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Donor–Acceptor Fluorophores for Visible-Light-Promoted Organic Synthesis: Photoredox/Ni Dual Catalytic $C(sp^3)$–$C(sp^2)$ Cross-Coupling

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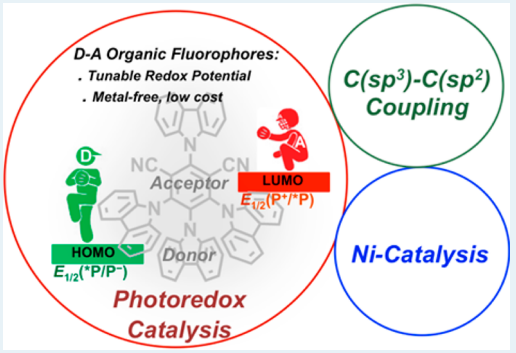
Supporting Information

ABSTRACT: We describe carbazolyl dicyanobenzene (CDCB)-based donor–acceptor (D–A) fluorophores as a class of cheap, easily accessible, and efficient metal-free photoredox catalysts for organic synthesis. By changing the number and position of carbazolyl and cyano groups on the center benzene ring, CDCBs with a wide range of photoredox potentials are obtained to effectively drive the energetically demanding $C(sp^3)$–$C(sp^2)$ cross-coupling of carboxylic acids and alkyltrifluoroborates with aryl halides via a photoredox/Ni dual catalysis mechanism. This work validates the utility of D–A fluorophores in guiding the rational design of metal-free photoredox catalysts for visible-light-promoted organic synthesis.



KEYWORDS: *donor–acceptor fluorophores, photoredox catalysis, nickel catalysis, visible light, cross-coupling*

Visible-light photoredox catalysis, the synthetic manifold mostly centered on ruthenium (Ru)- and iridium (Ir)-based photoredox catalysts, has recently received resurgent attention.[1] Thanks to the large collection of Ru- and Ir-complexes that cover a wide range of photoredox potentials for driving the intermolecular single-electron transfer (SET) processes,[2] many complicated organic transformations have now been realized,[3] including dual catalytic reactions.[4] Since Ru- and Ir-complexes are expensive, photocatalysts based on earth-abundant copper (Cu),[5] chromium (Cr),[6] and iron (Fe)[7] have been investigated. Nevertheless, for large-scale synthesis, organic dyes[8] with low cost, ease of availability, and low toxicity offer an intriguing alternative.[9] However, the general synthetic utility of organic dyes is still rather limited due to relatively few catalyst options. Therefore, it is highly desirable to design new organic photocatalysts with broad redox capabilities.

Donor–acceptor (D–A) molecular dyads have been extensively studied in chemical sensing,[10] optoelectronic materials,[11] organic photovoltaics,[12] and artificial photosynthetic systems.[13] D–A fluorophores are particularly interesting since their photoredox potentials are strongly dependent on the energy level of acceptor's LUMO (determining $E_{1/2}(P^+/{}^*P)$ and $E_{1/2}(P/P^-)$, P = photocatalyst, * = excited state) and donor's HOMO (determining $E_{1/2}({}^*P/P^-)$ and $E_{1/2}(P^+/P)$). In principle, by choosing donor–acceptor pairs with different electronic properties, D–A fluorophores with a wide range of photoredox potentials can be realized. In fact, the highly oxidative photocatalyst, 9-mesityl-10-methylacridinium (Acr^+-Mes),[14] is a D–A dyad.[15] However, tuning the photoredox potentials of Acr^+-Mes via structural modification is not straightforward.[16]

Herein, we describe carbazolyl dicyanobenzenes (CDCBs) as a versatile design platform to facilely construct D–A fluorophores at low cost. We choose CDCBs because dicyanoarenes and carbazole derivatives are strong electron acceptors[8b,f] and donors,[17] respectively, with appropriately aligned HOMO–LUMO energy levels. More importantly, by changing the number and position of carbazolyl and cyano groups on the center benzene ring, one can easily modify the photoredox potentials of the resulting D–A fluorophores. We further test the photocatalytic activities of CDCBs using two photoredox/Ni dual catalytic $C(sp^3)$–$C(sp^2)$ cross-coupling reactions and demonstrate their wide potential utility in visible-light-promoted organic synthesis.

Six CDCB-based D–A fluorophores, namely, 4CzIPN, 2CzIPN, 4CzPN, 2CzPN, 4CzTPN, and 2CzTPN (Figure 1) were prepared using a previously reported one-step nucleophilic substitution reaction followed by the simple recrystallization purification procedure.[18] Note that 2CzIPN and 2CzTPN are synthesized here for the first time. To demonstrate the versatility of this synthetic protocol, we prepared 4DPAIPN as an example in which a stronger electron donor diphenylamine is incorporated. It is gratifying that the costs for synthesizing these D–A fluorophores (e.g., ∼ $6/g for 4CzIPN and 4DPAIPN) were much lower than those of common Ru- and Ir-complexes (Supporting Information, S-2).

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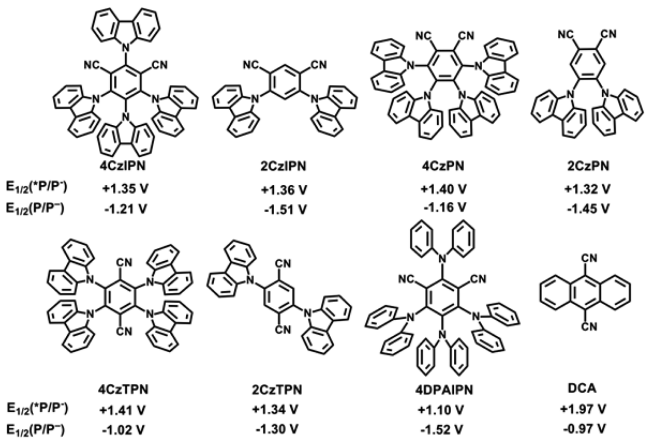


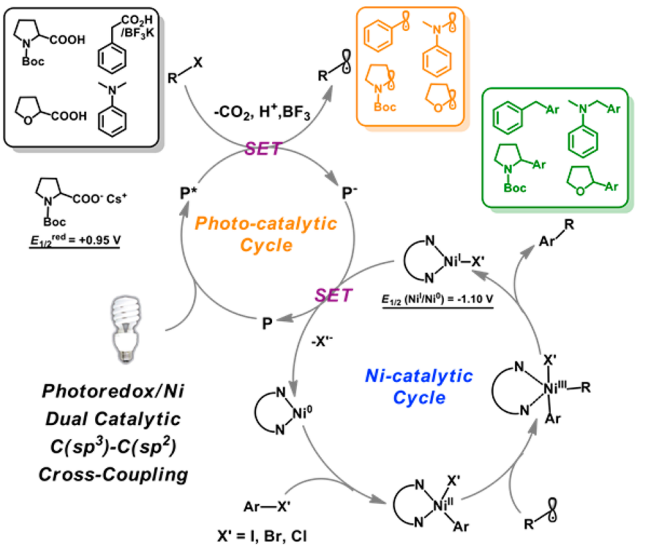
Figure 1. Structure and photoredox potentials (vs SCE; all potentials mentioned hereafter are against SCE) of the D−A fluorophores: 1,2,3,5-tetrakis(carbazol-9-yl)-4,6-dicyanobenzene (4CzIPN), 1,3-bis(carbazol-9-yl)-4,6-dicyanobenzene (2CzIPN), 1,2,3,4-tetrakis(carbazol-9-yl)-5,6-dicyanobenzene (4CzPN), 1,2-bis(carbazol-9-yl)-4,5-dicyanobenzene (2CzPN), 1,2,4,5-tetrakis(carbazol-9-yl)-3,6-dicyanobenzene (4CzTPN), 1,4-bis(carbazol-9-yl)-2,5-dicyanobenzene (2CzTPN), and 1,3-dicyano-2,4,5,6-tetrakis(*N*,*N*-diphenylamino)-benzene (4DPAIPN). DCA (9,10-dicyanoanthracene) is depicted here as a comparison. For simplicity, only $E_{1/2}(*P/P^-)$ and $E_{1/2}(P/P^-)$ are shown here. See Supporting Information, Table S1 for comprehensive values.

Upon visible light excitation, the nanosecond scale excited state of D−A fluorophores exhibits both strong oxidative ($E_{1/2}(*P/P^-)$ = +1.10 ∼ + 1.41 V) and reductive ($E_{1/2}(P^+/*P)$ = −0.99 ∼ − 1.41 V) capabilities that are comparable or superior to many metal complexes and organic dyes (Supporting Information, Table S1). Importantly, their relatively wide distribution of photoredox potentials is achieved simply by changing the number of donors (two or four carbazolyl), the positions of acceptors (*ortho-, meta-, or para*-dicyanobenzene), or the nature of donor (carbazolyl- or diphenylamino-). For example, increasing the number of carbazolyl groups from two to four anodically shifts $E_{1/2}(*P/P^-)$ and $E_{1/2}(P/P^-)$ (∼0.29 V), while inducing a smaller anodic shift on $E_{1/2}(P^+/*P)$ and $E_{1/2}(P^+/P)$ (<0.08 V) (Table S1). Further, when the carbazolyl moiety is changed to diphenylamine (as in 4DPAIPN), a cathodic shift of 0.18−0.31 V was observed for photoredox potentials (Table S1).

With their strong photoredox potentials in mind, we envision that the D−A fluorophores are suitable to promote organic transformations with high energetic demand such as the photoredox/Ni dual catalytic C(sp^3)−C(sp^2) cross-coupling[19] recently developed by the Molander group and the MacMillan/Doyle group independently.[20] The proposed reaction mechanism (Scheme 1) suggests that a highly oxidative photocatalyst ($E_{1/2}(*P/P^-)$ > + 1.10 V) is necessary to generate an organoradical (R·) from the C(sp^3) precursor (R−X, where X is CO_2^-, BF_3K, or H), which is subsequently captured by an aryl-Ni^{II} complex, forming a Ni^{III} species that readily undergoes reductive elimination.[21] Meanwhile, the reduced photocatalyst with a large $E_{1/2}$ (P/P^-) (<−1.10 V) facilitates a second SET to release a Ni^0 species, which further undergoes oxidative addition to Ar−X′, synchronizing and completing the two catalytic cycles.[22]

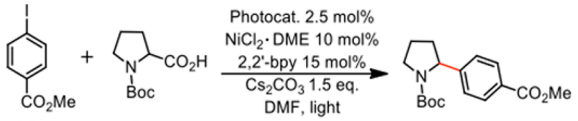
We first investigated the C(sp^3)−C(sp^2) cross-coupling of α-amino acids with aryl halides. We expect that the D−A

Scheme 1. Proposed Mechanism of Photoredox/Ni Dual Catalytic C(sp^3)−C(sp^2) Cross-Coupling[20]



fluorophores are sufficiently oxidative ($E_{1/2}(*P/P^-)$ = +1.10 ∼ + 1.41 V) to obtain an electron from the amino acid *N-tert*-butoxycarbonyl-proline (*N*-Boc-pro, $E_{1/2}^{red}$ = +0.95 V[23]) to generate the C(sp^3) radical, which is supported by a Stern−Volmer fluorescence quenching experiment between 4CzIPN and *N*-Boc-pro (in the form of its cesium salt, Figure S10). Encouraged by this result, we conducted the coupling reaction of *N*-Boc-pro with methyl 4-iodobenzoate in a reaction mixture consisting photocatalyst, bench stable $NiCl_2$·DME (DME = dimethoxyethane), bpy ligand (bpy = 2,2′-bipyridine), and Cs_2CO_3 under irradiation from a 26W white CFL (compact fluorescence lamp). This reaction is highly sensitive to the photoredox catalyst (Table 1 and Supporting Information, Table S2 and S4). Many common transition metal complexes (e.g., $[Ru(bpy)_3]^{2+}$ and $[Ru(bpz)_3]^{2+}$ (bpz = 2,2′-bipyrazine)) and organic dyes (e.g., eosin Y, Rose Bengal, methylene blue, and Acr^+-Mes) showed no activity (Table S4), likely due to

Table 1. Screening of Photocatalysts for Photoredox/Ni-Catalyzed Decarboxylative Cross-Coupling



entry	photocatalyst	% yield[a]	% residual photocatalyst[b]
1	4CzIPN	85	58
2	4DPAIPN	87	78
3	2CzIPN	56	11
4	4CzPN	15	0
5	2CzPN	20	0
6	4CzTPN	12	0
7	2CzTPN	<5	0
8	DCA	0	0
9[c]	$[Ir[dF(CF_3)ppy]_2(dtbbpy)]^{+d}$	83	65

[a]Isolated yield. [b]Measured by HPLC. [c]24 h to complete the reaction. [d][dF(CF_3)ppy] = 2-(2,4-difluorophenyl)-5-trifluoromethyl-pyridine, dtbbpy =4,4′-di*tert*-butyl-2,2′-bipyridine.

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their inferior redox potentials (Table S1). The D−A fluorophores, however, promoted this reaction with a variety of efficiencies. In particular, 4CzIPN and 4DPAIPN exhibited the best catalytic activity with isolated product yields of 85% and 87%, respectively, and 2CzIPN gave a moderate yield of 56%. The other four CDCB D−A fluorophores were weakly effective (5−20% yields). To our surprise, despite its strong redox potentials ($E_{1/2}$(*P/P$^-$) = +2.06 V and $E_{1/2}$ (P/P$^-$) = −1.00 V),[8b] DCA appeared to be ineffective. In fact, to the best of our knowledge, there have been no reports using organic photocatalysts for photoredox/Ni dual catalytic C(sp^3)−C(sp^2) cross-coupling reactions before our study. When the reaction was carried out using a less powerful blue LED (465 nm) in the presence of 4CzIPN, 77% yield can be achieved (Table S2, entry 6).

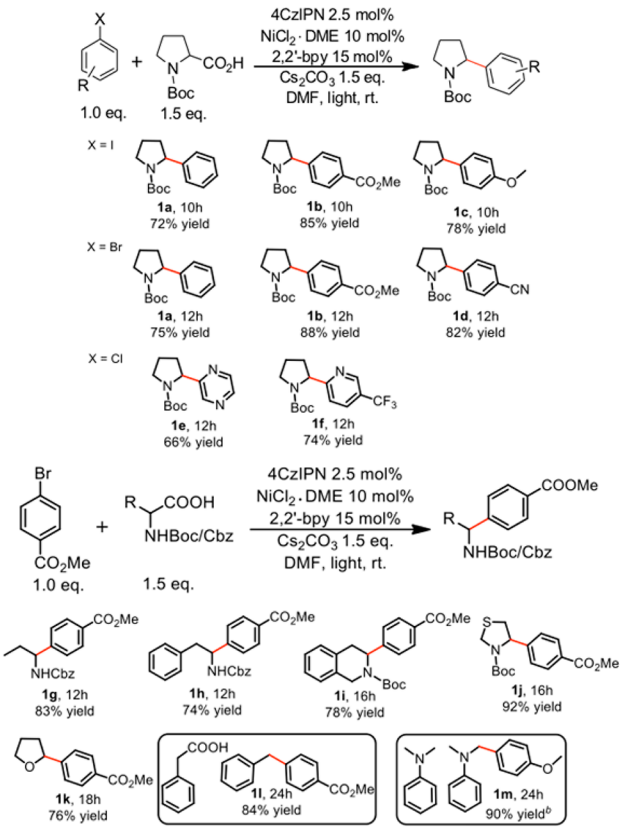
From a thermodynamic perspective, 4CzPN, 2CzPN, 4CzTPN, 2CzTPN, and DCA should favorably promote this coupling reaction. Thus, we tentatively attribute their low activities to the inferior stability under the reaction conditions. Indeed, the fluorescence spectra of the reaction mixture containing the four CDCB fluorophores exhibited a large blue shift (∼100 nm) of the emission maximum and the reaction solution containing DCA became nearly nonfluorescent (Figure S11). Moreover, HPLC analysis indicated that none of the four CDCB fluorophores and DCA can be recovered (entries 4−8, Table 1 and Supporting Information, S-8). On the other hand, 58%, 78%, and 11% of 4CzIPN, 4DPAIPN, and 2CzIPN, respectively, remained intact, which corresponds well with their product yields (entries 3−5, Table 1). Despite of its high activity, only 65% of [Ir[dF(CF$_3$)ppy]$_2$(dtbbpy)]$^+$ can be recovered (entry 9, Table 1).

To gain more insight into the drastic differences in catalytic efficiencies of the D−A fluorophores, we examined the effect of solvent on their photostability. The least active catalyst, 2CzTPN, was chosen for this study. UV−vis spectra of a deaerated solution of 2CzTPN (0.5 mM) before and after light irradiation (26 W CFL, 4h) showed that 2CzTPN is fairly stable in most common solvents except DMF (Figure S13). Further examination via UV−vis spectroscopy revealed that the photostability of the D−A fluorophores in DMF generally follows in the order of *meta* > *ortho* > *para* and tetrakiscarbazolyl > dicarbazolyl dicyanoarenes (Figure S12). DCA, with a *para*-dicyano structure and no carbazolyl-substitution, is extremely unstable: after 30 min irradiation, a significant decrease of absorption intensity accompanied by a blue shift (∼25 nm) was observed (Figure S12). Such photoinduced decomposition of cyanoarenes in DMF likely involves a nucleophilic substitution that can be inhibited in *meta*-dicyanoarenes and/or by bulky substitution groups.[24] Indeed, D−A fluorophores with these characteristics such as 4CzIPN and 4DPAIPN exhibit a significantly higher photostability in DMF (Figure S12). It should be emphasized here, however, that the inferior photostability of the D−A fluorophores based on *ortho*- or *para*-dicyanobenzene in DMF should not prevent their photocatalytic applications in other solvents.

Using 4CzIPN as the photoredox catalyst, we further optimized the Ni catalyst (Supporting Information, Table S3). No coupling product was detected in the absence of the ligand and the ligand's electronic effect is also significant.[19c,25] For example, 1,10-phenanthroline gave a comparably good yield (82%) as that of bpy; however, dtbbpy led to a significantly lower yield (30%), possibly due to the sluggish Ni^I reduction induced by electron-donating *tert*-butyl substituent. Moreover, bpy ligands with strong electron-donating (methoxy-) or strong electron-withdrawing (trifluoromethyl and methoxylcarbonyl) as well as the electron-deficient bpz ligand gave no coupling product.

With optimized photocatalyst (4CZIPN) and Ni catalyst (NiCl$_2$·DME + bpy), we tested the scope of the decarboxylative arylation reaction (Table 2). A wide range of electron-rich

Table 2. Photoredox/Ni-Catalyzed Decarboxylative Cross-Coupling of α-Amino Acids and Aryl Halides[a]



[a]Isolated yield. [b]NaOH was used as the base.

(methoxy, **1c**) and electron-deficient (methoxycarbonyl **1b**, cyano **1d**) aryl halides was suitable to this dual catalysis manifold (72−88%). Electron-deficient pyrazinyl (**1e**, 66%) and pyridinyl (**1f**, 74%) chlorides were also effective substrates. On the other hand, both *N*-Boc protected cyclic and *N*-benzyl carbamoyl (*N*-Cbz) protected acyclic α-amino acids (**1g**−**1j**) proved to be competent coupling partners. In particular, sulfur-containing *N*-Boc-4-thioproline was tolerant (**1j**, 92%), and no deactivation of the Ni catalyst was observed. Furthermore, decarboxylative arylation of tetrahydro-2-furoic acid and 2-phenylacetic acid proceeded smoothly forming the α-arylated ether (**1k**, 76%) and alkane (**1l**, 84%), respectively. Finally, 4CzIPN also exhibited an excellent activity for amine-based C(sp^3) precursors such as dimethylaniline (**1m**, 90%).

We next tested the photocatalytic activities of D−A fluorophores in the cross-coupling of alkyltrifluoroborates with aryl halides.[20a,d] Using the coupling of potassium benzyltrifluoroborate and methyl 4-bromobenzoate, we optimized the synthetic condition and found that a reaction consisting 4CzIPN as the photocatalyst, 2,2′-bpy and NiCl$_2$·DME as the metal catalyst in combination with 2,6-lutidine as

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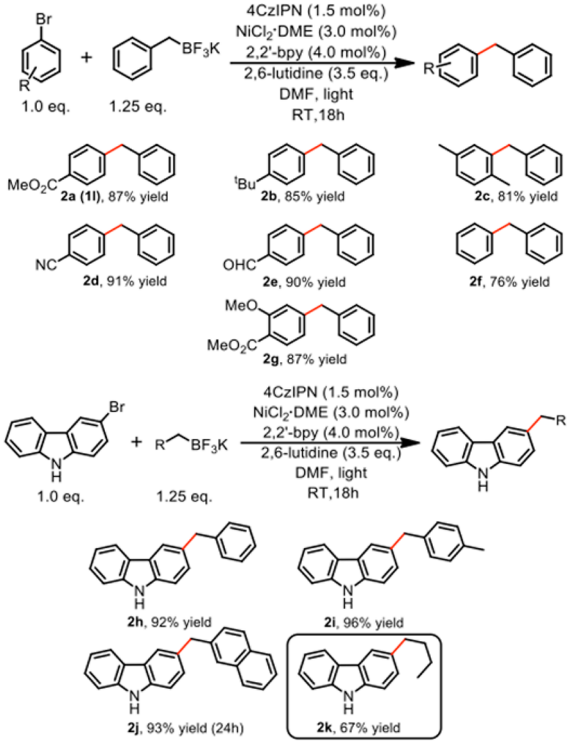
an additive proceeded smoothly with 87% yield of the coupling product (**2a** (also **1l**), Table 3). Compared to the previously

Table 3. Photoredox/Ni Dual-Catalyzed Cross-Coupling of Trifluoroborates and Aryl Bromides



reported reaction conditions,[20a] our procedure is simplified because it does not use highly air-sensitive $Ni(COD)_2$ (COD = 1,5-cyclooctadiene). Using a blue LED (465 nm) as the light source, an 86% yield was achieved (Table S5, entry 6). Other D−A fluorophores also effectively promote this reaction and give moderate to excellent yields (23% ∼ 91%) Table S6.

A range of structurally diverse aryl halides with various functional groups, including *tert*-butyl **2b**, methyl **2c**, cyano **2d**, and formyl **2e**, delivered the corresponding coupling products in good to excellent yield (81−91%). It is noteworthy that *ortho*-steric hindrance in **2c** was tolerated with no apparent decrease in yield. Additionally, the successful coupling between 3-bromo-9*H*-carbazole with benzylic trifluoroborate (**2h**, 92%) demonstrated the compatibility of this catalytic system with substrates containing active hydrogen functional groups. Further, the electronic effect of the benzylic trifluoroborate component is moderate considering that a slightly longer reaction time (24 h) was required to couple with 3-bromo-9*H*-carbazole (**2j**, 93%). Interestingly, propyl trifluoroborate can also be used as the $C(sp^3)$ radical precursor (**2k**, 67% yield), further manifesting the wider utility of 4CzIPN in direct functionalization of $C(sp^3)$−H bonds with aryl halides.

In conclusion, we have demonstrated that rationally designed donor−acceptor fluorophores can be used as highly efficient visible-light photoredox catalysts to promote organic transformations. Specifically, carbazolyl dicyanobenzene (CDCB) is a versatile platform to build D−A fluorophores with adjustable photoredox potentials by changing the number and position of carbazolyl and cyano groups on the center benzene ring. Due to their favorable photoredox potentials and excellent photostability in DMF, 4CzIPN exhibit a remarkable activity toward the energetically demanding photoredox/Ni dual catalytic $C(sp^3)$−$C(sp^2)$ cross-coupling of α-amino acids/alkyltrifluoroborates with aryl halides. The concept of D−A fluorophores can certainly be used to design other new metal-free photoredox catalysts, and this work validates its wide utility in visible-light-promoted organic synthesis.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acscatal.5b02204.

Materials, general procedures, synthesis, the cost calculations for D−A fluorophores, physical measurements, spectroscopic characterizations, CV diagrams, NMR spectra, and HPLC measurements (PDF)

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Notes

The authors declare no competing financial interest.

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