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Unusual Solid-State Luminescent Push−Pull Indolones: A General One-Pot Three-component Approach

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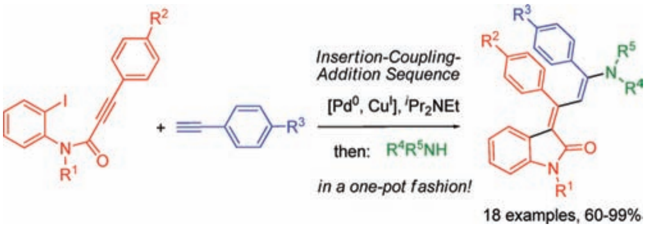
ABSTRACT



In a consecutive three-component cyclocarbopalladation, Sonogashira coupling, Michael addition sequence 4-aminopropenylidene indolones, i.e., terminally fixed push−pull chromophores, are obtained in yields as high as 99%. Most remarkable, however, is the pronounced orange red solid state fluorescence displaying large Stokes shifts of these merocyanines, in particular, since all chromophores are nonfluorescent in solution.

In recent years the productive concepts of multicomponent processes[1,2] and domino reactions[3,4] have considerably stimulated the synthetic scientific community. In particular, the combination of structural and functional diversity has initiated the quest of diversity oriented syntheses[5] with broad application in pharmaceutical lead discovery and development. However, with respect to functional π-electron systems, such as chromophores, fluorophores, and electrophores, required in molecule based electronics,[6] molecular photonics,[7] and biophysical analytics,[8] this approach is still quite novel.[9,10] However, in heterocyclic chemistry consecutive multicom-

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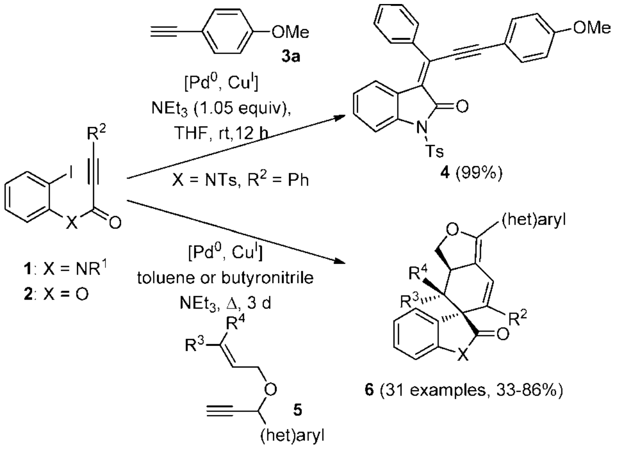
10.1021/ol101165m

ponent syntheses based upon transition metal catalysis,[11] such as the Pd/Cu-catalyzed generation of alkynones and alkenones, have paved the way to manifold classes of heterocycles.[12]

As early as 2000, we had developed a multicomponent method for the synthesis of chromophores[13] and fluorophores.[14] This was recently further extended by a domino insertion−coupling sequence of alkynoyl *o*-iodo anilides **1**,[15] or phenolates **2**, with *p*-anisyl acetylene (**3a**) or propargyl allyl ethers **5**, to give an enyne indolone **4** or highly fluorescent structurally rigidified butadienes **6** in a spirocyclic framework in good to excellent yields, displaying extraordinary large Stokes shifts and fluorescence quantum yields Φ_f as high as 62% (Scheme 1).[16] The latter spirocyclic lumophores **6** are formed in the sense of an insertion−coupling isomerization−Diels−Alder domino sequence, a quite general route to complex polycyclic frameworks that has recently found application in various domino sequences with other concluding pericyclic steps.[17]

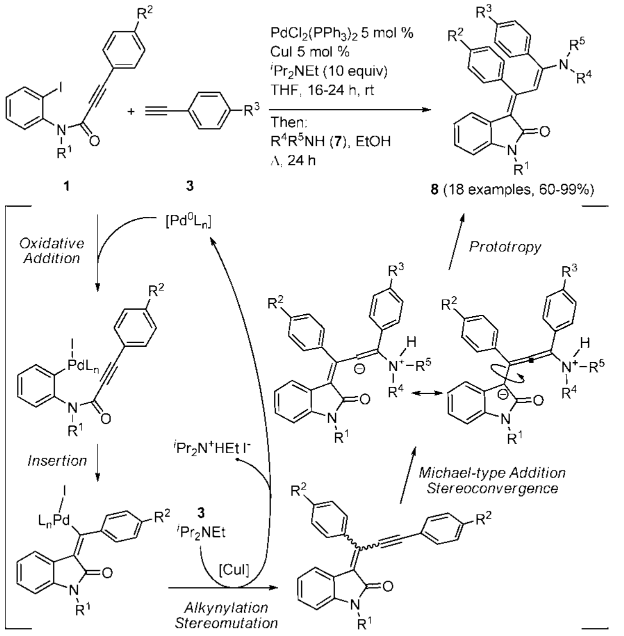
Scheme 1. Coupling of Alkynoyl *o*-Iodo Anilides **1** or Phenolates **2** with Terminal Alkynes **3** and Propargyl Allyl Ethers **5** Giving Rise to the Formation of Various Heterocycles in a Domino Fashion



Most interestingly the *Z*-configured enyne indolone **4**[18] represents a vinyl expanded ynamide and, therefore, Michael-type reactions can be conceived, eventually in a one-pot fashion as already successfully demonstrated with the three-component coupling-amine addition sequence to give enaminones.[19] Although Michael additions to ynones have been extensively studied, with the exception of a single example of an addition of diethyamine to a 2-fold acceptor-substituted enyne,[20] Michael-type additions have remained unexplored. Here, we communicate our findings on the three-component synthesis of push−pull butadienes on the basis of the indolone scaffold. Most remarkably, all representatives display intense orange to red luminescence in the solid state; however, surprisingly, in solution the same chromophores are completely nonemissive.

After reaction between alkynoyl *o*-iodo anilides **1** and terminal alkynes **3** at room temperature under Sonogashira conditions, the anticipated enyne indolones **4** (the reaction was monitored by TLC to ensure complete conversion) were not isolated but subsequently treated with ethanolic solutions of primary or secondary amines **7** at reflux to give 4-aminoprop-3-enylidene indolones **8** in good to excellent yields as crystalline solids with a bright orange red hue (Scheme 2, Table 1).[21] The structures of the 4-aminoprop-3-enylidene indolones **8** were unambiguously assigned by spectroscopic characterization and combustion analysis, and later corroborated by X-ray crystal structure analyses for compounds **8a**, **8k** (see the Supporting Information), and **8n** (Figure 1).[22]

Scheme 2. Three-Component Insertion−Coupling−Addition Synthesis of 4-Aminoprop-3-enylidene Indolones **8** and Mechanistic Rationale



This protocol shows a broad scope with respect to the electronic nature of the aryl substituents R² and R³ and the

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Table 1. Three-Component Synthesis of 4-Aminoprop-3-enylidene Indolones **8**

entry	*o*-iodo alkynylanilide **1**	alkyne **3**	amine **7**	4-aminoprop-3-enylidene indolones **8** (isolated yield)[a]
1	R^1 = Ac, R^2 = H (**1a**)	R^3 = OMe (**3a**)	R^4, R^5 = $(CH_2)_4$ (**7a**)	**8a** (89%)[b]
2	**1a**	**3a**	R^4, R^5 = $(CH_2CH_2)_2O$ (**7b**)	**8b** (60%)[b]
3	R^1 = Ac, R^2 = ^{t}Bu (**1b**)	R^3 = ^{t}Bu (**3b**)	**7a**	**8c** (97%)[b]
4	**1b**	**3b**	**7b**	**8d** (95%)[b]
5	**1a**	R^3 = CN (**3c**)	R^4 = ^{n}hexyl, R^5 = *p*-anisyl (**7c**)	**8e** (97%)
6	R^1 = Me, R^2 = H (**1c**)	**3a**	**7a**	**8f** (92%)
7	**1c**	R^3 = Cl (**3d**)	**7a**	**8g** (86%)
8	**1c**	**3a**	**7b**	**8h** (88%)
9	**1c**	**3d**	**7b**	**8i** (99%)
10	R^1 = SO_2Me, R^2 = OMe (**1d**)	**3d**	**7a**	**8j** (88%)
11	**1d**	**3c**	**7c**	**8k** (94%)
12	**1d**	**3a**	R^4 = H, R^5 = ^{i}propyl (**7d**)	**8*l*** (92%)
13	R^1 = SO_2Me, R^2 = Cl (**1e**)	R^3 = NO_2 (**3e**)	**7a**	**8m** (98%)
14	**1e**	**3a**	**7b**	**8n** (83%)
15	R^1 = SO_2Tol, R^2 = H (**1f**)	**3d**	**7a**	**8o** (87%)
16	**1f**	**3a**	**7b**	**8p** (80%)
17	**1f**	**3c**	**7c**	**8q** (95%)
18	**1f**	**3a**	**7d**	**8r** (93%)

[a] Reaction conditions: 1.00 equiv of alkynoyl *o*-iodo anilides **1** (0.1 M in THF), 1.10 equiv of terminal alkynes **3**, 0.05 equiv of $PdCl_2(PPh_3)_2$, 0.05 equiv of CuI, and 10.0 equiv of diisopropylethylamine; after stirring for 16−24 h at rt addition of 20.0 equiv of amine **7** (4 M in ethanol), heating to reflux temperature for 24 h in a sealed tube. [b] The acetyl group is cleaved, R^1 = H.

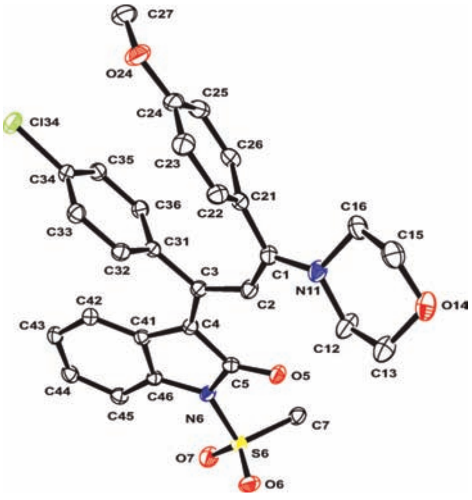

Figure 1. ORTEP plot of compound **8n** (hydrogen atoms are omitted for clarity).

cyclic, acyclic, primary, or secondary amine component. Moreover, the *E*,*E*-configured butadiene products **8** are formed with excellent diastereoselectivity. Interestingly, the insertion−coupling step occurs with stereomutation[18] and the Michael-type addition concludes in a stereoconvergent fashion as indicated by structural assignments from the crystallography and the occurrence of single sets of signals in all ^{13}C NMR spectra. Interestingly, when R^1 = Ac, this substituent is cleaved in the amine addition step, furnishing the 1*H* indolones **8a**−**d** (entries 1−4).

The 4-aminoprop-3-enylidene indolones **8** can be regarded as merocyanines or push−pull chromophores.[23] The longest wavelength absorption maxima are found between 446 and 488 nm (acetonitrile) and between 438 and 484 nm (THF) with significant extinction coefficients (Table 2 and Table SI-2 in the Supporting Information). A closer inspection reveals that the positive absorption solvochromicity is modest, indicating a relatively low polarity of the electronic ground state and a small charge transfer of S_0−S_1-transition character.[24] The electronic fine-tuning of the absorption maxima is achieved by the indolone *N*-substituent and by the terminal amino moiety.

Most interestingly, all merocyanines **8** are essentially nonfluorescent in solution. However, slightly red-shifted absorption maxima (492−502 nm) in the solid state spectra indicate J-aggregation[25] of the push−pull chromophores. Most remarkably the dyes **8** display intense orange red fluorescence with large Stokes shifts ($\Delta\nu \approx 2600$ cm^{-1}) and sharp emission maxima between 622 and 644 nm (Table 2, Figures 2 and 3). This effect is peculiar and apparently caused by packing and aggregation in the solid state. X-ray structure analyses reveal

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(18) The observed stereomutation deviates from the expected Pd-mediated *syn*-insertion of triple bonds, but the geometry has now unambigously been assigned by NOESY and the occurrence of a single set of signals in the ^{13}C NMR spectrum of compound **4**.

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Table 2. Electronic Spectral Data of Selected 4-Aminoprop-3-enylidene Indolones **8**[a]

entry	4-aminoprop-3-enylidene indolones **8**	$\lambda_{max,abs}$ [nm] (ε) in CH_3CN	$\lambda_{max,abs}$ [nm] (ε) in THF	$\lambda_{max,abs}$ [nm] film	$\lambda_{max,em}$ [nm] film
1	**8a**	456 (23200) 474 (21800 sh)	452 (12400)	472 sh 498	643
2	**8j**	458 (38900) 482 (47700)	464 (27500) 482 (28800)	473 sh 496	622
3	**8m**	480 (27800)	476 (14800)	494 470	639
4	**8n**	486 (34000)	474 (28600)	476 sh 502	644
5	**8r**	482 (45100)	478 (40100)	492	630

[a] Absorption Maxima in Solution and in the Solid State, and Emission Maxima in the Solid State.

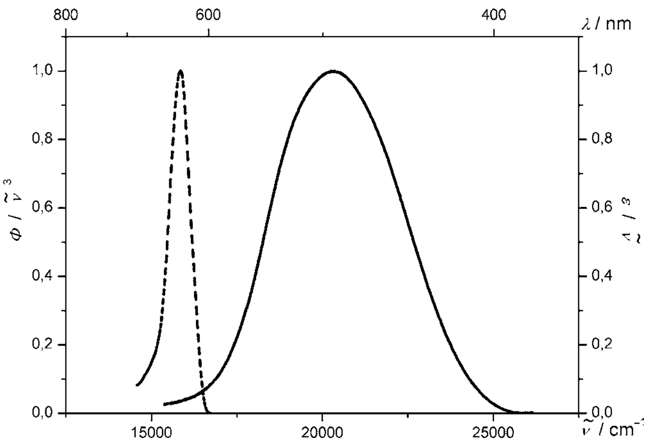

Figure 2. Normalized solid-state absorption (solid line) and emission spectra (dashed line) of compound **8r**.

that the coplanarity of the push−pull chromophore is stabilized by the parallel alignment of the aryl substituents (Figure 1) and short intermolecular distances between 3.96 to 5.08 Å in the crystal lattice (see the Supporting Information). The narrow red-shifted emission band (Figure 2) also accounts for aggregation induced emission[26] in the solid state and can be additionally rationlized by Davydov splitting.[27]

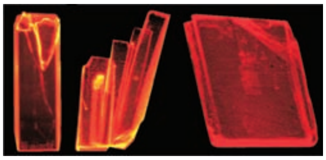

Figure 3. Photographs of solid-state fluorescent single crystals of the 4-aminoprop-3-enylidene indolones **8a** (left), **8m** (center), and **8n** (right) ($\lambda_{excitation}$ = 460 nm).

In conclusion we have disclosed a consecutive three-component insertion−coupling−addition sequence giving 4-aminoprop-3-enylidene indolones with a flexible substitution pattern in yields as high as 99%. Most remarkably, all representatives of these novel push−pull chromophores display intense solid-state fluorescence with large Stokes shifts, yet they are completely nonemissive in solution. Further studies addressing this unusual luminescence behavior by more detailed photophysical and computational investigations are currently underway.

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Supporting Information Available: Experimental details, NMR and selected solid state absorption and emission spectra of compounds **8**, and CIF files of compounds **8a**, **8k**, and **8n**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(21) **Typical procedure (8o):** In a flame-dried and nitrogen-flushed screw cap vessel, iodo phenylanilide **1e** (501 mg, 1.00 mmol) and alkyne **3d** (150 mg, 1.10 mmol) were dissolved in dry THF (10 mL). After degassing with a canula for 5 min diisopropylethylamine (1.7 mL, 10.0 mmol), $PdCl_2(PPh_3)_2$ (35.0 mg, 0.05 mmol), and CuI (10.0 mg, 0.05 mmol) were added to the reaction mixture. After stirring at rt for 16 h amine **7a** (1.6 mL, 20.0 mmol) dissolved in ethanol (5 mL) was added to the reaction mixture. Then the sealed reaction vessel was placed in a thermostat oil bath and heated to reflux temperature for 24 h. After cooling to rt the solvents were removed in vacuo and the residue was chromatographed on silica gel (hexanes/acetone 2:1) and crystallized from chloroform/pentane to give 506 mg (87%) of **8o** as a deep bright red solid: mp 248 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.80 (br, 2 H), 2.04 (br, 2 H), 2.40 (s, 3 H), 2.89 (br, 2 H), 3.71 (br, 2 H), 5.18 (d, $J = 7.7$ Hz, 1 H), 6.50 (dt, $J = 8.1$ Hz, $J = 0.9$ Hz, 1 H), 6.70 (m, 4 H), 6.86−6.92 (m, 3 H), 6.97 (m, 2 H), 7.10 (m, 1 H), 7.29 (d, $J = 8.0$ Hz, 2 H), 7.62 (s, 1 H), 7.87 (d, $J = 8.1$ Hz, 1 H), 8.03 (d, $J = 8.3$ Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.6 (CH_3), 25.2 (CH_2), 25.2 (CH_2), 49.9 (CH_2), 50.1 (CH_2), 104.5 (CH), 108.1 (C_{quat}), 112.3 (CH), 120.5 (CH), 122.7 (CH), 124.1 (CH), 126.7 (C_{quat}), 127.2 (CH), 127.6 (CH), 127.9 (CH), 128.2 (CH), 129.1 (CH), 129.5 (CH), 130.2 (CH), 133.9 (C_{quat}), 134.6 (C_{quat}), 134.9 (C_{quat}), 136.9 (C_{quat}), 139.5 (C_{quat}), 144.3 (C_{quat}), 160.5 (C_{quat}); HRMS calcd for $C_{34}H_{29}ClN_2O_3S$ 580.1587, found 580.1577. Anal. Calcd for $C_{34}H_{29}ClN_2O_3S$ (581.1): C 70.27, H 5.03, N 4.82, S 5.52, Cl 6.10. Found: C 70.02, H 4.99, N 4.97, S 5.64, Cl 6.27.

(22) Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication nos. CCDC 778168 (**8a**), CCDC 778169 (**8k**), and CCDC 778170 (**8n**). Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (Fax: + 44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk).

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