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A practical system to synthesize the multiple-substituted 2,5-dihydrofuran by the intermolecular dipolar cycloaddition reactions involving acceptor/acceptor-substituted diazo reagents

Shifa Zhu *, Lijuan Chen, Chao Wang, Renxiao Liang, Xiujun Wang, Yanwei Ren, Huanfeng Jiang

School of Chemistry and Chemical Engineering, South China University of Technology, Guangzhou 510640, PR China

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ABSTRACT

A practical system for synthesizing the multiple-substituted 2,5-dihydrofuran through intermolecular dipolar cycloaddition reactions of acceptor/acceptor diazo reagents, aldehydes, and acetylenedicarboxylate was developed. The reactions proceeded effectively under ambient temperature with low reactant ratios. The control reactions revealed that there are two competitive paths: one forms 1,3-dioxolane and the other forms 2,5-dihydrofuran. These two paths could be controlled by modifying the steric hindrance of the diazo reagents.

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1. Introduction

Dipolar cycloadditions (DC) are powerful reactions to rapidly build structurally complex heterocycles. The typical multicomponent nature of DC reactions has been used frequently in drug discovery chemistry.[1] Metal-catalyzed DC reactions involving carbonyl ylides can generate stereochemically complex molecules from three simple starting materials.[2] The scope of such DC reactions is broad when carbonyl ylides are formed by intramolecular processes.[1c] In contrast, analogous three component intermolecular reactions involving aldehydes, diazo compounds, and dipolarophiles had been relatively limited in terms of selectivity and substrate ratios. Because of competing dioxolane formation, excess dipolarophiles are often needed to diminish the side reaction.[3,4] However, this reaction is still highly desirable in terms of green chemistry (the dinitrogen molecule N_2 is the only by-product) and atom economic considerations when the carbonyl ylides are formed from the aldehydes and diazo compounds.

Recently, Fox and co-workers have reported an unusually three-component DC reaction of the carbonyl ylides from α-alkyl diazo compounds. With dirhodium tetrapivalate (Rh_2Piv_4) as the catalyst, the reactions can proceed at −78 °C with the substrates ratio close to equimolar (aldehyde/diazo compound/dipolarophile=1.0:1.1:1.1).[5]

We are very interested in the reactions involving the acceptor/acceptor-substituted diazo compounds, such as diazomalonate, diazoacetoacetate, nitro diazoacetate, and cyano diazoacetate; because these diazo compounds still remain undeveloped comparing to acceptor-substituted and donor/acceptor-substituted diazo compounds in the field of metal catalyzed selective carbene transfer reactions due to their inherent low reactivities.[6]

2,5-Dihydrofurans are a class of commonly observed structural units in natural products and unnatural products with biological potential.[7] Although many new methods have been developed for the efficient synthesis of 2,5-dihydrofurans.[8] However, it is still challenging to selectively synthesize multi-substituted 2,5-dihydrofuran. It is obvious that transitional metal catalyzed three component DC reactions involving aldehydes, diazo compounds, and acetylenedicarboxylate is one of the most efficient and straightforward methods to construct the multi-substituted 2,5-dihydrofurans structure (Scheme 1). In this paper, we want to report a practical system to synthesize the multiple-substituted 2,5-dihydrofuran by the intermolecular DC reactions involving different acceptor/acceptor-substituted diazo reagents.

2. Results

Initially, the DC reaction of different acceptor/acceptor-substituted diazo compound with benzaldehyde and dimethyl acetylenedicarboxylate (dipolarophiles) catalyzed by $Rh_2(OAc)_4$

* Corresponding author. Tel.: +86 20 8711 2906; fax: +86 20 8711 3735; e-mail address: zhusf@scut.edu.cn (S. Zhu).

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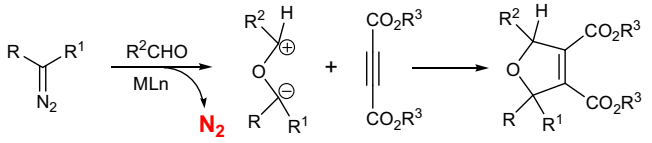
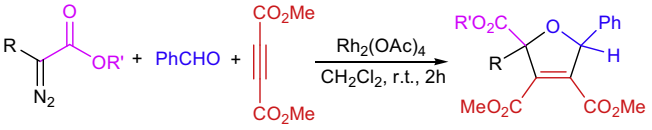


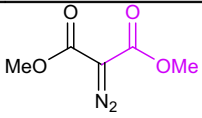
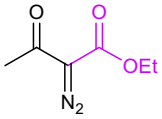
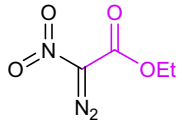
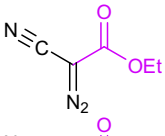
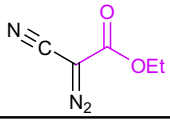
Scheme 1. The DC reactions of aldehydes, diazo compounds, and acetylenedicarboxylate.

was chosen as the model reaction. For practical purpose, the reactions were set at room temperature with aldehydes as limiting reagent; the substrates molar ratio of aldehyde/diazo/dipolarophile is 1.0:1.2:1.2, such low reaction temperature and substrates molar ratio for the acceptor/acceptor-substituted diazo compounds was never reported before. From the results listed in Table 1, diazo compounds **1a**–**4a** showed quite different activity in the DC reactions. For dimethyl diazomalonate **1a**, the desired dihydrofuran products **7a** could be formed in 41% isolated yield (Table 1, entry 1). Ethyl diazoacetoacetate **1b**, however, only trace amount of product **8a** was given (<5% by ^{1}H NMR) (entry 2). When nitro diazoacetate **1c** was used as the substrate, no any detectable amount of desired dihydrofuran product **9a** was observed, which could be attributed to the strong electron-withdrawing property of the $-NO_2$ group (entry 3). Unexpectedly, the cyano diazoacetate **1d** could furnish the desired product **10a** in 57% isolated yield, with cis/trans ratio being 67:33 (entry 4). When the reaction time was prolonged to 24 h, the yield of **10a** could be improved to 85% with the diastereoselectivity remaining unchanged (entry 5). It seems the reactivity order of these diazo compounds is **4a**>**1a**>**2a**>**3a**.

Table 1
The reactions of acceptor/acceptor diazo **1a**–**4a** with benzaldehyde **5a** and dimethyl acetylenedicarboxylate **6a**[a]

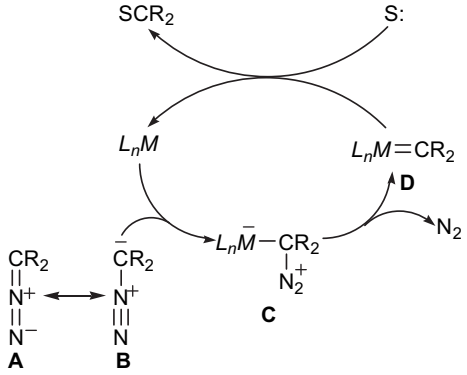


1a-4a **5a** **6a** **7-10**

Entry	Diazo compounds		Product	Yield[b]	dr[c]
1		**1a**	**7a**	41%	—
2		**2a**	**8a**	Trace[d]	—
3		**3a**	**9a**	ND[d]	—
4		**4a**	**10a**	57%	67:33
5[d]		**4a**	**10a**	85%	67:33

[a] [**5a**]=0.25 M, **5a**:(**1a**–**4a**):**6a**=1.0:1.2:1.2.
[b] Isolated yield.
[c] dr (cis/trans) was determined by ^{1}H NMR.
[d] The reaction time was 24 h.

To obtain a better understanding of the reactivity of diazo **1a**–**4a**, we turned our attentions to the theory calculation. As supposed from the reaction mechanism: the step **B**→**C** (the catalyst metal center was nucleophilically attacked by diazo carbon) and the step **C**→**D** (breaking the C–N_2 bond to release N_2 gas) were often believed to be the key steps for the reaction (Scheme 2).



Scheme 2. The proposed mechanism.

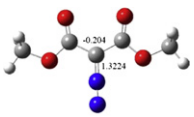
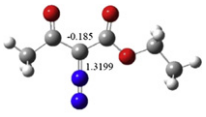
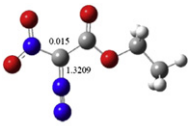
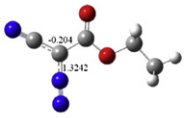
Natural bond orbital analysis provides an efficient method for investigating charge distribution in molecular systems.[9] The charge density of carbon atom and the C–N bond distance of the diazo moiety (C=N_2) could directly reflect the activities of the diazo compounds to some extent. The natural bonding orbital (NBO) population analysis of diazo carbon and the C–N bond distance (C=N_2) could be obtained by computer calculation using Gaussian software. The theoretical calculations were performed using the Gaussian 03 software package. The results are listed in Table 2.

The calculation results are well consistent with the trends found in Table 1. The NBO charge order is **4a**=**1a**<**2a**<<**3a**, which indicate the more negative of the diazo carbon, the more active of the diazo compound. The order of C–N bond distance is **4a**>**1a**>**2a**>**3a**, the longer C–N bond distance implies the easier happening the process of **C**→**D** (it also means that the nitrogen gas is more volatile in the intermediate **C**). Although C–N (**2a**) is a little bit larger than that of C–N (**3a**) by 0.0010 Å, however, the higher positive value of NBO charge (**3a**) dominates the reactivity expression in the catalytic process. Both the experimental results and calculation data supported that diazo **4a** is the most reactive diazo reagent. Therefore, cyano diazoacetates **4** were chosen as the diazo reagent for the model reaction to optimize the reaction conditions (Table 3).

As summarized in Table 3, the reaction is very sensitive to the solvents. DCM is the superior solvent for the reaction (Table 3, entry 1). Interestingly, **10a** was obtained only in 38% isolated yield without changing the diastereoselectivity when similar halogen solvent DCE was used (entry 2). Toluene and CH_3CN could be used as the solvents as well, although in relatively lower yields (entries 3, 4). With toluene being the solvent, the cis/trans ratio dropped to 52:48; with CH_3CN being the solvent, the cis/trans ratio increased to 77:23. When THF was used as the solvent, however, no desired product was detected; presumably the strong coordination capability of the oxygen atom in THF ring poisons the catalyst, which prohibited the reaction. In order to improve the diastereoselectivity of product, more bulky *tert*-butyl cyano diazoacetate (**4b**) was used for the reaction. It gave product **10a**′ in similar yield with the diastereoselectivity remaining unchanged (entry 6).

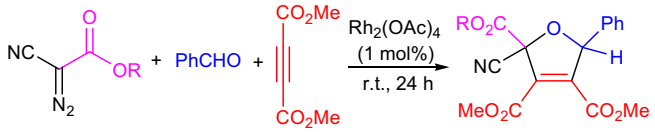
With the optimized reaction conditions in hand, the scope of the starting material was then investigated (Table 4). As summarized in the top part of Table 4, the yields of the products derived from aromatic aldehydes substituted by electron-withdrawing groups (**10c**, **10d**, and **10e**) are generally higher than electron-rich aromatic aldehydes (**10b**). The diastereoselectivities are generally moderate,

Table 2
The NBO charge and C–N bond distance data for **1a**–**4a**[a]

	 **1a**	 **2a**	 **3a**	 **4a**
NBO Charge	−0.204	−0.185	0.015	−0.204
C–N Bond distance	1.3224 Å	1.3199 Å	1.3209 Å	1.3242 Å

[a] The NBO charge and C–N bond distance were calculated by B3LYP/6-31+G(d) software.

Table 3
Optimization study[a]



4 **5a** **6a** **10**

Entry	R	Solvent	Product	Yield[b]	dr[c]
1	−Et (**4a**)	DCM	**10a**	85%	67:33
2	−Et (**4a**)	DCE	**10a**	38%	67:33
3	−Et (**4a**)	Toluene	**10a**	50%	52:48
4	−Et (**4a**)	CH_3CN	**10a**	45%	77:23
5	−Et (**4a**)	THF	**10a**	ND	—
6	$-Bu^t$ (**4b**)	DCM	**10a′**	89%	67:33

[a] The reaction was performed under N_2 atmosphere. [**5a**]=0.25 M, **5a**:**4**:**6a**=1.0:1.2:1.2.
[b] Isolated yield.
[c] dr (cis/trans) was determined by ^1H NMR.

ranging from 2:1 to 1:1. With the extremely electron-poor pentafluorobenzaldehyde (C_6F_5CHO) being the substrate, the desired product **10f** was formed with exceptional high diastereoselectivity (dr=95:5), albeit in a lower yield (32%). When cinnamaldehyde was used as the substrate, the desired product **10g** could be obtained in 60% yield. As for 2-furaldehyde, 21% of product **10h** could be formed. The unique bis-furan structure is interesting because it is often found in the natural products, biological, and medicinal molecules.

It's unusual that the yields derived from more bulky diazo reagent *tert*-butyl cyanodiazo-acetate (**4b**) (the bottom part of Table 4) are generally higher than those from the less bulky ethyl cyano diazoacetate (**4a**). For example, with pentafluorobenzaldehyde (C_6F_5CHO) as the substrate, the yield was enhanced from 32% (**10f**) to 69% (**10f′**); and with 2-furaldehyde as the substrate, the yield was increased from 21% (**10h**) to 31% (**10h′**). The electron-rich aldehydes, electron-poor aldehydes, α,β-unsaturated cinnamaldehyde, and the large 3,5-di-*tert*-butyl benzaldehyde all gave satisfactory yields of products. It's worth mentioning that the unprotected 4-hydroxyl benzaldehyde can also afford the corresponding 1,4-dihydrofuran **10l′** in 29% yield, which provided a direct way to synthesize the dihydrofuran with the unprotected −OH group. Furthermore, the aliphatic aldehyde (phenylpropyl aldehyde) furnished the desired 1,4-dihydrofuran **10m′** in lower yield (25%). When more bulky dipolarophiles, ethyl diethyl acetylenedicarboxylate **6b**, was used, the reaction proceeded efficiently as well (**10n′**). Mono-substituted alkyne, methyl propiolate, works for this reaction as well. It gave the corresponding product **10o′** in 46% yield.

To explore the reason why more bulky *tert*-butyl cyano diazoacetate **4b** gave more satisfactory yields of 1,4-dihydrofuran than less bulky ethyl cyano diazoacetate **4a**, we did a study of the products distribution with 4-nitrobenzaldehyde as the substrate. Besides the desired dihydrofuran products **10e** and **10e′** was isolated in 48% and 64%, the competing 1,3-dioxolane products **11a** and **11b** were formed as well. The isolated yields of **11a** and **11b** are 31% and 9%, respectively (Scheme 3).

It's obvious that the competing 1,3-dioxolane formation side reactions reduced the percentage of the desired 2,5-dihydrofuran. As depicted in Scheme 4, the reactions compete between path A and path B. The aldehyde and acetylenedicarboxylate compete as dipolarophiles for the carbonyl ylide intermediate **M**. When more bulky diazo reagent *tert*-butyl cyano diazoacetate **4b** was used, the resulting more bulky intermediate **M** prefer path A, in which dimethyl acetylenedicarboxylate served as dipolarophile. For less bulky ethyl cyano diazoacetate **4a**, the reaction prefer path B; it afforded 1,3-dioxolane **11** with the second molecular aldehyde being the dipolarophile.

To confirm this hypothesis, we revisited the similar reactions of dimethyl diazomalonate **1a** and its analogues diethyl diazomalonate **1a′**. The reaction results are perfectly consistent with our expectation again. The yield of dihydrofuran **7a** is only 41% when dimethyl diazomalonate **1a** was used as the diazo reagent. However, the yield of **7a′** doubled to 83% when diethyl diazomalonate **1a′** was used instead (Scheme 5).

In the literature, the issue of the reaction selectivity was often solved by using excess amount of dipolarphiles (often more than 4 equiv).[10] However, this strategy is undesirable in terms of green chemistry consideration. In this work, it was found that the 1,3-dioxolane formation could be easily depressed by increasing the steric hindrance of substituted group without using large excess dipolarphile.

3. Conclusions

We have developed a practical system to synthesize multiple-substituted dihydrofuran through the intermolecular DC reactions of the acceptor/acceptor diazo reagents, aldehydes, and acetylenedicarboxylate. The reactions proceeded effectively under ambient temperature with low reactants ratios. It was found that the reactions are competitive between two possible paths; one forms 2,5-dihydrofuran **10** and the other forms 1,3-dioxolane **11**. Unlike the strategies adopted in the literature, the issue of the reaction selectivity in this work was solved by simply increasing the steric hindrance of the substituted group of diazo reagents without using large excess dipolarphiles. With more bulky diazo reagents, the reaction preferred the former path, in which the 2,5-dihydrofuran products are furnished dominantly.

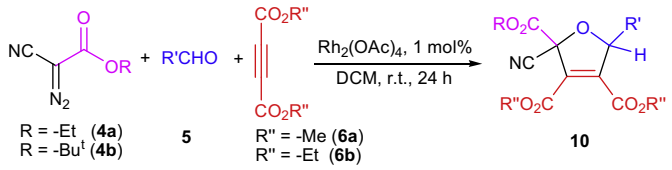
The results obtained in this work are an experimental insight concerning the intermolecular DC reactions of the acceptor/acceptor diazo reagents, and it would contribute to a better overall understanding of this synthetic methodology. Furthermore, owing to the low reactants ratio and mild reaction conditions, this system will be choice for the synthesis of multiple-substituted dihydrofuran and its derivatives.

4. Experimental section

4.1. General information

All the solvents were freshly distilled under N_2 from CaH_2 or Na. Liquid aldehydes (**5a**, **5b**, **5g**, **5h**) were purified by distillation at

Table 4
The reaction results of **4** with **5** and **6**[a]

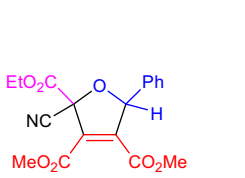


R = -Et (**4a**)
R = -Bu^t (**4b**)

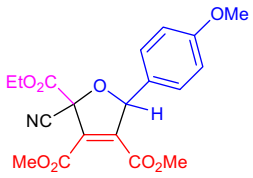
5

R" = -Me (**6a**)
R" = -Et (**6b**)

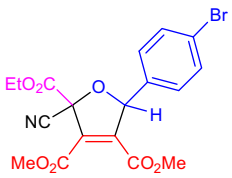
10



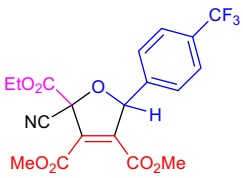
10a (85%)
dr = 67:33



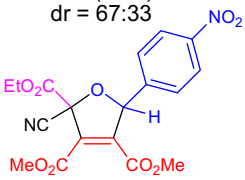
10b (38%)
dr = 53:47



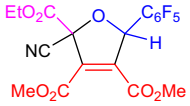
10c (59%)
dr = 62:38 [b]



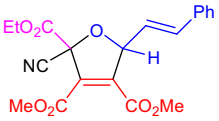
10d (48%)
dr = 53:47



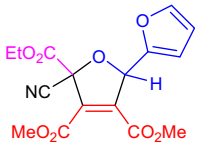
10e (48%)
dr = 58:42



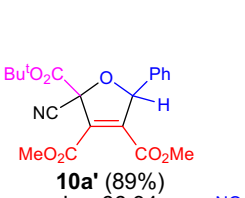
10f (32%)
dr = 95:5



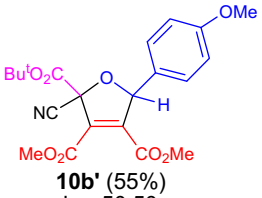
10g (60%)
dr = 66:34



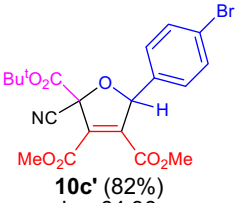
10h (21%)
dr = 56:44



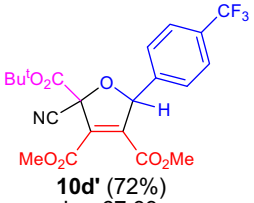
10a' (89%)
dr = 66:34



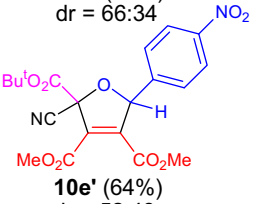
10b' (55%)
dr = 50:50



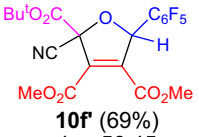
10c' (82%)
dr = 64:36



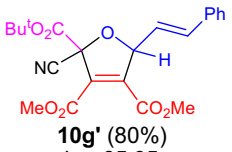
10d' (72%)
dr = 67:33



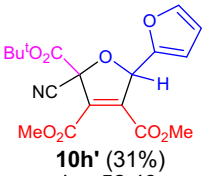
10e' (64%)
dr = 52:48



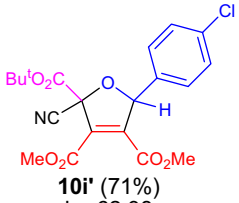
10f' (69%)
dr = 56:45



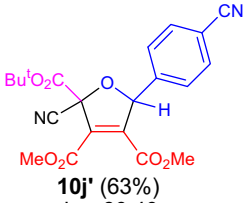
10g' (80%)
dr = 65:35



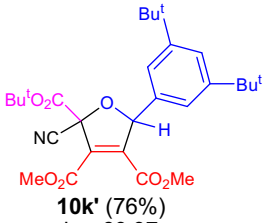
10h' (31%)
dr = 52:48



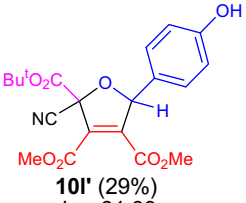
10i' (71%)
dr =62:38



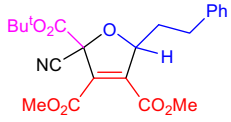
10j' (63%)
dr = 60:40



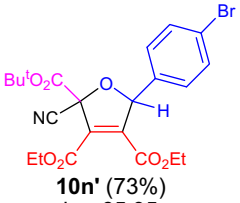
10k' (76%)
dr = 63:37



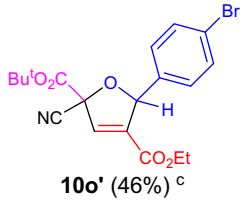
10l' (29%)
dr = 61:39



10m' (25%)
dr =62:38



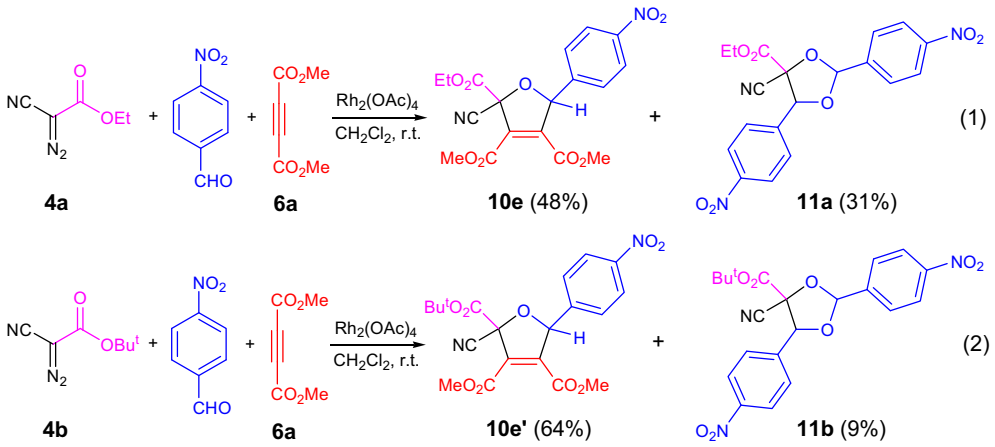
10n' (73%)
dr = 65:35



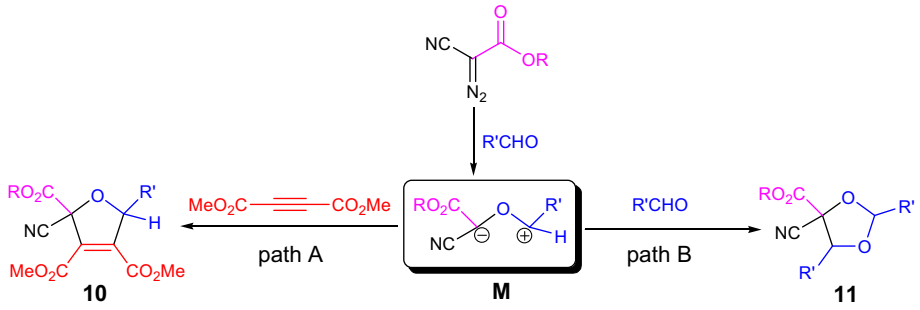
10o' (46%) [c]
dr = 75:25

[a] The reaction was performed in DCM under N_2 for 24 h [**5**]=0.25 M, **5a**: **4**:**6**=1.0:1.2:1.2. The yields refer to isolated yield and dr (cis/trans) was determined by ^{1}H NMR.
[b] The structure of the major isomers was determined by X-ray diffraction analysis.
[c] Methyl propiolate was used as the dipolarophile.

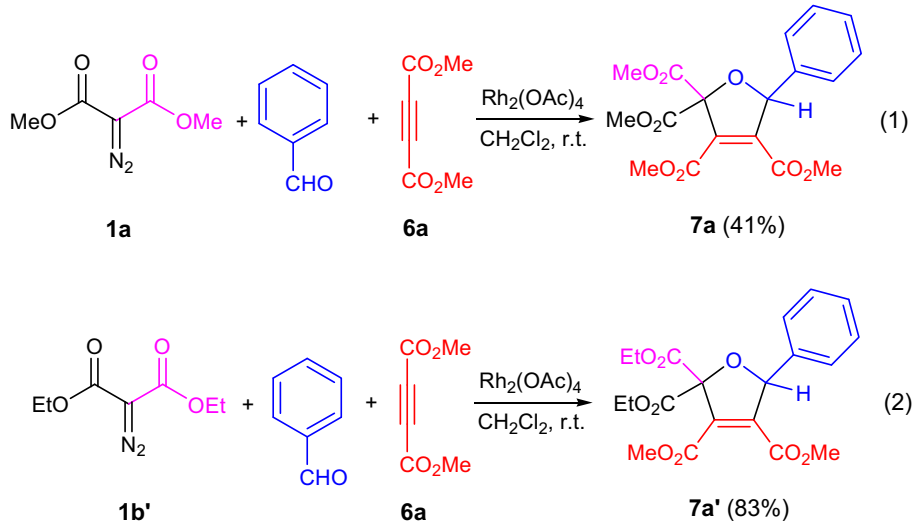
reduced pressure before use. Other reagents were used from commercial suppliers without further purification. All the reactions of α-cyano-diazoacetates catalyzed by $Rh_2(OAc)_4$ were carried out under a nitrogen atmosphere in an oven-dried glassware following standard Schlenk techniques. Yields of condition optimization and all dr ratios were determined by crude ^{1}H NMR of the reaction mixture. Chromatography was performed on silica gel. Products were visualized by UV and $KMnO_4$ stain. ^{1}H and ^{13}C NMR spectra were recorded on a Bruck DRX-400 DRX-600. High resolution mass spectra were measured on a Bruck Daltonics-APEXIII 7.0 TESLA



Scheme 3. The reaction products distribution of **4a** and **4b**.



Scheme 4. Two competing reaction paths.



Scheme 5. Reaction results of **1b** and **1b′**.

FTMS under electronic impact (EI) or on DSQ (Thermo) under electron spray ionization (ESI) mode. Infrared (IR) spectra are recorded on a Nicolet 210 spectrophotometer. Crystallographic data was collected on a Bruker-axs Smart APEX-II CCD diffractometer.

4.2. Synthesis of diazo reagent

4.2.1. Typical procedures for preparation α-cyano-diazoacetates. 4.2.1.1. Preparation of methyl cyanoacetate[10]. A dry round-bottom flask equipped with a magnetic stirrer was charged with 25 mL of a 1 M solution of cyano acid in MeCN and 1.3 mL MeOH (1.25 equiv), a 25 mL of 1.1 M solution of DCC in MeCN was added at stirring, the reaction mixture was stirred at room temperature for 2 h, it can be monitored by TLC with $KMnO_4$ stain. The reaction mixture was filtered through a Buchner funnel, the filtrate was purified using a short-path distillation.

4.2.1.2. Preparation of TfN_3 hexane solution[11]. Sodium azide (12.2 g, 187.5 mmol) was dissolved in distilled water (50 mL) and then hexane (30 mL) was added. The mixture was cooled on ice

bath for 2 min. Triflyl anhydride (6.2 mL, 37.5 mmol) was added slowly and the mixture was stirred for 2 h. The mixture was extracted with hexane (2×15 mL). The organic portions, containing the triflyl azide were pooled, washed once with saturated Na_2CO_3, and used without further purification.

4.2.1.3. Preparation of α-cyano-α-diazoacetates[6b]. To a stirred solution of the methyl cyanoacetate (2.47 g, 25 mmol) in acetonitrile (50 mL) under N_2 was added the above triflyl azide solution (60 mL) in hexane. Pyridine (4 mL, 50 mmol) was then added dropwise (over 5 min). The reaction mixture was stirred at room temperature for 24 h, after which the solvent was blowed away by the air flow (Note: Don't use rotary evaporator as it may cause potential explosion). Purification of the crude residue by flash chromatography on silica gel ($CHCl_3$) afforded the pure diazo ester as yellow oil.

*4.2.1.4. Ethyl cyano diazoacetate (**4a**).* Yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.35 (q, *J*=7.2 Hz, 2H), 1.34 (t, *J*=7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.3, 107.5, 63.1, 51.1, 14.0.

*4.2.1.5. tert-Butyl cyano diazoacetate (**4b**).* Yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.53 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.0, 106.7, 83.7, 50.1, 26.7.

4.3. Synthesis of the dihydrofuran and 1,3-dioxolane

All the reaction is conducted in schlenk tube under N_2 atmosphere; all the reactions were performed on a scale of diazo (0.25 mmol). $Rh_2(OAc)_4$ (1.0 mol %), aldehyde (0.30 mmol), dimethyl acetylenedicarboxylate **6a** or **6b** (0.30 mmol), solvent (1.0 mL), and diazo reagent was added in order. The dr ratio was determined by ^{1}H NMR of the crude reaction mixture, the products were purified by chromatography silica gel using ethyl acetate/petroleum.

*4.3.1. Tetramethyl 5-phenylfuran-2,2,3,4(5H)-tetracarboxylate (**7a**).* Yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45–7.34 (m, 5H), 6.21 (s, 1H), 3.87–3.85 (m, 9H), 3.64 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.3, 166.7, 161.6, 141.8, 136.2, 134.0, 129.4, 128.6, 128.0, 92.9, 90.1, 53.6, 53.5, 52.9, 52.6.

*4.3.2. 2,2-Diethyl 3,4-dimethyl 5-phenylfuran-2,2,3,4(5H)-tetracarboxylate (**7a′**).* Yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48–7.34 (m, 5H), 6.22 (s, 1H), 4.37–4.27 (m, 4H), 3.85 (s, 3H), 3.65 (s, 3H), 1.35–1.28 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.8, 166.2, 161.7, 141.4, 136.4, 134.5, 129.3, 128.5, 128.0, 93.1, 90.0, 62.9, 62.7, 52.7, 52.6, 14.0, 13.9. IR: 2988, 1732, 1667, 1441, 1261, 1140, 1093, 1042, 926, 859, 751, 701, 595, 519. HRMS (ESI): calcd for $C_{20}H_{22}O_9[M+Na]^+$, 429.1156, found 429.1150.

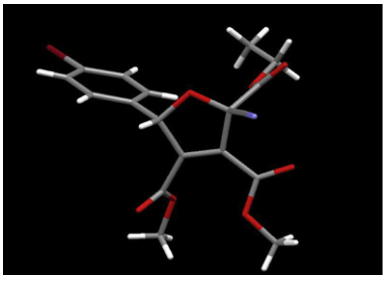
*4.3.3. 2-Ethyl 3,4-dimethyl 2-cyano-5-phenyl-2,5-dihydrofuran-2,3,4-tricarboxylate (**10a**).* Yellow oil, *cis*-^{1}H NMR (600 MHz, $CDCl_3$): δ 7.45–7.36 (m, 5H), 6.31 (s, 1H), 4.45–4.34 (m, 2H), 3.85 (s, 3H), 3.69 (s, 3H), 1.38 (t, *J*=7.2 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 162.7, 160.5, 158.4, 146.5, 133.6, 129.2, 128.0, 127.9, 127.2, 113.4, 90.6, 83.2, 63.4, 52.3, 52.2, 13.0. *trans*-^{1}H NMR (600 MHz, $CDCl_3$): δ 7.45–7.36 (m, 5H), 6.29 (s, 1H), 4.45–4.34 (m, 2H), 3.87 (s, 3H), 3.70 (s, 3H), 1.36 (t, *J*=7.2 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 162.8, 160.3, 158.6, 145.8, 133.8, 129.1, 128.2, 127.9, 126.5, 113.6, 91.1, 83.3, 63.4, 52.3, 52.2, 13.0. IR: 2958, 1756, 1638, 1496, 1439, 1257, 1207, 1176, 1134, 1055, 1025, 986, 923, 854, 777, 749, 699, 620, 481. HRMS (EI): calcd for $C_{18}H_{17}NO_7$ $[M]^+$, 359.1000, found 359.1001.

*4.3.4. 2-Ethyl 3,4-dimethyl 2-cyano-5-(4-methoxyphenyl)-2,5-dihydrofuran-2,3,4-tricarboxylate (**10b**).* Yellow oil, *cis*-^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38–7.27 (m, 2H), 6.94–6.89 (m, 2H), 6.28 (s, 1H), 4.42–4.35 (m, 2H), 3.86 (s, 3H), 3.81 (s, 3H), 3.71 (s, 3H), 1.38 (t, *J*=6.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.8, 161.6, 160.9, 159.4, 147.6, 129.8, 128.6, 127.7, 126.5, 114.2, 91.3, 83.8, 64.2, 55.3, 53.2, 53.1, 13.9. *trans*-^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38–7.27 (m, 2H), 6.94–6.89 (m, 2H), 6.25 (s, 1H), 4.42–4.35 (m, 2H), 3.88 (s, 3H), 3.81 (s, 3H), 3.72 (s, 3H), 1.37 (t, *J*=6.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.8, 161.4, 160.9, 159.6, 146.9, 129.1, 128.7, 127.2, 126.6, 114.5, 91.7, 83.8, 64.2, 55.3, 53.2, 53.1, 13.9. IR: 2955, 1750, 1642, 1600, 1442, 1369, 1344, 1285, 1207, 1153, 1084, 1024, 831, 757, 694, 616, 490. HRMS (ESI): calcd for $C_{19}H_{19}NO_8[M+Na]^+$, 412.1003, found 412.1005.

*4.3.5. 2-Ethyl 3,4-dimethyl 5-(4-bromophenyl)-2-cyano-2,5-dihydrofuran-2,3,4-tricarboxylate (**10c**).* White solid, mp 108–110 °C, *cis*-^{1}H NMR (600 MHz, $CDCl_3$): δ 7.54–7.51 (m, 2H), 7.35–7.33 (m, 2H), 6.27 (s, 1H), 4.47–4.35 (m, 2H), 3.87 (s, 3H), 3.72 (s, 3H), 1.39 (t, *J*=7.2 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 163.6, 161.2, 159.2, 146.5, 133.6, 132.1, 129.8, 129.4, 124.3, 114.1, 90.7, 84.1, 64.4, 53.3, 53.2, 13.9. IR: 2959, 2363, 1753, 1670, 1591, 1489, 1444, 1412, 1350, 1307, 1263, 1202, 1179, 1131, 1079, 1054, 1020, 985, 926, 843, 782, 744, 608, 502.

X-ray analysis of **10c**: (Table 5)

Table 5
Crystal data and structure refinement for **10c**



Identification code	f
Empirical formula	$C_{18}H_{16}BrNO_7$
Formula weight	438.23
Temperature	296 (2) K
Wavelength	0.71073 Å
Crystal system, space group	Monoclinic, *P*2(1)/*c*
Unit cell dimensions	*a*=8.6572 (12) Å alpha=90° *b*=17.480 (2) Å beta=100.143 (2)° *c*=13.1878 (18) Å gamma=90°
Volume	1964.5 (5) Å^3
Z, Calculated density	4, 1.482 Mg/m^3
Absorption coefficient	2.131 mm^{-1}
F(000)	888
Crystal size	0.27×0.22×0.15 mm
Theta range for data collection	1.95–25.20°
Limiting indices	$-10\le h\le 9$, $-19\le k\le 20$, $-15\le l\le 11$
Reflections collected/unique	10,105/3540 [*R*(int)=0.0451]
Completeness to theta=25.20	99.9%
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7405 and 0.5970
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	3540/0/248
Goodness-of-fit on F^2	1.026
Final *R* indices [$I>2\sigma(I)$]	*R*1=0.0501, *wR*2=0.1170
R indices (all data)	*R*1=0.1194, *wR*2=0.1453
Extinction coefficient	0.0024 (8)
Largest diff. peak and hole	0.465 and −0.686 e Å^{-3}

*4.3.6. 2-Ethyl 3,4-dimethyl 2-cyano-5-(4-(trifluoromethyl)-phenyl)-2,5-dihydrofuran-2,3,4-tricarboxylate (**10d**).* Yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67–7.60 (m, 4H), 6.37 (s, 1H), 4.50–4.35 (m, 2H), 3.88 (s, 3H), 3.72 (s, 3H), 1.40 (t, *J*=8.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.5, 161.0, 159.1, 146.2, 138.4, 130.3, 129.7, 128.5, 125.9 (m), 114.0, 90.6, 87.5, 84.2, 64.5, 53.4, 53.2, 13.9. IR:

2957, 2924, 2655, 1750, 1644, 1516, 1442, 1325, 1214, 1171, 1130, 1069, 1017, 849, 768, 697, 603. HRMS (ESI): calcd for $C_{19}H_{16}F_3NO_7[M+Na]^+$, 450.0771, found. 450.0781.

*4.3.7. 2-Ethyl 3,4-dimethyl 2-cyano-5-(4-nitrophenyl)-2,5-dihydrofuran-2,3,4-tricarboxylate (**10e**).* Yellow oil, *cis*-^{1}H NMR (400 MHz, $CDCl_3$): δ 8.29 (d, J=8.8 Hz, 2H), 7.59 (d, J=8.8 Hz, 2H), 6.40 (s, 1H), 4.46–4.38 (m, 2H), 3.91 (s, 3H), 3.75 (s, 3H), 1.39 (t, J=7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.2, 160.7, 159.2, 148.8, 144.7, 141.7, 130.1, 128.3, 124.3, 123.1, 114.1, 90.4, 84.5, 64.6, 53.5, 53.4, 13.9. *trans*-^{1}H NMR (400 MHz, $CDCl_3$): δ 8.26 (d, J=8.8 Hz, 2H), 7.70 (d, J=8.8 Hz, 2H), 6.42 (s, 1H), 4.46–4.38 (m, 2H), 3.89 (s, 3H), 3.73 (s, 3H), 1.39 (t, J=7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.4, 160.8, 159.1, 148.9, 145.4, 141.4, 130.5, 129.1, 124.1, 113.8, 90.0, 84.3, 64.7, 53.5, 53.4, 13.9. IR: 2959, 2853, 1752, 1641, 1528, 1441, 1350, 1262, 1208, 1139, 1098, 1055, 1020, 926, 859, 822, 782, 746, 697, 617, 486. HRMS (ESI): calcd for $C_{18}H_{16}N_2O_9[M+Na]^+$, 427.0748, found 427.0750.

*4.3.8. 2-Ethyl 3,4-dimethyl 2-cyano-5-(perfluorophenyl)-2,5-dihydrofuran-2,3,4-tricarboxylate (**10f**).* Yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.61 (s, 1H), 4.36 (q, J=8 Hz, 2H), 3.92 (s, 3H), 3.81 (s, 3H), 1.34 (t, J=7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) 162.0, 160.1, 159.4, 152.2, 147.0 (m), 144.5 (m), 140.1, 136.5 (m), 133.2, 113.4, 84.2, 79.7, 64.5, 53.5, 53.5, 13.7. ^{19}F NMR (360 MHz, CDDCl3) δ −140.74 to −140.82 (m, 2F), −149.64 to −149.77 (m, 1F), −160.51 to −160.64 (m, 2F). IR: 2959, 2362, 1751, 1653, 1510, 1440, 1264, 1207, 1128, 1100, 1027, 999, 926, 853, 768, 621. HRESI: calcd for $C_{18}H_{12}NO_7[M+Na]^+$, 472.0426, found 472.0427.

*4.3.9. (E)-2-Ethyl 3,4-dimethyl 2-cyano-5-styryl-2,5-dihydrofuran-2,3,4-tricarboxylate (**10g**).* Brown oil, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.58–5.92 (m, 8H), 4.43–4.35 (m, 2H), 3.88–3.84 (m, 3H), 3.81–3.74 (m, 3H), 1.39 (t, J=7 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.1, 163.7, 163.3, 162.1, 140.8, 135.0, 130.2, 128.9, 128.1, 115.2, 113.6, 102.6, 79.3, 64.6, 58.1, 53.2, 51.9, 13.9. IR: 2956, 2852, 1750, 1709, 1641, 1600, 1443, 1346, 1261, 1207, 1134, 1083, 1019, 855, 758, 693, 613, 491. HRMS (ESI): calcd for $C_{20}H_{19}NO_7[M+Na]^+$, 408.1054, found 408.1063.

*4.3.10. 2-Ethyl 3,4-dimethyl 2-cyano-5-(furan-2-yl)-2,5-dihydrofuran-2,3,4-tricarboxylate (**10h**).* Brown oil, *cis*-^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50–7.46 (m, 1H), 6.55–6.56 (m, 1H), 6.41–6.39 (m, 1H), 6.38 (s, 1H), 4.40–4.31 (m, 2H), 3.88 (s, 3H), 3.79 (s, 3H), 1.33 (t, J=7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.1, 161.0, 159.3, 147.2, 144.4, 143.4, 130.6, 114.1, 111.9, 111.1, 83.7, 83.7, 64.2, 53.3, 53.3, 13.8. *trans*-^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50–7.46 (m, 1H), 6.55–6.56 (m, 1H), 6.41–6.39 (m, 1H), 6.30 (s, 1H), 4.40–4.31 (m, 2H), 3.89 (s, 3H), 3.79 (s, 3H), 1.36 (t, J=7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.5, 160.9, 159.3, 147.2, 144.7, 142.9, 131.1, 113.9, 111.6, 112.0, 84.0, 83.4, 64.3, 53.3, 53.2, 13.9. IR: 2956, 2921, 2851, 1740, 1676, 1444, 1256, 1024, 744. HRMS (ESI): calcd for $C_{16}H_{15}NO_8[M+Na]^+$, 372.0690, found 372.0704.

*4.3.11. 2-tert-Butyl 3,4-dimethyl 2-cyano-5-phenyl-2,5-dihydrofuran-2,3,4-tricarboxylate (**10a′**).* Yellow oil, *cis*-^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47–7.38 (m, 5H), 6.29 (s, 1H), 3.87 (s, 3H), 3.69 (s, 3H), 1.57 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.3, 161.5, 159.4, 146.9, 134.7, 130.0, 129.4, 128.8, 128.1, 114.6, 91.2, 86.1, 84.9, 53.1, 54.0, 27.6. *trans*-^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47–7.38 (m, 5H), 6.27 (s, 1H), 3.89 (s, 3H), 3.71 (s, 3H), 1.55 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.4, 161.3, 159.7, 146.0, 135.0, 129.9, 129.7, 129.1, 127.4, 114.7, 91.8, 86.3, 84.8, 53.1, 53.0, 27.6. IR: 2960, 1750, 1673, 1440, 1266, 1205, 1157, 1026, 986, 923, 834, 748, 699, 620. HRMS (ESI): calcd for $C_{20}H_{21}NO_7[M+Na]^+$, 410.1210, found 410.1222.

*4.3.12. 2-tert-Butyl 3,4-dimethyl 2-cyano-5-(4-methoxyphenyl)-2,5-dihydrofuran-2,3,4-tricarboxylate (**10b′**).* Pale yellow oil, *cis*-^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39–7.28 (m, 2H), 6.93–6.88 (m, 2H), 6.24 (s, 1H), 3.87 (s, 3H), 3.81 (s, 3H), 3.70 (s, 3H), 1.56 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.5, 161.6, 160.8, 159.7, 146.2, 129.7, 129.0, 126.9, 114.8, 114.4, 90.9, 86.0, 84.4, 55.3, 53.1, 53.0, 27.6. *trans*-^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39–7.28 (m, 2H), 6.93–6.88 (m, 2H), 6.23 (s, 3H), 3.89 (s, 3H), 3.82 (s, 3H), 3.71 (s, 3H), 1.55 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.4, 161.4, 160.8, 159.5, 147.1, 129.5, 129.1, 126.8, 114.7, 114.2, 91.5, 86.1, 84.6, 55.3, 53.1, 53.0, 27.6. IR: 2959, 2844, 1748, 1616, 1515, 1441, 1259, 1160, 1028, 984, 837, 778, 734, 609, 540. HRMS (ESI): calcd for $C_{21}H_{23}NO_8[M+Na]^+$, 440.1316, found 440.1316.

*4.3.13. 2-tert-Butyl 3,4-dimethyl 5-(4-bromophenyl)-2-cyano-2,5-dihydrofuran-2,3,4-tricarboxylate (**10c′**).* Pale yellow oil, *cis*-^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56–7.24 (m, 4H), 6.23 (s, 1H), 3.89 (s, 3H), 3.73 (2, 3H), 1.55 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.2, 161.1, 159.6, 145.1, 134.1, 132.3, 130.3, 129.0, 124.2, 114.5, 91.0, 86.5, 84.7, 53.2, 53.1, 27.6. *trans*-^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56–7.24 (m, 4H), 6.24 (s, 1H), 3.88 (s, 3H), 3.71 (2, 3H), 1.57 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.2, 161.2, 159.3, 146.0, 133.9, 132.1, 129.9, 129.8, 124.33, 114.4, 90.4, 86.4, 84.9, 53.2, 53.1, 27.6. IR: 2984, 2955, 1752, 1644, 1591, 1486, 1439, 1399, 1369, 1337, 1278, 1208, 1154, 1095, 1011, 921, 833, 784, 476. HRMS (ESI): calcd for $C_{20}H_{20}BrNO_7[M+Na]^+$, 488.0315, found 488.0321.

*4.3.14. 2-tert-Butyl 3,4-dimethyl 2-cyano-5-(4-(trifluoromethyl)-phenyl)-2,5-dihydrofuran-2,3,4-tricarboxylate (**10d′**).* Yellow oil, *cis*-^{1}H NMR (400 MHz, $CDCl_3$): δ 7.69–7.50 (m, 4H), 6.34 (s, 1H), 3.89 (s, 3H), 3.71 (s, 3H), 1.58 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.1, 161.1, 159.3, 145.6, 138.8, 132.12, 131.8, 130.3, 128.5, 125.8 (m), 114.3, 90.3, 86.5, 85.0, 53.2, 53.1, 27.6. *trans*-^{1}H NMR (400 MHz, $CDCl_3$): δ 7.69–7.50 (m, 4H), 6.33 (s, 1H), 3.90 (s, 1H), 3.73 (s, 1H), 1.56 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.1, 160.91, 159.5, 144.6, 139.5, 132.1, 131.8, 130.3, 127.8, 126.1 (m), 114.4, 90.7, 86.6, 84.9, 53.2, 53.2, 27.6. IR: 2986, 2362, 1751, 1673, 1625, 1440, 1372, 1328, 1271, 1166, 1132, 1069, 1024, 990, 837, 775, 734, 672, 608. HRMS (ESI): calcd for $C_{20}H_{20}NO_7[M+Na]^+$, 478.1084, found 478.1094.

*4.3.15. 2-tert-Butyl 3,4-dimethyl 2-cyano-5-(4-nitrophenyl)-2,5-dihydrofuran-2,3,4-tricarboxylate (**10e′**).* Yellow oil, *cis*-^{1}H NMR (400 MHz, $CDCl_3$): δ 8.29–8.25 (m, 2H), 7.73–7.58 (m, 2H), 6.40 (s, 1H), 3.90 (s, 3H), 3.72 (s, 3H), 1.59 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.0, 160.7, 159.2, 184.8, 144.8, 141.8, 130.82, 129.1, 124.0, 114.1, 89.7, 86.8, 85.1, 53.3, 53.2, 27.6. *trans*-^{1}H NMR (400 MHz, $CDCl_3$): δ 8.29–8.25 (m, 2H), 7.73–7.58 (m, 2H), 6.38 (s, 1H), 3.91 (s, 3H), 3.74 (s, 3H), 1.57 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.9, 160.7, 159.4, 148.4, 143.8, 142.0, 131.3, 128.3, 124.2, 114.2, 90.2, 86.8, 85.0, 53.3, 53.3, 27.6. HRMS (ESI): calcd for $C_{20}H_{20}N_2O_9[M+Na]^+$, 455.1061, found 455.1070.

*4.3.16. 2-tert-Butyl 3,4-dimethyl 2-cyano-5-(perfluorophenyl)-2,5-dihydrofuran-2,3,4-tricarboxylate (**10f′**).* Yellow oil, *cis*-^{1}H NMR (400 MHz, $CDCl_3$): δ 6.58 (s, 1H), 3.94 (s, 3H), 3.79 (s, 3H), 1.51 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.9, 160.2, 159.8, 147.0 (m), 144.5 (m), 139.0, 136.4 (m), 134.3, 113.7, 86.8, 84.9, 79.4, 53.4, 53.4, 53.4, 27.5. *trans*-^{1}H NMR (400 MHz, $CDCl_3$): δ 6.60 (s, 1H), 3.94 (s, 3H), 3.78 (s, 3H), 1.56 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.9, 160.6, 159.6, 143.8 (m), 141.3 (m), 139.2, 138.9 (m), 133.9, 113.3, 87.1, 84.9, 80.3, 53.4, 53.34, 53.4, 27.7. IR: 2958, 1751, 1512, 1443, 1262, 1207, 1154, 1101, 996, 834, 782. HRMS (ESI): calcd for $C_{20}H_{16}F_5NO_7[M+Na]^+$, 500.0739, found 500.0747.

*4.3.17. (E)-2-tert-Butyl 3,4-dimethyl 2-cyano-5-styryl-2,5-dihydrofuran-2,3,4-tricarboxylate (**10g′**).* Yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.57–7.38 (m, 8H), 3.80–3.75 (m, 6H), 1.56–1.54 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.2, 163.8, 163.3,

160.4, 140.7, 135.0, 130.2, 128.9, 128.1, 115.6, 113.7, 113.7, 102.9, 87.1, 57.8, 53.0, 51.9, 27.7. IR: 2986, 2955, 1751, 1707, 1642, 1599, 1442, 1369, 1344, 1285, 1206, 1153, 1084, 1023, 831, 758, 693, 612, 490. HRMS (ESI): calcd for $C_{22}H_{23}NO_7$[M + Na]$^+$, 436.1367, found 436.1377.

*4.3.18. 2-tert-Butyl 3,4-dimethyl 2-cyano-5-(furan-2-yl)-2,5-dihydrofuran-2,3,4-tricarboxylate (**10h′**).* *cis*-^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49–7.45 (m, 1H), 6.54–6.52 (m, 1H), 6.40–6.39 (m, 1H), 6.35 (s, 1H), 3.89 (s, 3H), 3.78 (s, 3H), 1.51 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.1, 161.0, 159.7, 147.9, 144.2, 142.6, 131.9, 114.3, 111.6, 110.9, 86.0, 84.8, 83.4, 53.1, 27.6. *trans*-^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49–7.45 (m, 1H), 6.54–6.52 (m, 1H), 6.40–6.39 (m, 1H), 6.28 (s, 1H), 3.90 (s, 3H), 3.78 (s, 3H), 1.54 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.7, 160.9, 159.4, 147.5, 144.6, 142.1, 131.3, 114.1, 111.4, 110.9, 86.3, 84.0, 83.5, 53.1, 27.6. IR: 2958, 2929, 2855, 1748, 1636, 1442, 1372, 1276, 1208, 1155, 1079, 1022, 982, 924, 886, 834, 769, 599. HRMS (ESI): calcd for $C_{18}H_{19}NO_8$[M + Na]$^+$, 400.1003, found 400.1013.

*4.3.19. 2-tert-Butyl 3,4-dimethyl 5-(4-chlorophenyl)-2-cyano-2,5-dihydrofuran-2,3,4-tricarboxylate (**10i′**).* Yellow solid, mp 85.2–85.3 °C. *cis*-^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43–7.32 (m, 4H), 6.26 (s, 1H), 3.89–3.87 (m, 3H), 3.72–3.70 (m, 3H), 1.57 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.2, 161.3, 159.3, 146.1, 136.00, 133.4, 129.8, 129.5, 129.1, 114.4, 90.4, 86.4, 84.9, 53.2, 53.1, 27.6. *trans*-^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43–7.32 (m, 4H), 6.25 (s, 1H), 3.89–3.87 (m, 3H), 3.72–3.70 (m, 3H), 1.55 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.2, 161.1, 159.6, 145.2, 135.9, 133.6, 130.3, 129.3, 128.8, 114.5, 90.9, 86.4, 84.7, 53.2, 53.1, 27.6. IR: 2956, 2922, 1750, 1490, 1439, 1370, 1337, 1278, 1207, 1155, 1092, 1020, 835. HRMS (ESI): calcd for $C_{20}H_{20}ClNO_7$[M + Na]$^+$, 444.0821, found 444.0823.

*4.3.20. 2-tert-Butyl 3,4-dimethyl 2-cyano-5-(4-cyanophenyl)-2,5-dihydrofuran-2,3,4-tricarboxylate (**10j′**).* Yellow oil, *cis*-^{1}H NMR (400 MHz, $CDCl_3$): δ 7.75–7.29 (m, 4H), 6.34 (s, 1H), 3.89 (s, 3H), 3.72 (s, 3H), 1.56 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.7, 162.0, 160.9, 159.2, 144.9, 139.9, 132.6, 131.7, 128.7, 118.2, 114.12, 90.0, 86.8, 85.0, 53.3, 53.2, 27.6. *trans*-^{1}H NMR (400 MHz, $CDCl_3$): δ 7.75–7.29 (m, 4H), 6.32 (s, 1H), 3.91 (s, 3H), 3.74 (s, 3H), 1.58 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.8, 161.9, 160.7, 159.4, 144.0, 140.2, 132.8, 130.4, 128.0, 118.1, 114.3, 90.5, 86.8, 85.0, 53.3, 53.2, 27.6. IR: 2985, 2232, 1750, 1612, 1505, 1440, 1279, 1207, 1156, 1026, 990, 926, 834, 779, 734, 554, 470. HRMS (ESI): calcd for $C_{21}H_{20}N_2O_7$[M + Na]$^+$, 435.1163, found 435.1163.

*4.3.21. 2-tert-Butyl 3,4-dimethyl 2-cyano-5-(3,5-di-tert-butylphenyl)-2,5-dihydrofuran-2,3,4-tricarboxylate (**10k′**).* Yellow oil, *cis*-^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44–7.19 (m, 4H), 6.292 (s, 1H), 3.86 (s, 3H), 3.68 (s, 3H), 1.56 (s, 9H), 1.31 (s, 18H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.5, 161.8, 159.5, 151.3, 148.1, 133.7, 128.5, 122.4, 121.4, 114.8, 91.9, 85.8, 84.5, 53.0, 52.8, 34.9, 31.4, 27.6. *trans*-^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44–7.19 (m, 4H), 6.287 (s, 1H), 3.88 (s, 3H), 3.72 (s, 3H), 1.55 (s, 9H), 1.32 (s, 18H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.5, 161.5, 159.7, 151.6, 147.1, 134.0, 128.9, 123.7, 121.4, 114.9, 92.5, 86.0, 84.9, 53.0, 52.9, 34.9, 31.4, 27.6. IR: 2961, 1750, 1642, 1440, 1369, 1265, 1101, 1025, 882, 835, 622. HRMS (ESI): calcd for $C_{28}H_{37}NO_7$[M + Na]$^+$, 522.2462, found 524.2461.

*4.3.22. 2-tert-Butyl 3,4-dimethyl 2-cyano-5-(4-hydroxyphenyl)-2,5-dihydrofuran-2,3,4-tricarboxylate (**10l′**).* Pale yellow oil, *cis*-^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33–6.804 (m, H), 6.23 (s, 1H), 3.87 (s, 3H), 3.70 (s, 3H), 1.56 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.4, 161.5, 159.5, 157.3, 147.1, 129.9, 129.2, 126.7, 115.7, 114.6, 90.9, 86.2, 84.6, 53.1, 53.1, 27.6. *trans*-^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33–6.804 (m, H), 6.21 (s, 1H), 3.88 (s, 3H), 3.72 (s, 3H), 1.55 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.5, 161.7, 159.7, 157.2, 146.2, 129.4, 129.2, 126.8, 116.0, 114.8, 91.5, 86.3, 84.4, 53.1, 53.1, 27.6. IR: 2958, 1750, 1440, 1268, 1156, 1070, 1027, 990, 924, 835, 748, 698, 465. HRMS (ESI): calcd for $C_{20}H_{21}NO_8$[M+Na]$^+$, 426.1159, found 426.1175.

*4.3.23. 2-tert-Butyl 3,4-dimethyl 2-cyano-5-phenethyl-2,5-dihydrofuran-2,3,4-tricarboxylate (**10m′**).* Yellow oil, *cis*-^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31–7.27 (m, 2H), 7.22–7.17 (m, 3H), 5.40–5.36 (m, 1H), 3.87–3.85 (m, 6H), 2.84–2.74 (m, 2H), 2.12–2.07 (m, 2H), 1.54 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.3, 161.92, 159.5, 146.8, 140.6, 129.9, 128.5, 128.5, 128.5, 126.2, 114.6, 88.6, 85.8, 84.8, 53.0, 35.6, 30.8, 27.6. *trans*-^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31–7.27 (m, 2H), 7.22–7.17 (m, 3H), 5.40–5.36 (m, 1H), 3.87–3.85 (m, 6H), 2.84–2.74 (m, 2H), 2.12–2.07 (m, 2H), 1.53 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.4, 161.8, 159.6, 146.4, 140.5, 129.4, 128.5, 128.5, 126.2, 114.8, 88.2, 85.0, 84.3, 53.1, 35.2, 30.7, 27.6. IR: 2957, 1748, 1671, 1441, 1370, 1279, 1206, 1157, 1105, 1027, 835, 749, 702, 615, 473. HRMS (ESI): calcd for $C_{22}H_{25}NO_7$[M + Na]$^+$, 438.1523, found 438.1524.

*4.3.24. 2-tert-Butyl 3,4-diethyl 5-(4-bromophenyl)-2-cyano-2,5-dihydrofuran-2,3,4-tricarboxylate (**10n′**).* Brown oil, *cis*-^{1}H NMR (400 MHz, $CDCl_3$): δ 7.55–7.25 (m, 4H), 6.24 (s, 1H), 4.37–4.31 (m, 2H), 4.19–4.13 (m, 2H), 1.57 (s, 9H), 1.37–1.32 (m, 3H), 1.18–1.12 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.3, 160.82, 158.9, 146.0, 134.0, 131.9, 129.7, 129.7, 124.2, 114.5, 90.5, 86.3, 85.0, 62.6, 62.4, 27.6, 13.9, 13.8. *trans*-^{1}H NMR (400 MHz, $CDCl_3$): δ 7.55–7.25 (m, 4H), 6.22 (s, 1H), 4.37–4.31 (m, 2H), 4.19–4.13 (m, 2H), 1.55 (s, 9H), 1.37–1.32 (m, 3H), 1.18–1.12 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.3, 160.7, 159.1, 145.2, 134.3, 132.2, 130.0, 129.1, 124.0, 114.6, 91.0, 86.3, 84.9, 62.6, 62.4, 27.5, 13.9, 13.8. IR: 2985, 2938, 1752, 1674, 1593, 1485, 1372, 1260, 1157, 1020, 940, 837, 739, 582, 522, 466. HRMS (ESI): calcd for $C_{22}H_{24}BrN_4O_6$[M + Na]$^+$, 516.0628, found 516.0632.

*4.3.25. 2-tert-Butyl 4-ethyl 5-(4-bromophenyl)-2-cyano-2,5-dihydrofuran-2,4-dicarboxylate (**10o′**).* Colorless oil. *cis*-^{1}H NMR (400 MHz, $CDCl_3$): δ 7.46–7.42 (m, 2H), 7.29–7.19 (m, 2H), 6.68 (s, 1H), 6.08 (s, 1H), 4.12–4.01 (m, 2H), 1.50 (s, 1H), 1.12 (t, *J*=7.2 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.4, 160.5, 140.8, 136.0, 132.20, 131.6, 129.8, 123.4, 114.8, 89.0, 86.6, 83.8, 61.8, 27.8, 13.9. *trans*-^{1}H NMR (400 MHz, $CDCl_3$): δ 7.46–7.42 (m,2H), 7.29–7.19 (m, 2H), 6.67 (s, 1H), 6.08 (s, 1H), 4.12–4.01 (m, 2H), 1.49 (s, 1H), 1.13 (t, *J*=7.2 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.7, 160.5, 140.9, 136.1, 132.0, 131.9, 129.3, 123.4, 114.9, 89.7, 86.6, 83.7, 61.8, 27.9, 13.9. IR: 2983, 1732. HRMS (ESI): calcd for $C_{19}H_{20}BrNO_5$[M + Na]$^+$, 444.0423, found 444.0421.

*4.3.26. Ethyl 4-cyano-2,5-bis(4-nitrophenyl)-1,3-dioxolane-4-carboxylate (**11a**).* Pale yellow solid, mp 172.8–172.9 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.37 (d, *J*=8.8 Hz, 2H), 8.29 (d, *J*=8.8 Hz, 2H), 7.99 (d, *J*=8.8 Hz, 2H), 7.67 (d, *J*=8.8 Hz, 2H), 6.41 (s, 1H), 5.80 (s, 1H), 3.92–3.72 (m, 2H), 0.90 (t, *J*=7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.6, 149.5, 149.0, 139.7, 137.9, 128.9, 127.7, 124.0, 123.9, 115.4, 105.5, 86.8, 78.3, 63.9, 13.5. IR: 3119, 2922, 1741, 1605, 1521, 1394, 1346, 1247, 1213, 1123, 1081, 1008, 973, 851, 747, 695, 655, 567, 450. HRMS (ESI): calcd for $C_{19}H_{15}N_3O_8$[M + Na]$^+$, 436.0757, found 436.0760.

*4.3.27. tert-Butyl 4-cyano-2,5-bis(4-nitrophenyl)-1,3-dioxolane-4-carboxylate (**11b**).* Pale yellow solid, mp 162.8–163.8 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.37 (d, *J*=8.8 Hz, 2H), 8.30 (d, *J*=8.8 Hz, 2H), 8.00 (d, *J*=8.8 Hz, 2H), 7.70 (d, *J*=8.4 Hz, 2H), 6.37 (s, 1H), 5.77 (s, 1H), 1.09 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.1, 149.5, 148.9, 139.8, 138.3, 128.9, 127.9, 124.0, 123.8, 115.9, 105.2, 86.6, 86.4, 78.2, 27.2. IR: 3085, 3038, 2983, 2932, 2865, 1932, 1747, 1610, 1529, 1446,

1395, 1348, 1292, 1258, 1217, 1124, 1014, 975, 910, 851, 830, 770, 668, 624, 579, 450. HRMS (ESI): calcd for $C_{21}H_{19}N_3O_8[M + Na]^+$, 464.1070, found 464.1071.

4.4. Computational details

All theoretical calculations were performed using the Gaussian 03 software package.[12]

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tet.2011.05.028.

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