

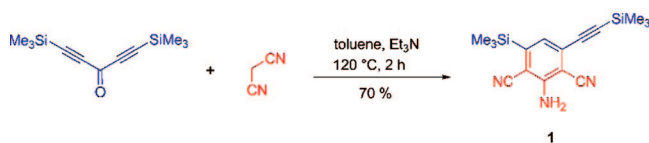
An Efficient and Facile Synthesis of Highly Substituted 2,6-Dicyanoanilines

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A one-pot procedure for the synthesis of substituted 2,6-dicyanoanilines starting from readily available yrones and malononitrile has been developed. For instance, penta-1,4-diyne-3-one is converted into the acetylene-substituted aniline derivative **1** in good yield. Upon photoexcitation, this chromophore shows a strong blue emission with a high quantum yield. The ground- and the excited-state geometries, charge distributions, and excitation energies of **1** have been evaluated by ab initio calculations.

Introduction

Multifunctionalized benzenes with electron donor (D) and/or acceptor (A) moieties such as 2,6-dicyanoaniline derivatives are of considerable interest; they are not only key constituents of a large number of bioactive compounds, both naturally and synthetically occurring,¹ but are also useful as versatile precursors for asymmetric syntheses,² as important substrates for nonlinear optical materials³ and molecular electronic devices.⁴ Thus, there is an ongoing effort in the exploration of efficient

methods for the synthesis of polysubstituted and functionalized benzenes starting from simple acyclic substrates, and a number of procedures have been developed with use of a variety of protocols.⁵ However, the control of both regio- and chemoselectivity remains a great challenge to organic chemists.⁶ Recently, Deng et al. reported on the one-pot tandem reaction of alkylidene malononitriles with nitroolefins in the presence of a base to yield polysubstituted benzenes.⁷

2,6-Dicyanoanilines are best prepared from 1-arylethylidene malononitrile and arylidene malononitrile and by a three-component reaction of aldehydes, ketones, and malononitrile.⁸ The reaction of malononitrile with α,β -unsaturated aldehydes or ketones is also reported to give 2,6-dicyanoanilines but the yields are low.⁹ To the best of our knowledge, although diversifications at positions C3, C4, and C5 of the 2,6-dicyanoaniline core have produced a large number of compound libraries,^{8–10} up to now there are no examples with the acetylenic functionality. This is presumably due to the lack of a suitable synthetic method since an alkynyl residue is expected to be problematic during the three-component coupling method as it opens many pathways for side reactions. Moreover, despite their attractiveness, only a few papers on the optical properties of 2,6-dicyanoanilines have been published so far.¹¹

We present here a facile way to prepare 2,6-dicyanoaniline derivatives **1–6** (Scheme 1) under mild reaction conditions from

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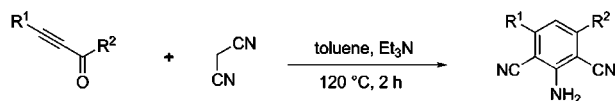
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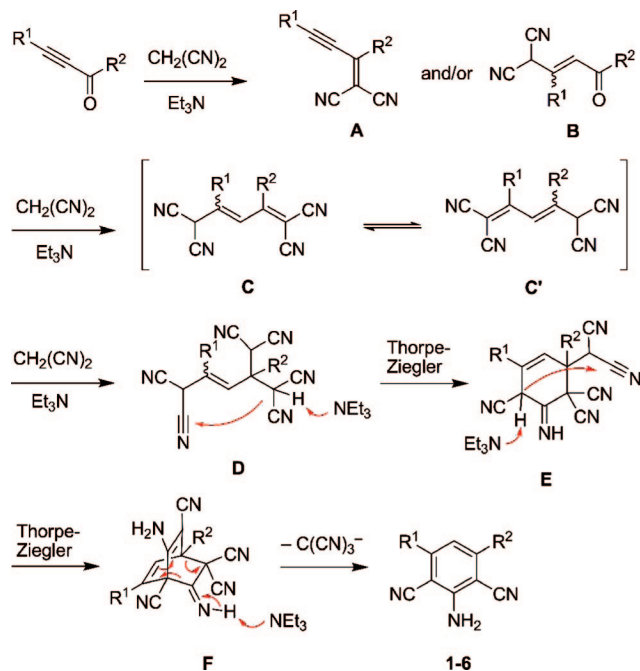
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SCHEME 1. Reactions of Ynone with Malononitrile



entry	R ¹	R ²	product	yield (%)
1	TMS	≡TMS	1	70
2	TMS	≡C(CH ₃)	2	32
3	Me	Ph	3	25
4	TMS	Me	4	63
5	Et	Me	5	61
6	TMS	H	6	16

SCHEME 2. Most Plausible Mechanism for the Formation of Substituted 2,6-Dicyanoanilines 1–6



the corresponding ynone and malononitrile. We report also the single-crystal X-ray structure analysis, the photophysical properties, and a theoretical investigation of the electronic structure of the 3-acetylenic-2,6-dicyanoaniline **1**.

The reaction of 1,5-bis(trimethylsilyl)penta-1,4-diyne-3-one¹² with 3 equiv of malononitrile in the presence of Et₃N (1 equiv) in refluxing toluene gives the tetrasubstituted aniline **1** in 70% yield (Scheme 1). This transformation under the same conditions has been tested with success on other ynone. The detailed experimental procedures and full spectroscopic characterizations of all new compounds are available in the Supporting Information.

A plausible reaction mechanism is depicted in Scheme 2. This mechanism is closely related to the one proposed by Victory et al. for the formation of 2,6-dicyanoanilines from enones and

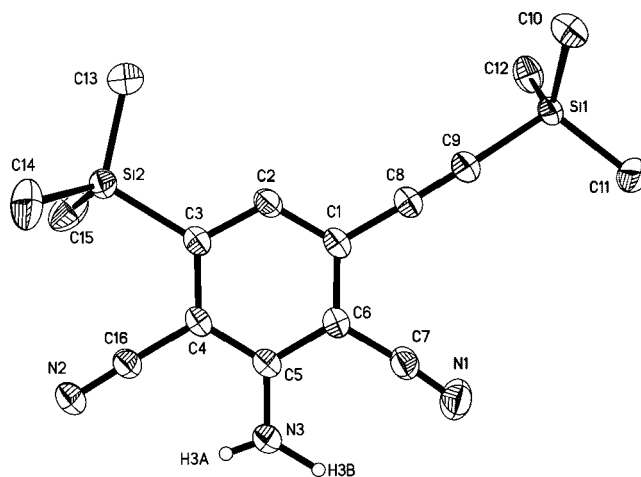


FIGURE 1. X-ray crystal structure of **1** (ORTEP, thermal ellipsoids set at the 50% probability level). Selected bond lengths [Å]: C1–C2 1.391(2), C2–C3 1.395(2), C3–C4 1.410(2), C4–C5 1.409(2), C5–C6 1.414(2), C6–C1 1.407(2), C1–C8 1.438(2), C8–C9 1.120(2), C9–Si1 1.853(1), C3–Si2 1.906(2), C5–N3 1.360(2), C7–N1 1.147(2), C16–N2 1.148(2). Hydrogen atoms are partially omitted for clarity.

malononitrile.^{10c} The first step of this process involves either a Knoevenagel condensation leading to the alkyldenemalononitrile **A**,¹³ or a conjugate addition leading to **B**. Reaction of **A** or **B** with a second equivalent of malononitrile affords the tautomeric intermediates **C** and **C'** that could undergo a second conjugate addition with a third molecule of malononitrile leading to **D**. Two consecutive Thorpe–Ziegler cyclizations afford intermediates **E** and **F**. Finally, intermediate **F** is unstable under basic conditions and evolves to **1–6** by a fragmentation process with elimination of the 1,1,1-tricyanomethyl anion. This mechanism is supported by the fact that best yields are obtained when at least 3 equiv of malononitrile are used.

Interestingly, the enone method according to Victory's mechanism gives a cyclohexadiene intermediate that has to be oxidized, presumably by air, to afford a stable aromatic derivative. In contrast to that method, the ynone method leads directly to an aromatic derivative. This may explain why it takes place under mild conditions and is high yielding.

Rod-like crystals of **1** were obtained by slow evaporation of a dichloromethane solution. The compound crystallizes in the triclinic crystal system, space group *P*1̄, with one molecule per asymmetric unit (Figure 1). With the exception of the methyl groups, the molecule is planar; the largest deviation from the least-squares plane (from all non-methyl atoms) is 0.164(1) Å for atom Si1.

In the crystal structure of **1**, two molecules related by an inversion center are arranged in close proximity to each other, so that they form a pair of N–H⋯NC hydrogen bonds (see the Supporting Information). Due to the bulky trimethylsilyl groups in meta-positions, the structure lacks π -stacking interactions.

The chromophore **1** strongly absorbs in the violet as evidenced by its yellow color. The UV–vis spectrum recorded in dichloromethane shows strong absorption bands around 370 nm and between 300 and 200 nm with extinction coefficients ϵ in the order of 1×10^4 to 4×10^4 L mol⁻¹ cm⁻¹ (Figure 2). Upon UV excitation, the chromophore shows an intense blue

(13) It has been demonstrated that the reaction of the corresponding vinyl malononitrile with malononitrile in CH₂Cl₂ in the presence of triethylamine gave **1** in 55% yield.

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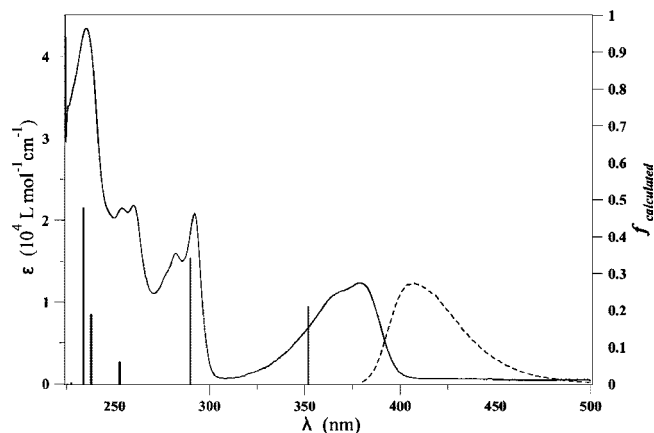


FIGURE 2. Electronic absorption (solid line) and emission fluorescence (dash line) spectra of **1** in deaerated dichloromethane solution; $\lambda_{\text{ex}} = 365$ nm, $\lambda_{\text{em}} = 405$ nm, at room temperature, together with the calculated oscillator strength.

fluorescence with emission maximum at 405 nm and a high quantum yield of 25% (using 9,10-diphenylanthracene as standard) while the Stokes shift amounts to 1900 cm^{-1} . Furthermore, the fluorescence–excitation spectrum (measured at 430 nm emission wavelength) agrees well with the corresponding absorption profile. The photophysical properties and high fluorescence quantum yield are in line with a recent study on dicyanoanilines.¹⁴ Compared to the 2,6-dicyanoaniline chromophore, both the absorption and emission of **1** are shifted about 20 nm to longer wavelengths.

To understand the ground- and excited-state electronic properties of chromophore **1**, density functional theory (DFT) as well as time-dependent DFT (TD-DFT) calculations were performed with the B3LYP functional and the TZVP (valence triple- ζ plus polarization) basis set, using the Turbomole 5.9 program.¹⁵ The minimum-energy geometry is calculated to have C_s symmetry and the central dicyanoaniline framework is planar in both ground and excited states. A planar geometry has previously been found for 2,6-dicyanoaniline itself and was rationalized by intramolecular hydrogen bonding between the amino and the cyano groups.¹⁶ We have checked this point (see the Supporting Information) by comparing the angles at the amino group in 2,6-dicyanoaniline to that in *p*-cyanoaniline (which has no N–H \cdots cyano contact). If the N lone pair donation into the electron-deficient 2,6-dicyano aromatic ring is the important mechanism, the amino group should be calculated planar or near-planar also in *p*-cyanoaniline. However, this is not the case. We conclude that the “side-on” N–H \cdots cyano hydrogen bonds are indeed responsible for the amino group planarity.

The vertical TD-DFT calculation predicts the $S_0 \rightarrow S_1$ excitation to be an intense ($f = 0.21$) $\pi \rightarrow \pi^*$ transition at 352 nm (3.52 eV) as shown with the stick spectrum in Figure 2. The transition is polarized within the molecular plane and approximately perpendicular to the amino substituent, in line with a benzenic 1L_b -type transition. Both the transition energy

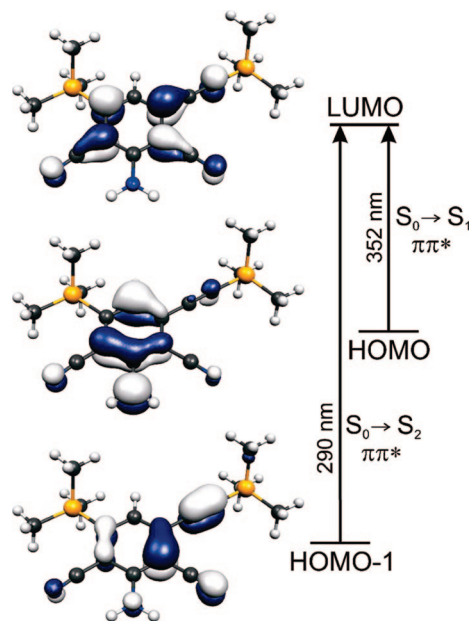


FIGURE 3. Molecular orbitals of **1** that are involved in the $S_0 \rightarrow S_1$ (HOMO to LUMO) and $S_0 \rightarrow S_2$ transitions (HOMO-1 to LUMO).

and intensity are in very good agreement with the longest-wavelength absorption (370 nm), for which the 320–410 nm energy-integrated absorption yields an oscillator strength $f = 0.16$. The $S_0 \rightarrow S_2$ excitation is predicted to be a $\pi \rightarrow \pi^*$ transition at 290 nm, with an oscillator strength of $f = 0.34$. This is in excellent agreement with the second UV absorption band observed at 291 nm with intensity similar to the $S_0 \rightarrow S_1$ band. The transition is polarized along the direction of the acetylene substituent.

According to the TD-DFT calculation, the $S_0 \rightarrow S_1$ electronic excitation is dominated by the HOMO \rightarrow LUMO contribution (93%). As Figure 3 shows, this corresponds partially to a π -electron flow from the amino N atom toward the benzene ring, where electron density spreads toward the two cyano and the acetylene substituents. The small Stokes shift indicates that the emission occurs from the locally excited S_1 $\pi \rightarrow \pi^*$ state. Adiabatic excited-state relaxation to a twisted intramolecular charge-transfer (TICT) state (as is characteristic for the TICT states of *m*- and *p*-cyanoanilines) is absent in this compound. The $S_0 \rightarrow S_2$ transition is dominated by the one-electron excitation from HOMO-1 to the LUMO (90%). This transition moves π -electron density from the C \equiv C bonding π orbital into the benzene ring.

In our study we developed a convenient and brief synthetic route to polysubstituted benzenes, highly functionalized with an amino group flanked by two carbonitrile substituents, and particularly in the cases of **1** and **2**, with ethynyl groups. Remarkably, this efficient one-pot procedure provides a new and straightforward entry to the regioselective formation of polysubstituted benzenes. Moreover, it is noteworthy that **1** has a promising topology and functionality as a useful substrate for Sonogashira coupling reactions and conjugate additions,¹⁷ thereby further generating molecular diversity and functionality.

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Experimental Section

General Procedure for the Preparation of 1–6. A mixture of the respective ynone (0.5 mmol), malononitrile (100 mg, 1.5 mmol), and triethylamine (50 mg, 0.5 mmol) in toluene (3.0 mL) was refluxed with stirring at 120 °C for 2 h. The solvent was removed under reduced pressure. Purification of the brownish oily residue by column chromatography on silica gel eluting with CH₂Cl₂ gave the desired compound as a light yellow solid.

Data for 2-Amino-4-(trimethylsilyl)-6-(trimethylsilylethynyl)isophthalonitrile (1) as an Example. Yield 110.5 mg (70%); mp 122–124 °C; ¹H NMR (300 MHz, CDCl₃) δ 6.97 (s, 1H), 5.15 (s, 2H), 0.41 (s, 9H), 0.30 (s, 9H); ¹³C NMR (75.5 MHz, CDCl₃) δ 152.93, 152.90, 131.81, 128.13, 118.34, 116.43, 107.34, 102.31, 102.20, 102.08, 1.22, 0.002; selected IR data (cm⁻¹, KBr pellet) 3479, 3362, 2959, 2924, 2218, 2160, 1735, 1637, 1538, 1403, 1253,

1062, 946, 845, 759, 671; HRMS, ESI (positive) calcd for C₁₆H₂₁N₃NaSi₂ 334.1172, found 334.1171.

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Supporting Information Available: General experimental details and characterization data for the prepared compounds **1–6** as well as the precursors 6-methyl-1-(trimethylsilyl)hepta-6-en-1,4-diyn-3-ol (**2a**) and 6-methyl-1-(trimethylsilyl)hepta-6-en-1,4-diyn-3-one (**2b**); copies of the ¹H and ¹³C spectra of all new compounds; CIF file for **1** (CCDC 656928) as well as the crystal packing and computational studies of **1**. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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