O$; 477.1967 (M+H) found: 477.1967.

*4.2.12. (2,7-Dimethyl-7H-indolo[3,2-b]acridin-6-yl)(phenyl)methanone (**3l**).* Yield: 68%; R_f=0.42 in 90% hexanes/10% EtOAc; mp 290–292 °C; IR (KBr): 3759, 2968, 2940, 2870, 1647, 1590, 1448, 1130 cm^{-1}; ^1H NMR (500 MHz, TMS, $CDCl_3$): 8.77 (s, 1H), 8.69 (s, 1H), 8.24 (d, *J*=7.5 Hz, 1H), 7.97–7.99 (m, 2H), 7.82 (d, *J*=9.0 Hz, 1H), 7.67 (s, 1H), 7.53–7.58 (m, 2H), 7.43 (m, 3H), 7.31 (t, *J*=7.0 Hz, 1H), 7.27–7.30 (m, 1H), 3.64 (s, 3H), 2.52 (s, 3H); ^{13}C NMR (125 MHz, TMS, $CDCl_3$): 199.4, 147.5, 146.6, 144.9, 140.8, 139.9, 139.3, 134.6, 134.0, 132.9, 132.5, 129.9, 129.1, 128.5, 127.3, 125.8, 122.1, 121.2, 121.0, 119.9, 115.1, 114.1, 108.3 (Aromatic C), 31.8, 21.7 (Aliphatic C); HRMS (ESI-MS) calcd for $C_{28}H_{20}N_2O$; 401.1654 (M+H), found: 401.1654.

*4.2.13. (2-Methoxy-7-methyl-7H-indolo[3,2-b]acridin-6-yl)(phenyl) methanone (**3m**).* Yield: 70%; R_f=0.48 in 90% hexanes/10% EtOAc; mp 302–304 °C; IR (KBr): 3012, 2950, 2980, 1647, 1595, 1458, 1110, 1080, 900 cm^{-1}; ^1H NMR (500 MHz, TMS, $CDCl_3$): 8.61 (s, 1H), 8.59 (s, 1H), 8.23 (d, *J*=8.0 Hz, 1H), 7.98 (d, *J*=7.5 Hz, 2H), 7.80 (d, *J*=9.5 Hz, 1H), 7.55 (t, *J*=7.5 Hz, 2H), 7.41 (t, *J*=7.5 Hz, 2H), 7.29–7.30 (m, 2H), 7.22 (d, *J*=8.0 Hz, 1H), 7.02 (s, 1H), 3.92 (s, 3H), 3.60 (s, 3H); ^{13}C NMR (125 MHz, TMS, $CDCl_3$): 199.5, 156.1, 145.7, 145.6, 144.9, 140.3, 139.9, 133.4, 133.0, 131.0, 129.9, 128.5, 128.4, 127.3, 125.3, 124.8, 122.0, 121.3, 121.1, 119.7, 118.7, 115.2, 108.3, 102.7 (Aromatic C), 55.4, 31.8 (Aliphatic C); HRMS (ESI-MS) calcd for $C_{28}H_{20}N_2O_2$; 417.1603 (M+H), found: 417.1603.

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Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.tet.2013.07.016.

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10. The CCDC deposition number of **3a** is 900312; molecular formula: $C_{26}H_{16}N_2O_1$, unit cell parameters: a=17.4997(15), b=4.9148(4), c=21.8498(16); space group $P21/n$. The CCDC deposition number of **3e** is 900313; molecular formula: $C_{30}H_{24}N_2O_1$, unit cell parameters: a=12.0524(17), b=13.4942(19), c=15.342(2); space group $P-1$. The CCDC deposition number of **3l** is 900314; molecular formula: $C_{28}H_{20}N_2O_1$, unit cell parameters: a=33.695(3), b=30.274(2), c=8.2167(7); space group *Fdd*2.
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13. The detailed crystal packing of **3a**, **3e** and **3l**. (See Supplementary data, pages S2–S4).