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Synthesis of Triazene-Substituted Homoconjugated Push-Pull

Chromophores by Formal [2+2] Cycloadditions

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ABSTRACT. 1-(4-ethynylphenyl)-3,3-dialkyltriaz-1-enes, well-known building blocks for branched dendrimer syntheses, were utilized as a new type of electron-donor component in formal [2+2] cycloadditions. The click-type, atom-economic reactions proceed efficiently under ambient conditions without any catalyst. The resulting products are structurally interesting push-pull chromophores and were investigated in the context of optoelectronic properties using UV/Vis spectroscopy, NMR studies, and computational chemistry.

Keywords: homoconjugation; push-pull chromophores; [2+2] cycloaddition; triazenes

INTRODUCTION

The growing interest in conjugated materials in large industrial areas such as textiles and electronics has been encouraging scientists for many years to develop atomic-economic, efficient reactions.¹ Most of the synthetic methods used to access conjugated systems are insufficient since they involve demanding synthetic steps. Accordingly, the rapid access to complex conjugated structures using short and economic methods is the major necessity in the field.

The introduction of a fundamental research project arises at this point. One of the most important organic transformations satisfying these conditions is the cycloadditions.² The most well-known reaction in this area, Diels-Alder [4+2] cycloaddition, has entered the literature in the early 20th century with Otto Diels and Kurt Alder's pioneering study.^{2,3} In addition to Diels Alder cycloadditions, another commonly used method to access carbocyclic materials is the [2+2] cycloadditions.⁴ [2+2] cycloadditions do not usually occur under thermal conditions, unlike [4+2] cycloadditions. In order to initiate these valuable transformations, starting materials should be stimulated by ultraviolet and/or visible light. Whether cycloaddition reactions take place thermally or photochemically can be determined by the well-known Woodward-Hoffmann rules.⁵ There are very few but quite important literatures that do not comply with the Woodward-Hoffmann predictions. For example, Reinhoudt reported the synthesis of thiepin derivatives by the thermal [2+2] cycloaddition reaction of highly polarized alkynes and alkenes having opposite electron densities.⁶ The resulting high-energy butene intermediates rearranged into thiepin derivatives without being isolated at room temperature. The reactions of tetracyanoethene (TCNE) and 7,7,8,8-tetracyano-p-quinodimethane (TCNQ) with activated alkynes give non-planar

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push–pull systems through [2+2] cycloaddition/retroelectrocyclization cascade.⁷ The highly reactive cyclobutene intermediates cannot be isolated similar to the ones obserbed in the thiepin synthesis.⁶ Thermal [2+2] cycloaddition reactions have not been able to find a wide range of applications for years due to limited substrate diversity, low yields, and instability of products.⁸

However, serendipitous findings are important in chemistry.⁹ An example of this is Trofimov's unexpected discovery of a thermal [2+2] cycloaddition of DDQ with pyrrole substituted electron-rich alkynes.¹⁰ An unsuccessful attempt to use DDQ as an oxidizing agent provided pyrrole-substituted homoconjugated [2+2] cycloadducts. At about the same time that Trofimov's work was published, Diederich and his group also reported a study on the reaction of DDQ with dialkylanilino (DAA)-substituted electron-rich alkynes.¹¹ Another important contribution of this study is the use of synthesized [2+2] cycloadducts in nonlinear optical applications.¹¹ Later, Trofimov,¹² Diederich,¹³ Shoji,¹⁴ and Swager¹⁵ groups have published a number of studies on the various alkyne derivatives which can be used in thermal [2+2] cycloaddition reactions. Results in those reports showed that the adducts produced in the cycloadditions of endocyclic double bonds were not suitable to undergo further retroelectrocyclization step.

Despite all the efforts on [2+2] cycloadditions, the limitation of this strategy, the poor substrate scope is still valid. The electron-rich alkyne derivatives used in these studies are limited to ferrocene, indole, azulene, and dialkylanilino-substituted substrates. Another issue is that electron-rich alkynes are generally very reactive and therefore difficult to maintain under ambient conditions. Our aim in this study was to

prepare a new type of stable electron-donor material that can undergo click-type [2+2] cycloaddition, thereby eliminating all the aforementioned synthetic limitations in the literature. Historically electron-rich triazenes have been utilized in dendrimer chemistry to mask aryl iodide substrates for branched dendrimer synthesis.¹⁶ Another important field where triazenes found application is medicinal chemistry.¹⁷ However, little has been reported on the electron-donor capabilities of triazene systems in the literature. Recently, Severin and co-workers have reported that 1-alkynyl and 1-allenyl triazenes can be utilized in cycloaddition and isomerization-type transformations.¹⁸ They benefited from the reactions of lithium amides with nitrous oxide and alkynyl Grignard reagents while synthesizing 1-alkynyl triazenes.¹⁹ Armed with the previous studies, we aimed to investigate the reactivity of 1-(4-ethynylphenyl)-3,3-dialkyltriaz-1-enes in [2+2] cycloadditions with electron-deficient DDQ.

RESULTS AND DISCUSSION

The key alkyne substrates are designed considering several crucial points such as donor strength, reactivity, and solubility. The target triazene-functionalized substrates **4a–f** were obtained via simple-to-perform synthetic routes (Scheme 1).²⁰ The reaction sequence to access **4a–f** began with the preparation of iodobenzenes **2a–f** from commercially available 4-iodoaniline (**1**). Compounds **2a–f** were accessed by trapping the in situ formed diazonium salt from (**1**) with corresponding dialkylamines. Sonogashira cross-coupling of **2a–f** with an excess of ethynyltrimethylsilane afforded **3a–f**, which then underwent alkyne deprotection to give **4a–f** in yields 30–77%. The ¹H-NMR studies showed that alkyl signals are relatively broad compared to the rest of the peaks due to restricted free rotation around the N–N bond as observed in the earlier literature reports.²¹ Unfortunately, our attempts to prepare 1-(4-ethynylphenyl)-3,3-

diphenyl triaz-1-enes failed due to the insufficient nucleophilic character of the diphenylamine.



Scheme 1. Three-step synthesis of electron-rich alkynes 4a–f.

Expanding the scope of [2+2] cycloadditions is crucial to access homoconjugated push–pull dyes with enhanced electronic and optical properties. With this motivation, triazene-capped alkyne substrates **4a–f** were tested for their reactivities towards formal [2+2] cycloadditions. In this part of the study, DDQ is selected as an electron-poor olefin substrate although it is commonly known as an oxidizing agent for dehydrogenation reactions.²² The reason behind this selection is the electron accepting power of DDQ with its high reduction potential ($E_{red 1} = + 0.16$ V, cyclic voltammetry

data in CH₂Cl₂ against the Fc⁺/Fc couple).^{13b} Scheme 2 depicts the homoconjugated dyes (\pm)-**6a**–**f** that were obtained from alkynes **4a**–**f** in yields changing from 19% to 73% using formal [2+2] cycloadditions. The reason for low yield as in the case of compound (\pm)-**6c** is probably due to competing oxidation reactions as reported earlier for DDQ cycloadditions.^{13a,15} Additionally, we have not observed any correlation between the electron-donor strength of the 1-(4-ethynylphenyl)-3,3-dialkyltriaz-1-enes and the yields of the homoconjugated chromophores (\pm)-**6a**–**f**.



Scheme 2. Formal [2+2] Cycloadditions of Triazene-substituted Electron-rich Alkynes with DDQ.

To the best of our knowledge, there is no systematic study for the electron-donor capabilities of triazene systems in the literature. However, Weringa and Janssen have established electron-donation order for *N*-substituted aniline structures.²³ Isolated homoconjugated push–pull dyes (\pm)-**6a**–**f** are all dark-orange colored solids that are very stable under ambient conditions for weeks. Next, we sought to characterize the resulting products in the context of optoelectronic properties.

A key question is about the strength of the donor group: are the triazene-based donor group strong enough to initiate intramolecular charge transfer (ICT) to the acceptor CN moieties? In order to answer this question, we examined the absorption behavior of the homoconjugated dyes. It should also be noted that the efficiency of the electron delocalization is hindered due to a quaternary carbon atom in between electron-rich triazene groups and electron-poor CN groups. Almost all of the designed donor-acceptor (D–A)-type chromophore structures are planar to keep efficient π -conjugation.²⁴ There are only a few studies on the chromophore structures in which donor and acceptor groups are not parallel to each other.²⁵ These results make the non-linear homoconjugated chromophore architectures considerably more attractive.

UV/Vis spectroscopy provided solid evidence for the ICT behavior of the dark orange-colored homoconjugated chromophores at room temperature in dichloromethane. Compounds (\pm)-**6a**–**f** feature intramolecular charge-transfer bands of moderate intensity (ε values between 3100 and 3800 M⁻¹cm⁻¹, see Figure 1 for details): $\lambda_{max} = 440$ nm (2.82 eV, 3700 M⁻¹cm⁻¹, (\pm)-**6a**), 442 (2.81 eV, 3800 M⁻¹cm⁻¹, (\pm)-**6b**),

438 (2.83 eV, 3100 $M^{-1}cm^{-1}$, (±)-6c), 428 (2.90 eV, 3600 $M^{-1}cm^{-1}$, (±)-6d), 430 (2.88 eV, 3800 $M^{-1}cm^{-1}$, (±)-6e), and 448 (2.77 eV, 3500 $M^{-1}cm^{-1}$, (±)-6f).



Figure 1. UV/Vis spectra of homoconjugate chromophores (±)-**6a** (black line), (±)-**6b** (yellow line), (±)-**6c** (purple line), (±)-**6d** (blue line), (±)-**6e** (red line), and (±)-**6f** (green line) in CH₂Cl₂ at 298 K.

Cycloadducts (\pm)-**6a**–**f** shows positive solvatochromism which further supports ICT behavior (Figure S1 in the SI).²⁶ Less polar (e.g. toluene) solutions of chromophores (\pm)-**6a**–**f** are yellow and more polar solutions (e.g. dichloromethane) are dark orange. The corresponding bathochromic shift for low energy bands is approximately 25 nm. None of the chromophores are emissive in both solution and solid-state. After analyzing the ICT behavior of the homoconjugated chromophores in detail by experimental studies, the electronic properties of the cycloadducts were also

analyzed with the help of computational chemistry (Figure 2). HOMO and LUMO orbital depictions support ICT process involving transfer of electron density from electron-rich triazene groups to the CN groups, which confirms the donor nature of the proposed substrates with the HOMO is localized on the triazene unit while the LUMO is on the CN groups and electron-deficient dichloro-dicyano-substituted cyclohexenedione structure.



Figure 2. HOMO-LUMO orbital depictions of (\pm) -6a.

Optimized molecular structure of the triazene-substituted dyes (\pm)-**6a**–**f** were obtained at the B3LYP/6-31G(d)²⁷ level of theory with the CPCM solvation model in CH₂Cl₂. The vertical optical transitions were calculated by time-dependent density functional theory (TD-DFT) at the CAM-B3LYP/6-31G(d) level of theory, again with the CPCM solvation model in CH₂Cl₂ using the software package Gaussian 09.²⁸ The lowest-energy transitions are mostly composed of HOMO to LUMO excitations and observed in the region of 500 nm. The computed transition energies are in good agreement with the experimental values (Tables S1–S6 in the SI). These values are consistent with the values computed for the known substances in the literature.^{13,29–31} Figure 3 depicts the calculated and experimental UV/Vis spectra for the selected homoconjugated dye (\pm)-**6a**. Although the computational results are slightly off for the

high energy absorption bands, the results for the low energy ICT band is remarkable with only 3 nm difference.



Figure 3. Calculated (not shifted, scaled by 0.6, red line) TD-DFT:CAM-B3LYP/6-31G* level of theory in CH₂Cl₂ and experimental (blue line) UV/Vis absorption spectrum of (\pm) -**6a**.

CONCLUSION

In summary, we reported an elegant, one-step synthesis of triazene-substituted structurally complex homoconjugated push–pull chromophores starting from easily accessible and stable 1-(4-ethynylphenyl)-3,3-dialkyltriaz-1-enes. The electron-rich 1- (4-ethynylphenyl)-3,3-dialkyltriaz-1-enes were used for the first time in the activation of [2+2] cycloaddition transformations. The reported [2+2] cycloadditions occurred under ambient conditions without any catalyst loading. The flexibility of the selected method allowed for the easy variation of triazene substituents and rapid access to new push–pull systems. Optoelectronic properties of the chromophores were investigated in

detail by UV/Vis studies. All homoconjugated dyes featured intramolecular chargetransfer and positive solvatochromism which confirmed intramolecular charge transfer behavior of the chromophores. Electronic/optical properties of the reported cycloadducts were also investigated using computational chemistry. Theoretical calculations indicated that target triazene-substituted alkynes are highly efficient donor structures. This work expands the scope of formal [2+2] cycloadditions. Posttransformations of the reported dyes to generate molecules with extended conjugation, as well as optoelectronic device applications, are now being further investigated.

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DEDICATION

This paper is dedicated to Prof. François Diederich on the occasion of his retirement.

REFERENCES

- (1) (a) Trost, B. M. Angew. Chem. Int. Ed. Engl. 1995, 34, 259–281. (b) Kolb, H. C.;
 Finn, M. G.; Sharpless, K. B. Angew. Chem. Int. Ed. 2001, 40, 2004–2021.
- (2) Nicolaou, K. C.; Snyder, S. A.; Montagnon, T.; Vassilikogiannakis, G. Angew. Chem. Int. Ed. 2002, 41, 1668–1698.
- (3) Diels, O.; Alder, K. Justus Liebigs Ann. Chem. 1928, 460, 98–122.
- (4) Rabinovich, D.; Schmidt, G. M. J. J. Chem. Soc. B 1967, 144-149.

- (5) Woodward, R. B.; Hoffmann, R. Angew. Chem. Int. Ed. Engl. 1969, 8, 781-853.
- (6) Reinhoudt, D. N.; Kouwenhoven, C. G. Tetrahedron 1974, 30, 2093-2098.
- (7) (a) Kivala, M.; Diederich, F. Acc. Chem. Res. 2009, 42, 235–248. (b) Kato, S.-i.; Diederich, F. Chem. Commun. 2010, 46, 1994–2006. (c) Misra, R.; Maragani, R.; Gautam, P.; Mobin, S. M. Tetrahedron Letters 2014, 55, 7102–7105. (d) Misra, R.; Gautam, P. Org. Biomol. Chem. 2014, 12, 5448–5457. (e) Misra, R.; Gautam, P.; Maragani, R. Tetrahedron Letters 2015, 56, 1664–1666. (f) Michinobu, T.; Diederich, F. Angew. Chem. Int. Ed. 2018, 57, 3552–3577.
- (8) Reinhoudt, D. N. Adv. Heterocyc. Chem. 1977, 21, 253-321.
- (9) Bosenman, M. F. J. Creat. Behav. 1988, 22, 132-138.
- (10) Trofimov, B. A.; Sobenina, L. N.; Stepanova, Z. V.; Ushakov, I. A.; Sinegovskaya, L. M.; Vakul'skaya, T. I.; Mikhaleva, A. I. *Synthesis* 2010, *3*, 470–476.
- (11) Kato, S-i.; Beels, M. T. R.; La Porta, P.; Schweizer, W. B.; Boudon, C.; Gisselbrecht, J.-P.; Biaggio, I.; Diederich, F. Angew. Chem. Int. Ed. 2010, 49, 6207–6211.
- (12) (a) Trofimov, B. A.; Sobenina, L. N.; Stepanova, Z. V.; Ushakov, I. A.; Mikhaleva, A. I.; Tomilin, D. N.; Kazheva, O. N.; Alexandrov, G. G.; Chekhlov, A. N.; Dyachenko, O. A. *Tetrahedron Lett.* 2010, *51*, 5028–5031. (b) Sobenina, L. N.; Stepanova, Z. V.; Ushakov, I. A.; Mikhaleva, A. I.; Tomilin, D. N.; Kazheva, O. N.; Alexandrov, G. G.; Dyachenko, O. A.; Trofimov, B. A. *Tetrahedron*, 2011, *67*, 4832–4837.
- (13) (a) Dengiz, C.; Dumele, D.; Kato, S-i.; Zalibera, M.; Cias, P.; Schweizer, W. B.;
 Boudon, C.; Gisselbrecht, J.-P.; Gescheidt, G.; Diederich, F. *Chem. Eur. J.* 2014,

20, 1279–1286. (b) Dengiz, C.; Prange, C.; Gawel, P.; Trapp, N.; Ruhlmann, L.; Boudon, C.; Diederich, F. *Tetrahedron* **2016**, *72*, 1213–1224.

- (14) (a) Shoji, T.; Maruyama, M.; Shimomura, E.; Akifumi, M.; Ito, S.; Yasunami, M.; Higashi, J.; Toyota, K.; Morita, N. *Heterocycles* 2014, *88*, 319–329. (b) Shoji, T.; Higashi, J.; Ito, S.; Yasunami, M.; Morita, N. *Heterocycles* 2011, *83*, 2271–2274.
- (15) Dengiz, C.; Swager, T. M. Synlett 2017, 28, 1427–1431.
- (16) (a) Moore, J. S.; Xu, Z. *Macromolecules* 1991, *24*, 5893–5894. (b) Pesak, D. J.;
 Moore, J. S. Macromolecules 1997, *30*, 6467–6482.
- (17) (a) Marchesi, F.; Turriziani, M.; Tortorelli, G.; Avvisati, G.; Torino, F.; De Vecchis, L. *Pharmacol. Res.* 2007, *56*, 275–287. (b) Newell, D. R.; Foster, B. J.; Carmichael, J.; Harris, A. L.; Jenns, K.; Gumbrell, L. A.; Calvert, A. H.; Triazenes: Chemical, Biological and Clinical Aspects, Springer, Berlin, Heidelberg, 1990, pp.119–131.
- (18) (a) Perrin, F. G.; Kiefer, G.; Jeanbourguin, L.; Racine, S.; Perrotta, D.; Waser, J.; Scopelliti, R.; Severin, K. *Angew. Chem. Int. Ed.* 2015, *54*, 13393–13396. (b) Jeanbourguin, L.; Scopelliti, R.; Tirani, F. F.; Severin, K. *Org. Lett.* 2017, *19*, 2070–2073. (c) Suleymanov, A. A.; Scopelliti, R.; Tirani, F. F.; Severin, K. *Org. Lett.* 2018, *20*, 3323–3326.
- (19) Kiefer, G.; Riedel, T.; Dyson, P. J.; Scopelliti, R.; Severin, K. Angew. Chem. Int.
 Ed. 2015, 54, 302–305.
- (20) Block, M. A. B.; Hecht, S. *Macromolecules* **2008**, *41*, 3219–3227.
- (21) Zarei, A.; Khazdooz, L.; Aghaei, H.; Azizi, G.; Chermahini, A. N.; Hajipour, A.
 R. *Dyes Pigm.* 2014, *101*, 295–302.
- (22) Walker, D.; Hiebert, J. D. Chem. Rev. 1967, 67, 153–195.
- (23) Weringa, W. D.; Janssen, M. J. Rec. Trav. Chim. Pays-Bas 1968, 87, 1372–1380.

- (24) (a) Yamashita, Y.; Tomura, M. J. Mater. Chem. 1998, 8, 1933–1944. (b) Meier,
 H. Angew. Chem. Int. Ed. 2005, 44, 2482–2506.
- (25) (a) Iwamura, H.; Makino, K. J. Chem. Soc. Chem. Commun. 1978, 720–721. (b)
 Yamamura, K.; Nakazawa, T.; Murata, I. Angew. Chem. Int. Ed. Engl. 1980, 19, 543
 –545. (c) Yamamura, K.; Nakasuji, K.; Yamochi, H.; Murata, I.; Yasuoka, N.;
 Kusunoki, M. Chem. Lett. 1986, 969–972. d) Gleiter, R.; Doerner, T.; Irngartinger,
 H. Liebigs Ann. 1996, 381–391. (e) Kim, Y.; Zhu, Z.; Swager, T. M. J. Am. Chem.
 Soc. 2004, 126, 452–453. (f) Cao, J.; Lu, H.-Y.; Chen, C.-F. Tetrahedron 2009, 65, 8104–8112.
- (26) (a) Bures, F.; Pytela, O.; Kivala, M.; Diederich, F. J. Phys. Org. Chem. 2011, 24, 274–281. (b) Solvents and Solvent Effects in Organic Chemistry, 4th ed.; Reichardt, C., Welton, T., Eds.; Wiley-VCH: Weinheim, Germany, 2010.
- (27) (a) Lee, C.; Yang, W.; Parr, R. G. Phys. Rev. B: Condens. Matter Mater. Phys.
 1988, 37, 785–789. (b) Becke, A. D. J. Chem. Phys. 1993, 98, 5648–5652.
- (28) Frisch, et al. Gaussian 09, D.01 ed.; Gaussian, Inc., Wallingford, CT, 2009. See the Supporting Information for full reference.
- (29) Jödicke, C. J.; Lüthi, H. P. J. Am. Chem. Soc. 2003, 125, 252-264.
- (30) Jödicke, C. J.; Lüthi, H. P. J. Chem. Phys. 2002, 117, 4146–4156.
- (31) Jacquemin, D.; Wathelet, V.; Perpéte, E. A.; Adamo, C. J. Chem. Theory Comput. 2009, 5, 2420–2435.

Graphical Abstract



-up to 73% isolated yield -mild, catalyst free, atom economic, click-type synthesis -regioselective [2+2] cycloaddition -triazene-substituted new donor substrate a synt ubstrate whether the synthesis of

HIGHLIGHTS

- This work expands the scope of formal [2+2] cycloadditions.
- The reported cycloadditions occur under ambient conditions without any catalyst.
- n d tria The flexibility of the method allowed for the easy variation of triazenes.