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The [2 + 2] Cycloaddition–Retroelectrocyclization and [4 + 2] Hetero-Diels–Alder Reactions of 2-(Dicyanomethylene)indan-1,3-dione with Electron-Rich Alkynes: Influence of Lewis Acids on Reactivity

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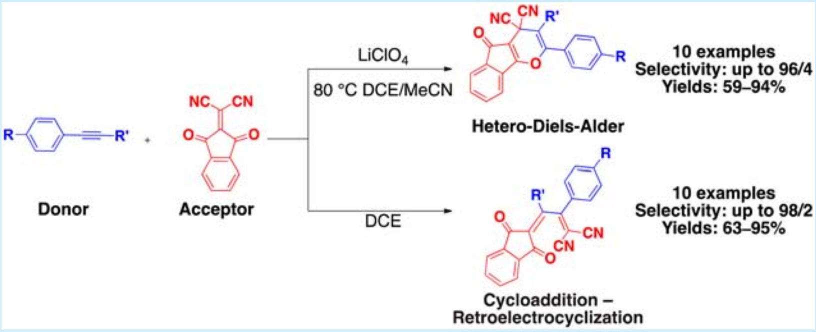
Ⓢ *Supporting Information*



ABSTRACT: The reaction of electrophilic 2-(dicyanomethylene)indan-1,3-dione (DCID) with substituted, electron-rich alkynes provides two classes of push–pull chromophores with interesting optoelectronic properties. The formal [2 + 2] cycloaddition–retroelectrocyclization reaction at the exocyclic double bond of DCID gives cyanobuta-1,3-dienes, and the formal [4 + 2] hetero-Diels–Alder (HDA) reaction at an enone moiety of DCID generates fused 4*H*-pyran heterocycles. Both products can be obtained in good yield and excellent selectivity by carefully tuning the reaction conditions; in particular, the use of Lewis acids dramatically enhances formation of the HDA adduct.

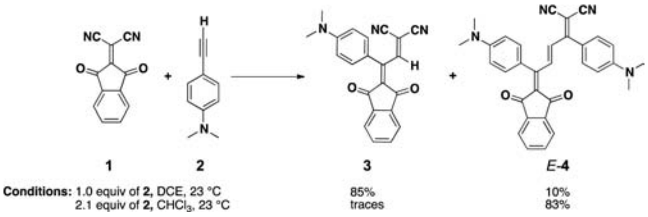
The formal [2 + 2] cycloaddition–retroelectrocyclization (CA–RE) reaction between electron-rich alkynes and electron-deficient olefins yielding push–pull-substituted buta-1,3-dienes is a versatile, well-studied transformation.[1] It is a "click"-type reaction[2] that is high yielding, atom-economic, requires no catalyst, proceeds under mild conditions, and exhibits excellent chemo- and regioselectivity. CA–RE reactions of electron-rich alkynes with electron-deficient alkenes, such as tetracyanoethene (TCNE),[3a] 7,7,8,8-tetracyano-*p*-quinodimethane (TCNQ),[3b] and others[1,3c–e] have been used as a convenient, robust method for preparing nonplanar, *π*-conjugated, donor–acceptor (D–A) chromophores that exhibit intense, low-energy, intramolecular charge-transfer (CT) bands. Some of them have found application in devices for all-optical switching.[4]

To this end, we became interested in 2-(dicyanomethylene)-indan-1,3-dione (DCID) **1** as an acceptor for the formation of new push–pull chromophores. DCID was first described in the literature in 1968,[5] but has received little attention as an electron acceptor because of its facile rearrangement to 2,3-dicyano-1,4-naphthoquinone upon chemical reduction.[6] DCID can be prepared in good yield as yellow, air-stable crystals by reaction of ninhydrin with malononitrile in water.[5]

Herein we show that DCID exhibits two modes of reactivity with electron-rich alkynes: the expected CA–RE reaction involving the dicyanovinyl moiety, and a previously unseen hetero-Diels–Alder (HDA) pathway. The properties of the resulting two classes of chromophores are reported.

In an initial experiment, the CA–RE reaction of **1** with 1 equiv of *N*,*N*-dimethylanilinoacetylene (DMA-acetylene) **2** afforded **3** (85% yield) as the major product and oligoene *E*-**4** as a minor product (10% yield) (Scheme 1). By mixing 2.1

Scheme 1. CA–RE Reaction of 1 with 2



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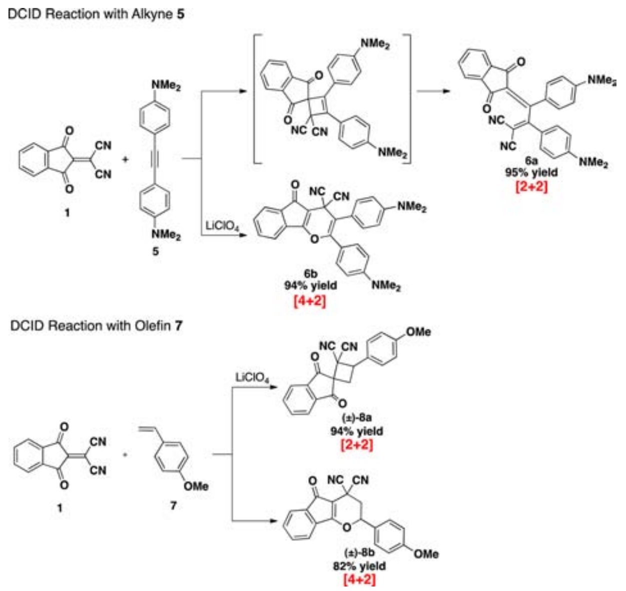
equiv of **2** with 1 equiv of DCID in $CHCl_3$, *E*-**4** was obtained in one pot in 83% yield. Only the *E*-isomer was observed, confirmed by X-ray analysis (Figure S1, Supporting Information (SI)), in accordance with our previous work.[7]

When DCID was reacted with bis-DMA-acetylene **5**, oligoene formation was suppressed and the expected CA−RE product **6a** was isolated as the major product (90% yield), along with the unexpected, fused 4*H*-pyran **6b** (10% yield), the product of an inverse electron demand HDA reaction (Scheme 2).[8] In view of the interest in 4*H*-pyran derivatives in natural products and biologically active compounds[9] as well as in optoelectronics,[10] we investigated ways to control the selectivity of this transformation to bias formation of 4*H*-pyran **6b**.[11]

Scheme 2. Differences in the Reactivity of Electron-Donating Olefins and Alkynes with DCID



Hall et al. studied the influence of Lewis acids, such as $ZnCl_2$ and $LiClO_4$, on the cycloaddition of cyano- and carbomethoxy-substituted olefins with donor-substituted alkenes.[12] In the absence of Lewis acids, the [4 + 2] HDA pathway to yield 3,4-dihydro-2*H*-pyrans was preferred, whereas Lewis acids promoted the [2 + 2] cycloaddition pathway. We observed the same selectivity in the transformation of DCID with 4-vinylanisole **7** (Scheme 2), yielding cyclobutane (±)-**8a** and dihydropyran (±)-**8b**.

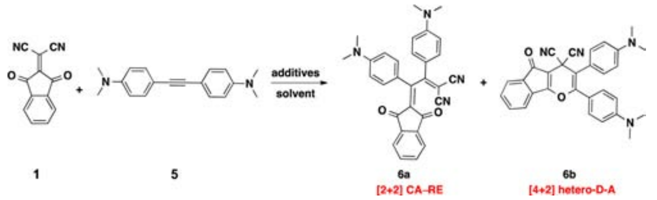
Intriguingly, Lewis acids have the opposite effect on DCID reactivity with donor-substituted alkynes. In this case, the addition of 1.0 equiv of different Lewis acids activates the enone moiety of DCID for the HDA reaction. We tested the efficiency of various Lewis acids to promote the HDA reaction of DCID with alkyne **5** (Table 1). The best selectivity (**6a**/**6b** = 5:95) was obtained with $LiClO_4$ in the presence of a mixed-solvent system at 80 °C (Table 1, entry 10). In the absence of Lewis acid, the CA−RE pathway dominates. Putative mechanisms for the formal [2 + 2] and [4 + 2] reactions of DCID with donor-substituted alkynes are presented in section S4 in the SI. There, the difference in the effect of Lewis acids on cycloadditions with donor-activated alkenes and alkynes is also briefly discussed.

With optimized conditions in hand, we evaluated the scope of the reaction with a series of different donor-substituted alkynes **9**−**21** (Table 2).

In general, good to excellent yields and chemoselectivities were obtained starting from anilino-substituted alkynes. The CA−RE transformation was consistently preferred in the absence of Lewis acid, providing buta-1,3-dienes **22a**−**30a**, while addition of $LiClO_4$ afforded 4*H*-pyrans **22b**−**30b** with excellent selectivity. In contrast, the use of alkynes with less activating donor substitutents, such as anisyl[7] or ferrocenyl,[13] led to no reaction. The reaction of DCID with asymmetric alkynes **20** and **21** gave mixtures of regioisomers that were inseparable by either chromatography or recrystallization.

The majority of the new products described herein were characterized by X-ray crystallographic analysis. Figure 1 shows

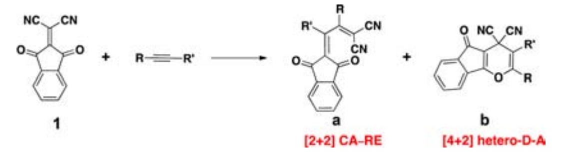
Table 1. Selected Results for the Chemoselectivity in the Reaction of DCID with Bis-DMA-acetylene

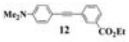
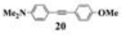


entry	additive	solvent	ratio[a]	yield (%) **6a**	yield (%) **6b**
1	–	DCM	75:25	75	25
2	–	MeCN	85:15	82	14
3	–	DCE	90:10	90	10
4	$TiCl_4$	DCE	28:72	27	70
5	$AlCl_3$	DCE	34:66	32	63
6	$BF_3{\cdot}Et_2O$	DCE	35:65	33	61
7	$ZnCl_2$	DCE	20:80	19	76
8	$LiClO_4$	DCE	14:86	14	86
9	$LiClO_4$	DCE	10:90[b]	10	90
10	$LiClO_4$	DCE/MeCN (98:2)	5:95[b]	5	95

[a] All reactions were conducted using 1.0 equiv of **1**, 1.05 equiv of **5**, and 1.0 equiv of additive on 0.15 mmol scale at 0.1 M concentration, 3 h at 25 °C. DCM = dichloromethane; DCE = 1,2-dichloroethane. Ratio and yield determined by ^1H NMR using dibromomethane as the internal standard. [b] Reaction conducted at 80 °C.

Table 2. CA–RE and HDA Reaction of DCID with Various Donor-Substituted Alkynes[a]



entry	donor	product	condition A ratio	condition A yield(%) **a**	condition A yield(%) **b**	condition B ratio	condition B yield(%) **a**	condition B yield(%) **b**
1	 **5**	**6a/6b**	95:5	95	5	5:95	5	94
2	 **9**	**22a/22b**	85:15	65	11	5:95	5	85
3	 **10**	**23a/23b**	80:20	76	18	13:87	13	87
4	 **11**	**24a/24b**	95:5	95	5	10:90	9	91
5	 **12**	**25a/25b**	94:6	70	4	5:95	3	66
6	 **13**	**26a/26b**	94:6	94	6	5:95	4	80
7	 **14**	**27a/27b**	94:6	85	5	4:96	4	81
8	 **15**	**28a/28b**	94:6	89	6	4:96	4	91
9	 **16**	**29a/29b**	90:10	63	7	8:92	6	59
10	 **17**	**30a/30b**	98:2	83	2	10:90	8	74
11	 **18**	-	-[b]	-	-	-[b]	-	-
12	 **19**	-	-[b]	-	-	-[b]	-	-
13	 **20**	-	-[c]	-	-	-[c]	-	-
14	 **21**	-	-[c]	-	-	-[c]	-	-

[a] Condition A: 1.05 equiv of alkyne and 1.0 equiv of **1** on 0.15 mmol scale in 0.1 M MeCN for 3 h at 25 °C. Condition B: 1.05 equiv of alkyne, 1.0 equiv of **1**, and 1.0 equiv of $LiClO_4$ on 0.15 mmol scale in 0.1 M DCE/MeCN 98:2 at 80 °C for 2 h. Fc = ferrocenyl. Ratios determined by yields of isolated compounds. [b] No reaction. [c] Regioisomers observed.

the crystal structures of **6a**, **23a**, **24b**, and **30b**. Crystallographic data are summarized in section S5 in the SI.

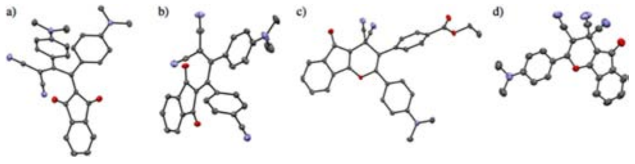


Figure 1. ORTEP representation of the molecular structures of CA–RE adducts **6a** (a) and **23a** (b) and HDA adducts **24b** (c) and **30b** (d). Thermal ellipsoids are shown at the 50% probability level. Hydrogen atoms not shown. *T* = 100 K.

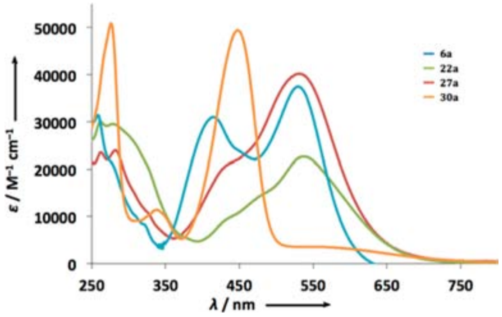


Figure 2. UV–vis spectra of selected CA–RE products in CH_2Cl_2 at 25 °C.

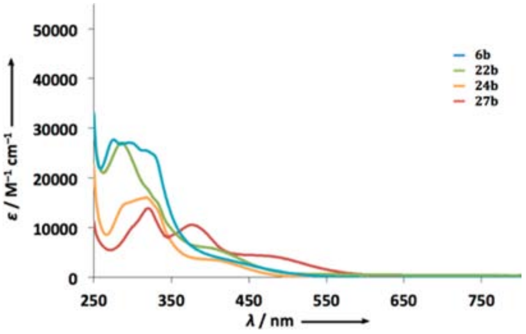


Figure 3. UV–vis spectra of selected HDA products in CH_2Cl_2 at 25 °C.

Figures 2 and 3 depict the UV–vis spectra of selected CA–RE and HDA products, recorded in CH_2Cl_2 at 25 °C. The CA–RE products feature intense intramolecular charge transfer (ICT) bands with λ_{max} values in the range of 450–545 nm (ε = 22500 to 49000 M^{-1} cm^{-1}). The ICT bands of the HDA products are hypsochromically shifted and less intense ($\lambda_{max} \approx$ 290–487 nm, ε = 10000–26000 M^{-1} cm^{-1}; see Figures S12 and S13 in the SI). The ICT nature of these bands was confirmed by protonation with CF_3COOH, leading to attenuation of the band, followed by neutralization with NEt_3, which reconstituted the initial transition (Figures S18–S49 in the SI)

The redox properties of compounds **3**, *E*-**4**, **6a/b**, and **22–30a/b** were studied by cyclic voltammetry (CV) and rotating-disc voltammetry (RDV) in CH_2Cl_2 + 0.1 M $n\mathrm{Bu}_4\mathrm{NPF}_6$. All potentials are given versus ferrocene, used as internal standard reference (for details, see section S9 in the SI).

By CV, compounds commonly exhibit one or two, usually reversible oxidation waves corresponding to the oxidation of the anilino moieties. At least two, mostly reversible reduction waves are observed, corresponding to the electron transfer to the extended DCID acceptor in the CA–RE products and the tricyclic acceptor moiety in the HDA products. The reduction of the CA–RE products is more facile, with $E^{o}_{red,1}$ occurring between −0.53 and −1.17 V, than the reduction of the HDA adducts, with $E^{o}_{red,1}$ occurring between −0.84 and −1.50 V. On the other hand, the HDA adducts ($E^{o}_{ox,1}$ between +0.34 and +0.78 V) are easier to oxidize than the CA–RE products ($E^{o}_{ox,1}$ between +0.63 and +0.88 V; Table S27). From the CV data (Tables S26 and S27 in the SI), we calculated a highest occupied–lowest unoccupied molecular orbital (HOMO–LUMO) energy gap of 1.80 and 1.84 eV for **26a** and **26b**, respectively, in agreement with the optical gaps obtained from the lowest-energy absorption maximum or the end-absorption in the UV–vis spectra (for the optical gaps of other chromophores, see Table S27 in the SI). Both CA–RE and HDA products feature positive solvatochromism (Figures S16 and S17).

The vertical optical transitions of the optimized structures of **3**, **4**, **6a–30a** and **6b–30b** were calculated by time-dependent density functional theory (TD-DFT) using the software package Gaussian 09 (see section S8 in the SI).[14] In all cases, the computed transition energies are slightly larger than the experimental values (Tables S12–S25 in the SI). Differences between computed excitation energies and experimental absorption maxima are in the range of 0.12–0.43 eV for **6a–30a** and in the range of 0.07–0.63 eV for **6b–30b**, well within the expected range for anilino-cyano-type push–pull chromophores.

In summary, DCID reacts with electron-rich anilinoalkynes in two different and useful ways. Depending on the reaction conditions, push–pull buta-1,3-dienes are obtained by the CA–RE reaction or tricyclic 4*H*-pyrans by the [4 + 2] HDA reaction. The presence of Lewis acids, such as $LiClO_4$, greatly enhances the formation of the HDA cycloaddition over the CA–RE reaction. This is the opposite to the effect of the Lewis acids on cycloadditions with electron-rich olefins. Optoelectronic applications and device applications of the new push–pull chromophores as well as the rapid construction of complex 4*H*-pyran derivatives are now being further investigated.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Synthesis, NMR spectra, X-ray crystallography details, CIF files, electrochemical data, UV–vis spectra, and DFT calculations. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.5b01598.

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Notes

The authors declare no competing financial interest.

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