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NHC-Ag(I)-Catalyzed Three-Component 1,3-Dipolar Cycloaddition To Provide Polysubstituted Dihydro-/Tetrahydrofurans

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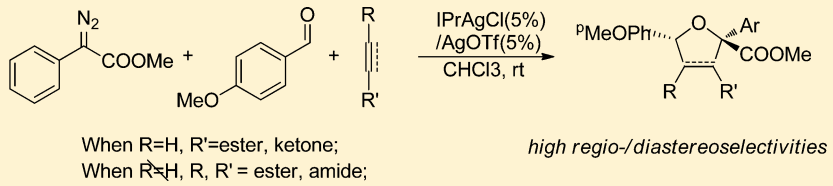
Supporting Information



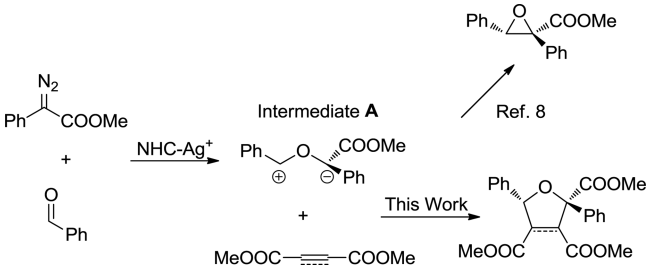
ABSTRACT: A new method was developed to synthesize polyfunctionalized dihydrofuran and tetrahydrofuran derivatives from the three-component [2 + 2 + 1] cycloaddition of the diazoesters with aryl/alkenyl aldehydes and alkyne/olefin dipolarophiles by using a Ag(I) *N*-heterocyclic carbene complex as the catalyst. A carbonyl ylide intermediate was generated, which undertook an *endo*-type 1,3-dipolar cycloaddition to provide the desired dihydro-/tetrahydrofurans in high regio- and diastereoselectivities by using α-aryl or α-alkenyl diazoesters.

1,3-Dipolar cycloaddition (DC) is an important approach for hetereocycle synthesis.[1] In this field, DC reactions that make use of silver salts as the catalysts have attracted much attention from organic chemists.[1b,c] Most of these studies focused on the dipolar cycloadditions of azomethine ylides with olefins to provide polysubstituted pyrrolidine derivatives, in which silver salts usually behave as the Lewis acid catalysts.[2,3]

On the other hand, metal-catalyzed DC reactions involving carbonyl ylides can generate stereochemically complex molecules from three simple starting materials.[4] These reactions are highly desirable in terms of green chemistry and were commonly mediated by Rh(II) complexes as the carbene transfer catalysts.[5] Nevertheless, regio- and diastereoselectivities were usually an issue for many of these transformations.[6]

We have recently described a silver mediated carbene transfer reaction to synthesize oxirane molecules from the reaction of diazocarbonyl substrates with aryl aldehydes by using a Ag(I) *N*-heterocyclic carbene complex[7] as the catalyst (Scheme 1, ref 8 reaction).[8] It was proposed that a carbonyl ylide was generated as the reaction intermediate.[9] As an extension of this reaction, we herein want to report the first example of silver-catalyzed carbonyl ylide's DC reaction with electron-deficient alkynes and olefins to provide a series of 2,5-dihydrofurans and tetrahydrofurans with high regio- and diastereoselectivities (Scheme 1).[10]

Scheme 1. NHC-Ag(I) Mediated [2 + 2 + 1] Carbene Cycloaddition



The reaction of methyl phenyldiazoacetate **1a** with benzaldehyde **2a** and electron-deficient diethyl acetylenedicarboxylate (dipolarophile) **3a** was chosen as the model system for our initial investigation. Following the previous reaction procedure, an *N*-heterocyclic carbene ligated silver complex was employed as the catalyst.[8] As shown in Table 1, a mixture of **1a** (0.1 mmol) and 1 mol equiv of **2a** and **3a** in CH_2Cl_2 was treated with 5 mol % equiv of IPrAgCl/AgOTf in the condition of 50 mg of 4 Å molecular sieves. Twenty-four hours later, 2,5-dihydrofuran **4a** was obtained in 32% yield, together with the formation of the oxirane product **7a** in 10% yield. (Table 1, entry 1). Other NHC ligands, such as SIPrAgCl and ICyAgCl, were evaluated, which led to slightly reduced yields (Table 1, entries 2−3). Different silver cocatalysts (Table 1, entries 4−9) were then screened. It was found that $AgBF_4$, $AgSbF_6$, $AgPF_6$, $AgNTf_2$, and $AgClO_4$ gave the desired product in low to moderate yields, while Ag_2CO_3 gave no reaction. Exploration of various solvents found that $CHCl_3$ was the best reaction medium (Table 1, entries 10−13). Improving **2a**'s and **3a**'s equivalence could enhance **4a**'s yield (Table 1, entry 14). When substrates **1a** and **2a** were added via syringe pump, **4a**'s yield could be improved to 91% (Table 1, entry 15). In the control experiments, either the sole silver complex IPrAgCl or the cocatalyst AgOTf gave no desried

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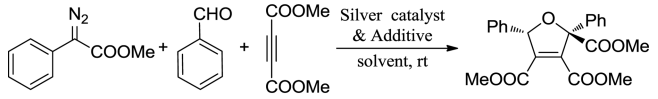
Table 1. Silver Mediated Carbonyl Ylide Cycloaddition of Phenyldiazoacetate 1a with Benzaldehyde 2a and Diethyl Acetylenedicarboxylate 3a[a]



1a 2a 3a 4a

	Ag catalyst (mol %)	additive (mol %)	solvent/time (h)	yield (%)[b]
1	IPrAgCl (5)	AgOTf (5)	DCM/12	32
2	SIPrAgCl (5)	AgOTf (5)	DCM/12	23
3	ICyAgCl (5)	AgOTf (5)	DCM/12	27
4	IPrAgCl (5)	$AgBF_4$ (5)	DCM/12	24
5	IPrAgCl (5)	$AgSbF_6$ (5)	DCM/12	16
6	IPrAgCl (5)	$AgPF_6$ (5)	DCM/12	18
7	IPrAgCl (5)	$AgNTf_2$ (5)	DCM/12	30
8	IPrAgCl (5)	Ag_2CO_3 (5)	DCM/12	ND
9	IPrAgCl (5)	$AgClO_4$ (5)	DCM/12	13
10	IPrAgCl (5)	AgOTf (5)	DCE/12	34
11	IPrAgCl (5)	AgOTf (5)	$CHCl_3$/12	42
12	IPrAgCl (5)	AgOTf (5)	toluene/12	13
13	IPrAgCl (5)	AgOTf (5)	1,4-dioxane/12	<5%
14[c]	IPrAgCl (5)	AgOTf (5)	$CHCl_3$/12	78
15[d]	IPrAgCl (5)	AgOTf (5)	$CHCl_3$/12	91
16	AgOTf (5)	no	DCM/24	<5
17	IPrAgCl (5)	no	DCM/24	ND
18	AgOTf (5)/Ph_3P (5)	no	DCM/24	25

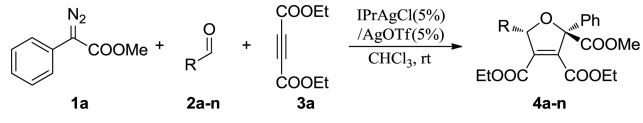
[a]Unless noted, all reactions were carried out on a 0.1 mmol scale in 2 mL of solvent at rt with the addition of 50 mg of 4 Å molecular sieves. [b]The reaction yields were determined by ^1H NMR spectral data. [c]2 mol equiv of **1a** and 5 mol equiv of **3a** were used. [d]**1a** and **2a** in 1 mL of $CHCl_3$ were added via syringe over 2 h. ND = No product **4a** detected. **4a**'s structure only shows relative configuration.

product (Table 1, entries 16–17).[10] Utilization of phosphine ligand Ph_3P led to a low reaction yield (Table 1, entry 18).

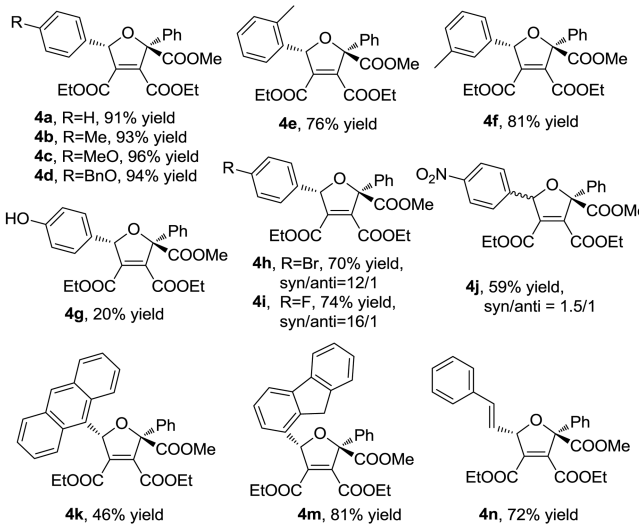
The structure of compound **4a** could be deduced from **5e**'s X-ray structure,[11] and confirmed by the NOESY spectral data for **4c**, *cis*-**4j**, and *trans*-**4j**, in which the two phenyl groups are positioned on the same side of the dihydrofuran ring.[12] Nevertheless, in Rh(III) mediated α-alkyl-α-diazoester's carbonyl ylide cycloaddition reaction, reported by the Fox group in 2009, the sole phenyl group positions on the same side with the ester group. Moreover, it is notable that only one isomer was obtained in Table 1's reaction.[13]

With the optimal reaction conditions in hand, the substrate scope was explored and a series of 2,5-dihydrofuran and tetrahydrofuran derivatives were synthesized. At first, various aromatic and α,β-unsaturated aldehydes were tested by using methyl phenyldiazoacetate **1a** and diethyl acetylenedicarboxylate **3a** as the reaction partners. As shown in Table 2, several *para*-, *ortho*-, and *meta*-substituted benzaldehydes were scrutinized. Both electron-donating and electron-withdrawing benzaldehydes worked very well in this silver carbene mediated [2 + 2 + 1] cycloaddition reaction. Electron-rich *p*-alkoxy benzaldehydes afforded **4c** and **4d** in high reaction yields (Table 2, **4c–d**). **4g**'s low yield was due to the phenol group's lability.[14] It was proposed that intermediate **A** was formed from the nucleophilic addition of aldehyde onto the silver carbenoid ester (Scheme 1). Thus, the aldehyde's nucleophilicity might affect the reaction yield. The electron-poor *p*-halo substituted benzaldehydes provided the desired dihydrofurans in relatively low yields, together with the formation of a small amount of *trans* isomers (Table 2, **4h–i**). In the reaction of *p*-nitro benzaldehyde, the desired cycloadduct **4j** was obtained in 59% yield with a ratio of *cis*/*trans* = 1.5/1 (Table 2, **4j**). The reactions of bulky aromatic and α,β-unsaturated aldehydes went smoothly, provided **4k–n** in moderate to good yields (Table 2).

Table 2. NHC-Ag^+ Mediated Carbonyl Ylide Cycloaddition of 1a, 3a with Various Aldehydes[a,b]



1a 2a-n 3a 4a-n



[a]Unless noted, all reactions were carried out on a 0.1 mmol scale in 2 mL of CH_2Cl_2 at rt with the addition of 50 mg of 4 Å molecular sieves (**1a**/**2**/**3a** = 2/1/5). [b]The structures of products **4a–n** only show their relative configuration.

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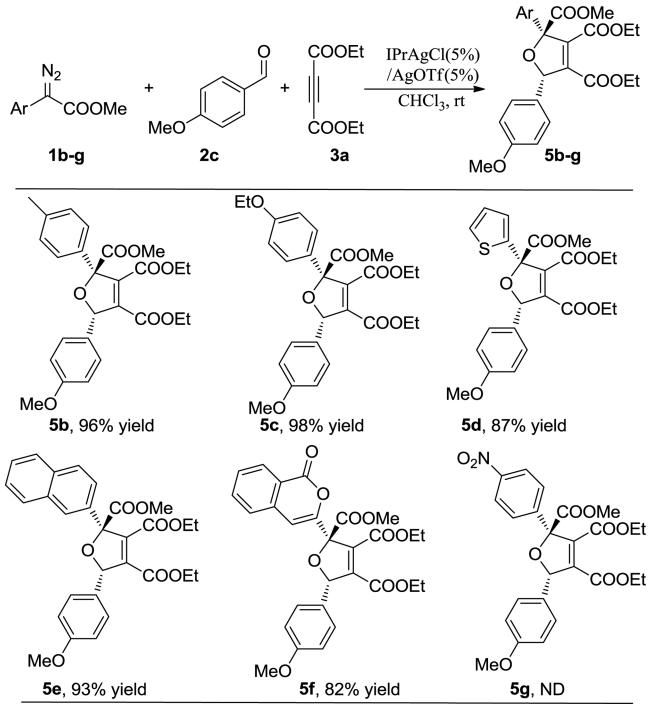
Next, various diazoesters were investigated. Both phenyl and vinyl diazoesters reacted smoothly with **2c** and **3a**, which provided a series of desired dihydrofuran cycloadducts in good to excellent yields (Table 3, **5b–f**), in which only *cis* isomers were detected, whereas, when α-nitrophenyl diazoester was utilized, no desired dihydrofuran product was obtained (Table 3, **5g**).

Table 3. NHC-Ag$^+$ Mediated Carbonyl Ylide Cycloaddition of 2c, 3a with Various Diazoesters[a,b]



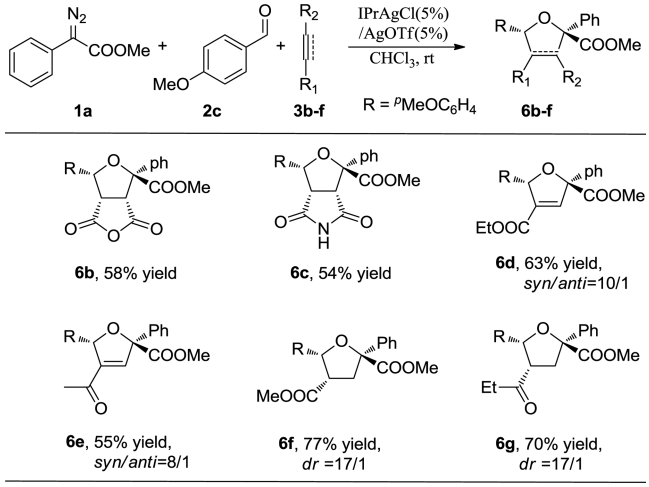
[a]Unless noted, all reactions were carried out on a 0.1 mmol scale in 2 mL of CH_2Cl_2 at rt with the addition of 50 mg of 4 Å molecular sieves (**1**/**2c**/**3a** = 2/1/5). [b]The structures of products **5b–g** only show their relative configuration.

Other electron-deficient olefin and alkyne dipolarophiles were explored too. As shown in Table 4, [3 + 2] dipolar cycloaddition of carbonyl ylides with maleic anhydride **3b** and maleimide **3c** yielded the corresponding *endo*-selective THF cycloadducts **6b** and **6c** in moderate yields, without the formation of other diastereoisomers. When unsymmetric alkyne substrates, such as ethyl acetylenecarboxylate **3d** and 3-butynone **3e**, were utilized, dihydrofuran products **6d** and **6e** were readily obtained, together with the formation of a small amount of *trans* isomers (Table 4, **6d–e**). Notably, there were no regioisomers detected. Likewise, the reactions of vinyl ester and vinyl ketone provided *endo*-selective THF cycloadducts in good yields with high diastereoselectivities (Table 4, **6f–g**).

In the reaction of **1a**, **2c**, and acrylonitrile **3h**, *endo*-**6h** was obtained in 52% yield, together with the formation of *exo*-**6h** in 22% yield. In addition, the *exo*-**6h** was an inseparable mixture of *cis*/*trans* isomers in a ratio of *cis*/*trans* = 2/1 (Scheme 2).

A plausible mechanism was proposed. As shown in Scheme 3, the reaction's high regioselectivity could be rationalized by an asynchronous transition state[15] and determined by their inherent charge distribution from both the carbonyl ylide intermediates and the dipolarophiles. The high *cis*/*trans* selectivities of **4h–j** and **6d–e** and the high diastereoselectivities of **6f–g** might be owing to the preference of the *endo* transition state **I** over **II**.

Table 4. NHC-Ag$^+$ Mediated Carbonyl Ylide Cycloaddition of 1a, 2c with Various Dipolarophiles[a,b]



[a]Unless noted, all reactions were carried out on a 0.1 mmol scale in 2 mL of CH_2Cl_2 at rt with the addition of 50 mg of 4 Å molecular sieves (**1a**/**2c**/**3** = 2/1/5). [b]The structures of products **6b–g** only show their relative configuration.

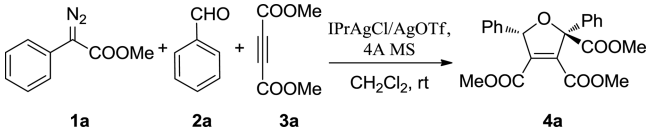
Otherwise, a possible configuration isomerization during the process of the asynchronous *endo* transition state **I** could also lead to the formation of the minor isomers. Moreover, based on acrylonitrile **3h**'s result (Scheme 2), an *exo* transition state is also possible in some cases.

In summary, a new method was developed to synthesize polyfunctionalized dihydrofuran and tetrahydrofuran derivatives from the three-component [2 + 2 + 1] cycloaddition of the diazoesters with aryl/alkenyl aldehydes and alkyne/olefin dipolarophiles by using a Ag(I) *N*-heterocyclic carbene complex as the catalyst, in which carbonyl ylide intermediate **A** was involved. The *endo*-type 1,3-dipolar cycloaddition provided the desired dihydro-/tetrahydrofurans in high regio- and diastereoselectivities by using α-aryl or α-alkenyl diazoesters.

EXPERIMENTAL SECTION

General Conditions. All reactions were run under an inert atmosphere (N_2) with flame-dried glassware using standard techniques for manipulating air-sensitive compounds. CH_2Cl_2 was obtained by fresh distilled over calcium hydride. Commercial reagents were used as supplied or purified by standard techniques where necessary. Column chromatography was performed using 200–300 mesh silica with the proper solvent system according to TLC analysis using UV light to visualize the reaction components. Unless otherwise noted, nuclear magnetic resonance spectra were recorded on a 400 MHz spectrometer. NMR data were reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet, and brs = broad singlet), coupling constant in Hz and integration. Chemical shifts for ^{13}C NMR spectra were recorded in parts per million from tetramethylsilane using the central peak of deuterochloroform (77.0 ppm) as the internal standard. IR spectra were recorded on an FTIR spectrometer (KBr) and reported in reciprocal centimeters (cm^{-1}). HRMS data were recorded on an orbitrap MS analyzer by using ESI ionization with 100 000 (fwhm) maximum resolution.

General Procedure for Ag(I) Mediated Carbonyl Ylide Cycloaddition of 1a with 2a and 3a.



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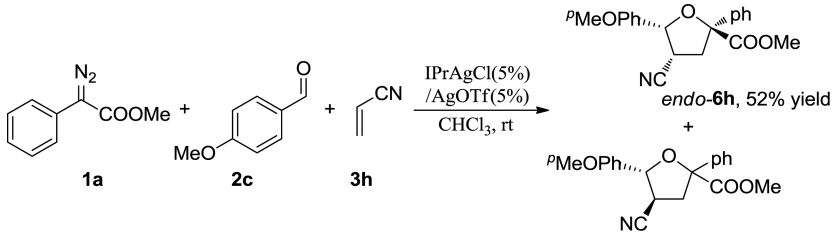
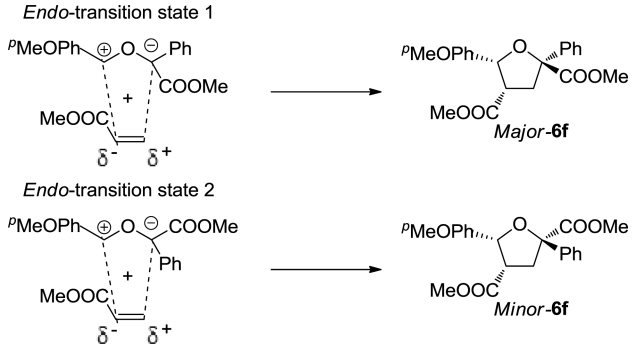
Scheme 2. Trapping the Carbonyl Ylide with Acrylonitrile 3h



Scheme 3. A Plausible *Endo*-Type Dipolar Cycloaddition Mechanism To Provide THF Cycloadducts in High Regio- and Diastereoselectivities



To a solution of IPrAgCl/AgOTf (5 mol %) in dry $CHCl_3$ (2 mL) was added 50 mg of activated 4 Å MS and diethyl acetylenedicarboxylate **3a** (71 mg, 0.5 mmol). Three minutes later, a solution of phenyldiazoacetate **1a** (35.2 mg, 0.2 mmol) and benzaldehyde 2a (10.6 mg, 0.1 mmol) in $CHCl_3$ (1 mL) was added via syringe pump in 2 h. The reaction was stirred at rt until complete consumption of the starting material **2a** with TLC monitoring. Then, the reaction mixture was concentrated in vacuum, and the residue was purified by flash chromatography over silica gel column using hexane/EtOAc (20/1) as the eluent to afford **4a** (36 mg, 91% yield) as a colorless oil.

3,4-Diethyl 2-Methyl (2S,5R*)-2,5-Diphenyl-2,5-dihydrofuran-2,3,4-tricarboxylate* ***4a.*** Obtained as a colorless oil in 91% yield (36 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54−7.51 (m, 2H), 7.40−7.32 (m, 8H), 6.24 (s, 1H), 4.25 (q, J = 7.1 Hz, 2H), 4.13−4.06 (m, 2H), 3.86 (s, 3H), 1.24, 1.09 (2 t, J = 7.1 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.3, 162.3, 161.8, 140.1, 138.9, 137.3, 129.1, 128.9, 128.2, 128.1, 127.2, 94.6, 87.9, 61.8, 61.5, 53.1, 13.9, 13.8. IR (neat, cm^{-1}): 3132, 3034, 2987, 2073, 1747, 1732, 1660, 1398, 1371, 1261, 1151, 1118, 1064, 1028, 975, 862, 754, 698, 545, 418; HRMS (ESI) Calcd for $C_{24}H_{24}O_7Na$ [M + Na]$^+$: 447.1420; Found: 447.1395.

3,4-Diethyl 2-Methyl (2S,5R*)-2-Phenyl-5-(p-tolyl)-2,5-dihydrofuran-2,3,4-tricarboxylate* ***4b.*** Obtained as a colorless solid in 93% yield (40 mg); mp 68−70 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.53−7.51 (m, 2H), 7.38−7.35 (m, 3H), 7.24 (d, J = 8.0 Hz, 2H), 7.15 (d, J = 7.9 Hz, 2H), 6.21 (s, 1H), 4.24 (q, J = 7.1 Hz, 2H), 4.10 (q, J = 7 Hz, 2H), 3.86, 2.34 (2 s, 6H), 1.24 (t, J = 7.2 Hz, 3H), 1.11 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.4, 162.4, 161.9, 140.1, 138.9, 138.7, 137.3, 134.3, 129.2, 128.8, 128.2, 128.1, 127.2, 94.5, 87.8, 61.8, 61.5, 53.1, 21.3, 13.9, 13.8; IR (neat, cm^{-1}): 3132, 3008, 2073, 1732, 1608, 1400, 1261, 1149, 1120, 1028, 979, 860, 698; HRMS (ESI) Calcd for $C_{25}H_{26}O_7Na$ [M + Na]$^+$: 461.15762; Found: 461.15608.

3,4-Diethyl 2-Methyl (2S,5R*)-5-(4-Methoxyphenyl)-2-phenyl-2,5-dihydrofuran-2,3,4-tricarboxylate* ***4c.*** Obtained as a colorless oil in 96% yield (43.5 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.52−7.49 (m, 2H), 7.37−7.34 (m, 3H), 7.27, 6.86 (2 d, J = 8.7 Hz, 4H), 6.19 (s, 1H), 4.24 (q, J = 7.1 Hz, 2H), 4.13−4.06 (m, 2H), 3.86, 3.79 (2 s, 6H), 1.23 (t, J = 7.2 Hz, 3H), 1.11 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.3, 162.3, 162.0, 160.1, 140.1, 138.6, 137.3, 129.6, 129.4, 128.8, 128.1, 127.1, 113.9, 94.4, 87.5, 61.8, 61.5, 55.3, 53.1, 13.8. IR (neat, cm^{-1}): 3170, 2958, 2360, 2069, 1732, 1612, 1514, 1396, 1251, 1176, 1029, 975, 837, 698, 543; HRMS (ESI) Calcd for $C_{25}H_{26}O_8Na$ [M + Na]$^+$: 477.1525; Found: 477.1505.

3,4-Diethyl 2-Methyl (2S,5R*)-5-(4-(Benzyloxy)phenyl)-2-phenyl-2,5-dihydrofuran-2,3,4-tricarboxylate* ***4d.*** Obtained as a colorless oil in 94% yield (50 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.52−7.50 (m, 2H), 7.41−7.34 (m, 7H), 7.31−7.26 (m, 3H), 6.93(d, J = 8.5 Hz, 2H), 5.03 (s, 2H), 4.23 (q, J = 7.1 Hz, 2H), 4.11−4.06 (m, 2H), 3.84 (s, 3H), 1.22, 1.08 (2 t, J = 7.1 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.3, 162.3, 162.0, 159.4, 140.1, 138.7, 137.4, 136.8, 129.7, 128.8, 128.6, 128.1, 128.0, 127.5, 127.2, 114.9, 94.4, 87.6, 70.0, 61.8, 61.5, 53.5, 53.1, 13.9, 13.8; IR (neat, cm^{-1}): 2983, 2360, 2343, 1745, 1716, 1600, 1514, 1454, 1369, 1259, 1176, 1024, 975, 835, 746, 698; HRMS (ESI) Calcd for $C_{31}H_{30}O_8Na$ [M + Na]$^+$: 553.1838; Found: 553.1818.

3,4-Diethyl 2-Methyl (2S,5R*)-2-Phenyl-5-(o-tolyl)-2,5-dihydrofuran-2,3,4-tricarboxylate* ***4e.*** Obtained as a colorless solid in 75% yield (33 mg); mp 64−66 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49−7.47 (m, 2H), 7.36−7.33 (m, 3H), 7.22−7.14 (m, 4H), 6.54 (s, 1H), 4.26 (q, J = 7.1 Hz, 2H), 4.10 (q, J = 7.3 Hz, 2H), 3.87, 2.51 (2 s, 6H), 1.25, 1.09 (2 t, J = 7.1 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.4, 162.4, 162.0, 140.2, 139.3, 137.1, 135.5, 130.6, 128.9, 128.7, 128.1, 127.2, 126.2, 94.5, 83.9, 61.8, 61.5, 53.1, 19.3, 13.9, 13.8. IR (neat, cm^{-1}): 3126, 2983, 2848, 2358, 2330, 1738, 1658, 1400, 1267, 1153, 1020, 740, 698; HRMS (ESI) Calcd for $C_{25}H_{26}O_7Na$ [M + Na]$^+$: 461.15762; Found: 461.15618.

3,4-Diethyl 2-Methyl (2S,5R*)-2-Phenyl-5-(m-tolyl)-2,5-dihydrofuran-2,3,4-tricarboxylate* ***4f.*** Obtained as a colorless solid in 81% yield (35.5 mg); mp 67−70 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54−7.52 (m, 2H), 7.40−7.35 (m, 3H), 7.25−7.21 (m, 1H), 7.16−7.13 (m, 3H), 6.21 (s, 1H), 4.25 (q, J = 7.2 Hz, 2H), 4.14−4.08 (m, 2H), 3.86, 2.31 (2 s, 6H), 1.24, 1.11 (2 t, J = 7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.3, 162.3, 161.9, 140.2, 138.7, 138.1, 137.4, 137.1, 129.8, 129.0, 128.8, 128.4, 128.1, 127.2, 125.2, 94.6, 88.0, 61.8, 61.5, 53.1, 21.4, 13.9, 13.8; IR (neat, cm^{-1}): 2983, 2954, 1747, 1732, 1716, 1660, 1448, 1369, 1257, 1026, 975, 833, 773, 748, 698; HRMS (ESI) Calcd for $C_{25}H_{26}O_7Na$ [M + Na]$^+$: 461.15762; Found: 461.15531.

3,4-Diethyl 2-Methyl (2S,5R*)-5-(4-Hydroxyphenyl)-2-phenyl-2,5-dihydrofuran-2,3,4-tricarboxylate* ***4g.*** Obtained as a colorless oil in 20% yield (8.8 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51−7.48 (m, 2H), 7.38−7.35 (m, 3H), 7.22 (d, J = 8.4 Hz, 2H), 6.77 (d, J = 8.5 Hz, 2H), 6.17 (s, 1H), 4.91 (s, 1H), 4.24 (q, J = 7.1 Hz, 2H), 4.13−4.07 (m, 2H), 3.86 (s, 3H), 1.23, 1.11 (2 t, J = 7.1 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.3, 162.3, 162.0, 156.2, 140.1, 138.7, 137.3, 129.8, 129.6, 128.8, 128.1, 127.1, 115.4, 94.4, 87.5, 61.8, 61.5, 53.0, 29.7, 13.8, 13.7. IR (neat, cm^{-1}): 3439, 3383, 3157, 3130, 2924, 2357, 1726, 1612, 1597, 1444, 1402, 1265, 1138, 1066, 950, 912, 854; HRMS (ESI) Calcd for $C_{24}H_{24}O_8Na$ [M + Na]$^+$: 463.1369; Found: 463.1345.

3,4-Diethyl 2-Methyl (2S,5R*)-5-(4-(2-Methoxy-2-oxo-1-phenylethoxy)phenyl)-2-phenyl-2,5-dihydrofuran-2,3,4-tricarboxylate* ***4gs.*** Obtained as a colorless oil in 26% yield (15 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56 (d, J = 7.2 Hz, 2H), 7.50−7.48 (m, 2H), 7.41−7.36 (m, 6H), 7.27−7.25 (m, 2H), 6.91 (s, J = 8.6 Hz, 2H), 6.17 (s, 1H), 5.63 (s, 1H), 4.26−4.21 (m, 2H), 4.13−4.05 (m, 2H), 3.86, 3.73 (2 s, 6H), 1.25−1.22 (m, 3H), 1.08 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.2, 162.3, 161.8, 157.8, 140.0, 138.7, 137.3, 135.1, 130.7,

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129.7, 129.1, 128.8, 128.1, 127.1, 127.0, 115.5, 115.4, 94.4, 87.3, 61.8, 61.5, 53.1, 32.7, 13.8, 13.7. IR (neat, cm^{-1}): 3062, 2983, 2360, 2343, 1738, 1610, 1512, 1265, 1238, 1024, 732, 698; HRMS (ESI) Calcd for $C_{33}H_{32}O_{10}Na$ $[M + Na]^+$: 611.1893; Found: 611.1876.

3,4-Diethyl 2-Methyl (2S,5R*)-5-(4-Bromophenyl)-2-phenyl-2,5-dihydrofuran-2,3,4-tricarboxylate* ***4h.*** Obtained as a colorless oil in 70% yield (35 mg); ^1H NMR (400 MHz, $CDCl_3$): δ 7.50−7.45 (m, 4H), 7.40−7.37 (m, 3H), 7.21 (d, J = 8.4 Hz, 2H), 6.19 (s, 1H), 4.25 (q, J = 7.1 Hz, 2H), 4.15−4.07 (m, 2H), 3.86 (s, 3H), 1.24, 1.13 (2 t, J = 7.1 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.0, 162.3, 161.5, 139.5, 139.1, 137.1, 136.5, 131.7, 129.8, 129.0, 128.2, 127.1, 123.2, 94.8, 87.2, 61.9, 61.7, 53.2, 13.9, 13.8; IR (neat, cm^{-1}): 3132, 2953, 2073, 1732, 1608, 1400, 1271, 1230, 1172, 1157, 1056, 995, 860, 698, 547; HRMS (ESI) Calcd for $C_{24}H_{23}O_7BrNa$ $[M + Na]^+$: 525.05249, 527.0504; Found: 525.05072, 527.04820.

3,4-Diethyl 2-Methyl (2S,5R*)-5-(4-Fluorophenyl)-2-phenyl-2,5-dihydrofuran-2,3,4-tricarboxylate* ***4i.*** Obtained as a colorless solid in 74% yield (33 mg); mp 65−67 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 7.51−7.49 (m, 2H), 7.39−7.37 (m, 3H), 7.34−7.30 (m, 2H), 7.02 (t, J = 8.6 Hz, 2H), 6.22 (s, 1H), 4.25 (q, J = 7.1 Hz, 2H), 4.11 (m, 2H), 3.86 (s, 3H), 1.24 (t, J = 7.2 Hz, 3H), 1.11 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.1, 164.3, 162.3, 161.9, 161.6, 139.5, 139.2, 137.1, 133.3, 130.1, 130.0, 128.9, 128.2, 127.1, 115.6, 115.4, 94.6, 87.1, 61.9, 61.6, 53.1, 13.8, 13.7; IR (neat, cm^{-1}): 2983, 2954, 1738, 1660, 1606, 1510, 1369, 1315, 1263, 1224, 1014, 977, 842, 829, 698, 532; HRMS (ESI) Calcd for $C_{24}H_{23}FO_7Na$ $[M + Na]^+$: 465.13255; Found: 465.13083.

3,4-Diethyl 2-Methyl (2S,5R*)-5-(4-Nitrophenyl)-2-phenyl-2,5-dihydrofuran-2,3,4-tricarboxylate cis-***4j.** Obtained as a colorless oil in 35% yield (16.5 mg); ^1H NMR (400 MHz, $CDCl_3$): δ 8.18 (d, J = 8.7 Hz, 2H), 7.50−7.48 (m, 4H), 7.42−7.40 (m, 3H), 6.32 (s, 1H), 4.27 (q, J = 7.1 Hz, 2H), 4.17−4.08 (m, 2H), 3.87 (s, 3H), 1.26, 1.15 (2 t, J = 7.1 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.7, 162.2, 161.1, 148.2, 144.5, 140.4, 138.2, 136.8, 129.3, 129.0, 128.4, 127.1, 123.7, 95.3, 86.6, 62.2, 61.9, 53.3, 13.9, 13.8; IR (neat, cm^{-1}): 2922, 1732, 1448, 1369, 1313, 1265, 1020, 975, 736, 698; HRMS (ESI) Calcd for $C_{24}H_{23}NO_9Na$ $[M + Na]^+$: 492.12705; Found: 492.12480.

3,4-Diethyl 2-Methyl (2R,5R*)-5-(4-Nitrophenyl)-2-phenyl-2,5-dihydrofuran-2,3,4-tricarboxylate trans-***4j.** Obtained as a colorless oil in 23% yield (11 mg); ^1H NMR (400 MHz, $CDCl_3$): δ 8.25, 7.74 (2 d, J = 8.7 Hz, 4H), 7.52−7.49 (m, 2H), 7.44−7.39 (m, 3H), 6.24 (s, 1H), 4.29, 4.10 (2 q, J = 7.1 Hz, 4H), 3.87 (s, 3H), 1.28, 1.12 (2 t, J = 7.1 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.3, 161.9, 161.2, 148.3, 144.5, 139.6, 137.9, 137.4, 129.0, 128.5, 126.4, 123.7, 94.8, 87.1, 62.2, 61.9, 53.3, 29.7, 13.9, 13.8; IR (neat, cm^{-1}): 3124, 2991, 2358, 2341, 1728, 1523, 1412, 1350, 1265, 1151, 1120, 1066, 858, 746, 696; HRMS (ESI) Calcd for $C_{24}H_{23}NO_9Na$ $[M + Na]^+$: 492.12705; Found: 492.12480.

3,4-Diethyl 2-Methyl (2S,5R*)-5-(Anthracen-9-yl)-2-phenyl-2,5-dihydrofuran-2,3,4-tricarboxylate* ***4k.*** Obtained as a colorless oil in 46% yield (24 mg); ^1H NMR (400 MHz, $CDCl_3$): δ 8.51 (s, 1H), 8.46 (br, 2H), 8.01 (d, J = 8.8 Hz, 2H), 7.73 (s, 1H), 7.68−7.65 (m, 2H), 7.44 (br, 2H), 7.37−7.36 (m, 3H), 4.34 (q, J = 7.1 Hz, 2H), 3.97 (s, 3H), 3.84−3.75 (m, 2H), 1.31 (t, J = 7.1 Hz, 3H), 1.28−1.22 (m, 2H), 0.60 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.3, 162.7, 161.6, 143.0, 138.1, 136.0, 131.5, 130.2, 129.2, 128.9, 128.1, 127.3, 125.5, 124.9, 93.6, 82.0, 61.9, 61.2, 53.2, 13.9, 13.2; IR (neat, cm^{-1}): 3126, 3111, 1728, 1404, 1396, 1255, 1018, 975, 732, 700; HRMS (ESI) Calcd for $C_{32}H_{28}O_7Na$ $[M + Na]^+$: 547.17327; Found: 547.17068.

3,4-Diethyl 2-Methyl (2S,5R*)-5-(9H-Fluoren-1-yl)-2-phenyl-2,5-dihydrofuran-2,3,4-tricarboxylate* ***4m.*** Obtained as a colorless oil in 81% yield (41.4 mg); ^1H NMR (400 MHz, $CDCl_3$): δ 7.77 (t, J = 7.4 Hz, 2H), 7.58−7.53 (m, 4H), 7.43−7.38 (m, 5H), 7.31 (td, J = 7.4, 0.9 Hz, 1H), 6.34 (s, 1H), 4.29 (q, J = 7.1 Hz, 2H), 4.14−4.08 (m, 2H), 3.89, 3.87 (2 s, 6H), 1.27, 1.11 (2 t, J = 7.1 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.3, 162.4, 161.9, 143.6, 143.5, 142.6, 141.2, 140.1, 138.9, 137.3, 135.7, 128.9, 128.2, 127.2, 127.1, 126.8, 125.1, 125.0, 120.1, 119.9, 94.6, 88.2, 61.9, 61.6, 53.1, 36.9, 13.9, 13.8; IR (neat, cm^{-1}): 3126, 3005, 2071, 1732, 1660, 1400, 1371, 1265, 1151, 1028, 975, 860, 767, 736, 698; HRMS (ESI) Calcd for $C_{31}H_{28}O_7Na$ $[M + Na]^+$: 535.17327; Found: 535.17170.

3,4-Diethyl 2-Methyl (2S,5R*)-2-Phenyl-5-((E)-styryl)-2,5-dihydrofuran-2,3,4-tricarboxylate* ***4n.*** Obtained as a colorless oil in 71% yield (32 mg); ^1H NMR (400 MHz, $CDCl_3$): δ 7.52 (dd, J = 8.1, 1.8 Hz, 2H), 7.41−7.28 (m, 7H), 7.25−7.23 (m, 1H), 6.72 (d, J = 15.7 Hz, 2H), 6.23 (q, J = 7.6 Hz, 2H), 5.87 (d, J = 7.6 Hz, 1H), 4.22 (quint, J = 7.3 Hz, 4H), 3.85 (s, 3H), 1.25, 1.21 (2 t, J = 7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.1, 162.2, 161.9, 139.1, 138.4, 137.7, 136.0, 134.9, 128.9, 128.6, 128.3, 128.2, 127.1, 126.9, 124.9, 94.7, 86.7, 61.8, 53.1, 14.0, 13.8; IR (neat, cm^{-1}): 3176, 2983, 2355, 1745, 1732, 1660, 1448, 1371, 1265, 1155, 1026, 966, 860, 748, 696; HRMS (ESI) Calcd for $C_{26}H_{26}O_7Na$ $[M + Na]^+$: 473.15762; Found: 473.15517.

3,4-Diethyl 2-Methyl (2S,5R*)-5-(4-Methoxyphenyl)-2-(p-tolyl)-2,5-dihydrofuran-2,3,4-tricarboxylate* ***5b.*** Obtained as a colorless oil in 96% yield (44.7 mg); ^1H NMR (400 MHz, $CDCl_3$): δ 7.40 (d, J = 8.2 Hz, 2H), 7.28 (d, J = 8.6 Hz, 2H), 7.18 (d, J = 8.1 Hz, 2H), 6.86 (d, J = 8.6 Hz, 2H), 6.19 (s, 1H), 4.25(q, J = 7.1 Hz, 2H), 4.13−4.06 (m, 2H), 3.84, 3.77 (2 s, 6H), 2.34 (s, 3H), 1.25 (t, J = 7.2 Hz, 3H), 1.11 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.5, 162.4, 162.0, 160.1, 139.9, 138.7, 138.6, 134.5, 129.6, 129.5, 128.8, 127.1, 113.8, 94.4, 87.4, 61.7, 61.5, 55.2, 53.0, 21.2, 13.9, 13.8; IR (neat, cm^{-1}): 3130, 2985, 2358, 2067, 1728, 1660, 1612, 1514, 1412, 1249, 1174, 1029, 975, 835, 819, 538; HRMS (ESI) Calcd for $C_{26}H_{28}O_8Na$ $[M + Na]^+$: 491.16819; Found: 491.16674.

Triethyl (2S,5R*)-2-(4-Ethoxyphenyl)-5-(4-methoxyphenyl)-2,5-dihydrofuran-2,3,4-tricarboxylate* ***5c.*** Obtained as a colorless oil in 99% yield (50.5 mg); ^1H NMR (400 MHz, $CDCl_3$): δ 7.42 (d, J = 8.8 Hz, 2H), 7.28−7.26 (m, 2H), 6.86 (t, J = 7.9 Hz, 4H), 6.15 (s, 1H), 4.32 (q, J = 7.0 Hz, 2H), 4.27−4.18 (m, 2H), 4.12−4.07 (m, 2H), 4.03 (q, J = 7.0 Hz, 2H), 3.79 (s, 3H), 1.40 (t, J = 7.0 Hz, 3H), 1.31, 1.24, 1.11 (3 t, J = 7.1 Hz, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.9, 162.5, 162.1, 160.0, 159.2, 140.0, 138.8, 129.6, 129.5, 128.6, 113.9, 113.8, 94.1, 87.2, 63.4, 62.2, 61.7, 61.4, 55.2, 14.8, 14.1, 13.9; IR (neat, cm^{-1}): 3126, 2981, 2073, 1737, 1732, 1610, 1514, 1396, 1251, 1180, 1111, 1029, 983, 835, 806, 543; HRMS (ESI) Calcd for $C_{28}H_{32}O_9Na$ $[M + Na]^+$: 535.19440; Found: 535.19216.

Triethyl (2S,5R*)-5-(4-Methoxyphenyl)-2-(thiophen-2-yl)-2,5-dihydrofuran-2,3,4-tricarboxylate* ***5d.*** Obtained as a colorless oil in 86.5% yield (41 mg); ^1H NMR (400 MHz, $CDCl_3$): δ 7.35−7.33(m, 3H), 7.24 (dd, J = 3.6, 1.0 Hz, 1H), 7.01−6.99 (m, 1H), 6.88(d, J = 8.7 Hz, 2H), 6.16 (s, 1H), 4.35 (q, J = 7.1 Hz, 2H), 4.28−4.20 (m, 2H), 4.09 (q, J = 6.9 Hz, 2H), 3.80 (s, 3H), 1.35 (t, J = 7.2 Hz, 3H), 1.25, 1.10 (2 t, J = 7.1 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.6, 162.0, 161.7, 160.2, 140.9, 140.4, 137.6, 129.8, 129.0, 127.0, 126.7, 113.8, 91.3, 87.8, 62.6, 61.7, 61.5, 55.3, 14.1, 13.9, 13.8; IR (neat, cm^{-1}): 3205, 3084, 2983, 1732, 1610, 1514, 1369, 1251, 1176, 1028, 979, 835, 711; HRMS (ESI) Calcd for $C_{24}H_{26}O_8SNa$ $[M + Na]^+$:497.12461; Found: 497.12162.

(2S,5R*)-3,4-Diethyl 2-Methyl 5-(4-Methoxyphenyl)-2-(naphthalen-2-yl)-2,5-dihydrofuran-2,3,4-tricarboxylate* ***5e.*** Obtained as a colorless solid in 93% yield (47 mg); mp 101−103 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 8.03−8.01 (m, 1H), 7.98−7.96 (m, 1H), 7.88−7.83 (m, 2H), 7.52 (t, J = 7.6 Hz, 1H), 7.45−7.43 (m, 2H), 7.06, 6.68 (2 d, J = 8.7 Hz, 4H), 6.39 (s, 1H), 4.33−4.24 (m, 2H), 4.19−4.10 (m, 2H), 3.69 (d, J = 8.5 Hz, 6H), 1.27, 1.17 (2 t, J = 7.1 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ172.0, 163.4, 159.7, 140.5, 139.8, 135.3, 134.1, 130.9, 130.2, 129.9, 129.2, 128.8, 126.5, 126.1, 125.7, 124.9, 124.8, 113.6, 95.5, 88.6, 62.3, 61.6, 55.2, 53.2, 13.9, 13.8; IR (neat, cm^{-1}): 3170, 2985, 2358, 1732, 1612, 1514, 1394, 1369, 1251, 1174, 1029, 993, 860, 821, 750, 543; HRMS (ESI) Calcd for $C_{29}H_{28}O_8Na$ $[M + Na]^+$: 527.16819; Found: 527.16654.

Triethyl (2R,5R*)-5-(4-Methoxyphenyl)-2-(1-oxo-1H-isochromen-3-yl)-2,5-dihydrofuran-2,3,4-tricarboxylate* ***5f.*** Obtained as a colorless oil in 82% yield (44 mg); ^1H NMR (400 MHz, $CDCl_3$): δ 8.28(d, J = 7.9 Hz, 1H), 7.70 (t, J = 7.3 Hz, 1H), 7.53 (t, J = 7.5 Hz, 1H), 7.43−7.40 (m, 3H), 6.89 (d, J = 8.6 Hz, 2H), 6.72, 6.18 (2 s, 2H), 4.37, 4.29 (2 q, J = 7.1 Hz, 4H), 4.14−4.08 (m, 2H), 3.79 (s, 3H), 1.35, 1.25, 1.12 (3 t, J = 7.1 Hz, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.4, 161.5, 161.4, 161.1, 160.4, 151.5, 141.0, 136.2, 135.7, 134.8, 129.8, 129.7, 129.0, 128.9, 126.5, 121.1, 114.0, 105.5, 91.8, 88.7, 62.9, 62.1, 61.7, 55.3, 14.1, 13.9, 13.8; IR (neat, cm^{-1}): 3124, 2983, 2349, 1747, 1732, 1610,

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1514, 1400, 1249, 1031, 999, 835, 759, 736, 688; HRMS (ESI) Calcd for $C_{29}H_{28}O_{10}Na$ [M + Na]$^+$: 559.15802; Found: 559.15543.

Methyl (1R,3S*,3aR*,6aS*)-3-(4-Methoxyphenyl)-4,6-dioxo-1-phenyltetrahydro-1H,3H-furo[3,4-c]furan-1-carboxylate* ***6b***. Obtained as a colorless oil in 58% yield (22.2 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.61−7.60 (m, 2H), 7.50−7.44 (m, 3H), 7.38, 6.99 (2 d, J = 8.6 Hz, 4H), 5.27 (d, J = 8.0 Hz, 1H), 4.77 (d, J = 8.4 Hz, 1H), 3.93−3.87 (m, 1H), 3.84, 3.81 (2 s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.2, 167.7, 167.5, 160.2, 133.4, 129.3, 128.7, 127.4, 125.9, 125.2, 114.2, 90.4, 81.7, 55.3, 54.0, 53.6, 51.9; IR (neat, cm^{-1}): 3126, 3030, 2358, 2341, 1788, 1732, 1614, 1516, 1402, 1138, 1068, 935, 856, 746, 667, 617; HRMS (ESI) Calcd for $C_{21}H_{18}O_7Na$ [M + Na]$^+$: 405.09502; Found: 405.09309.

Methyl (1R,3S*,3aR*,6aS*)-3-(4-Methoxyphenyl)-4,6-dioxo-1-phenylhexahydro-1H-furo[3,4-c]pyrrole-1-carboxylate* ***6c***. Obtained as a colorless oil in 54% yield (20.7 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.17 (br, 1H), 7.77−7.75 (m, 2H), 7.48−7.43 (m, 4H), 7.40−7.38 (m, 1H), 6.94 (d, J = 8.8 Hz, 2H), 5.53 (d, J = 7.2 Hz, 1H), 3.90−3.84 (m, 2H), 3.83, 3.69 (2 s, 6H), 3.57−3.52 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.2, 174.5, 170.6, 159.7, 139.2, 131.1, 128.4, 127.3, 125.9, 114.2, 89.4, 81.8, 58.4, 56.0, 55.4, 53.3; IR (neat, cm^{-1}): 3259, 2924, 2358, 1722, 1716, 1614, 1516, 1251, 1174, 1029, 825, 738, 702; HRMS (ESI) Calcd for $C_{21}H_{19}NO_6Na$ [M + Na]$^+$: 404.11101; Found: 404.10894.

4-Ethyl 2-Methyl (2R,5R*)-5-(4-Methoxyphenyl)-2-phenyl-2,5-dihydrofuran-2,4-dicarboxylate* ***6d***. Obtained as a colorless oil in 63% yield (23.9 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.53−7.51 (m, 2H), 7.40−7.34 (m, 3H), 7.25 (d, J = 2.2 Hz, 1H), 7.11 (d, J = 8.7 Hz, 2H), 6.78 (d, J = 8.6 Hz, 2H), 6.15(d, J = 2.1 Hz, 1H), 4.13−4.03 (m, 2H), 3.77 (d, J = 3.6 Hz, 6H), 1.16 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.4, 162.1, 159.7, 139.1, 138.4, 137.2, 131.1, 129.3, 128.7, 128.5, 125.8, 113.6, 93.2, 87.8, 61.0, 55.2, 53.0, 14.0; IR (neat, cm^{-1}): 3203, 3064, 2358, 1755, 1716, 1612, 1514, 1248, 1109, 1031, 831, 756, 731, 698; HRMS (ESI) Calcd for $C_{22}H_{22}O_6Na$ [M + Na]$^+$: 405.13141; Found: 405.12903.

Methyl (2R,5R*)-4-Acetyl-5-(4-methoxyphenyl)-2-phenyl-2,5-dihydrofuran-2-carboxylate* ***6e***. Obtained as a colorless oil in 55% yield (19.4 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.55−7.53 (m, 2H), 7.42−7.35 (m, 3H), 7.15 (d, J = 2 Hz, 1H), 7.11, 6.79 (2 d, J = 8.7 Hz, 4H), 6.19(d, J = 2 Hz, 1H), 3.77 (d, J = 7.6 Hz, 6H), 2.28 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 193.8, 171.4, 171.2, 159.7, 144.1, 142.9, 139.0, 138.2, 131.0, 129.2, 129.1, 128.7, 128.5, 128.2, 127.8, 127.5, 125.6, 114.1, 113.7, 93.2, 87.9, 87.0, 60.4, 55.3, 55.2, 53.1, 52.9, 28.2, 28.0, 21.1, 14.2; IR (neat, cm^{-1}): 2954, 2839, 1749, 1732, 1681, 1610, 1514, 1369, 1247, 1091, 1029, 904, 827, 734, 698; HRMS (ESI) Calcd for $C_{21}H_{20}O_5Na$ [M + Na]$^+$: 375.12084; Found: 375.11932.

Dimethyl (2R,4R*,5S*)-5-(4-Methoxyphenyl)-2-phenyltetrahydrofuran-2,4-dicarboxylate* ***6f***. Obtained as a colorless oil in 77% yield (28.5 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.64−7.62 (m, 2H), 7.42−7.34 (m, 3H), 7.18, 6.81 (2 d, J = 8.7 Hz, 4H), 5.48 (d, J = 9.3 Hz, 1H), 3.76, 3.73 (2 s, 6H), 3.61−3.55 (m, 1H), 3.20 (s, 3H), 3.18−3.15 (m, 1H), 2.73−2.68 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.7, 171.2, 159.4, 139.8, 130.3, 128.4, 128.1, 125.5, 113.3, 87.9, 82.0, 55.2, 53.0, 51.6, 49.6, 38.4; IR (neat, cm^{-1}): 3176, 3151, 3103, 2347, 1732, 1612, 1514, 1408, 1392, 1249, 1172, 975, 840, 700, 621; HRMS (ESI) Calcd for $C_{21}H_{22}O_6Na$ [M + Na]$^+$: 393.13141; Found: 393.13013.

Methyl (2R,4R*,5S*)-5-(4-Methoxyphenyl)-2-phenyl-4-propionyltetrahydrofuran-2-carboxylate* ***6g***. Obtained as a colorless oil in 70% yield (25.7 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.61−7.59 (m, 2H), 7.40−7.32 (m, 3H), 7.15, 6.81 (2 d, J = 8.7 Hz, 4H), 5.47 (d, J = 9.3 Hz, 1H), 3.76, 3.63 (2 s, 6H), 3.70−3.66 (m, 1H), 3.08−3.03 (m, 1H), 2.81−2.76 (m, 1H), 2.03−1.87 (m, 2H), 0.57 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 208.2, 173.9, 159.6, 139.9, 130.0, 128.6, 128.4, 128.0, 125.5, 113.7, 87.6, 82.0, 55.7, 55.2, 53.0, 38.0, 37.2, 7.2; IR (neat, cm^{-1}): 3124, 2953, 2839, 1732, 1714, 1612, 1514, 1448, 1400, 1257, 1174, 1070, 1029, 972, 835, 731, 700; HRMS (ESI) Calcd for $C_{22}H_{24}O_5Na$ [M + Na]$^+$: 391.15214; Found: 391.14981.

Methyl (2R,4S*,5S*)-4-Cyano-5-(4-methoxyphenyl)-2-phenyltetrahydrofuran-2-carboxylate endo-***6h**. Obtained as a colorless oil in 52% yield (17.5 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.61−7.59 (m, 2H), 7.44−7.35 (m, 5H), 6.93 (d, J = 8.7 Hz, 2H), 5.28 (d, J = 6.9 Hz, 1H), 3.80, 3.73 (2 s, 6H), 3.58−3.46 (m, 2H), 2.65−2.61 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.8, 160.0, 139.0, 128.7, 128.5, 127.8, 125.2, 118.3, 114.0, 87.2, 81.3, 55.3, 53.3, 41.0, 36.3; IR (neat, cm^{-1}): 2954, 2922, 2358, 2330, 1732, 1612, 1514, 1448, 1251, 1174, 1068, 1031, 912, 837, 731, 698; HRMS (ESI) Calcd for $C_{20}H_{19}NO_4Na$ [M + Na]$^+$: 360.12118; Found: 360.12009.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b02422.

X-ray structure for compound **5e**; NOESY spectral data for **4c**, *cis*/*trans*-**4j**, **6a**, and **6e**; and copies of ^{1}H and ^{13}C NMR spectra for all new compounds (PDF)

Crystallographic data for **5e** (CIF)

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Notes

The authors declare no competing financial interest.

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(12) X-ray structure for **5e**; NOESY spectral data for **4c**, *cis*/*trans*-**4j**, **6b**, and **6f**; and the detailed reaction procedure are provided in the Supporting Information. The relative stereochemistry of **6b−c** and **6f−g** was deduced from NOESY spectral data for **6b** and **6f**.

(13) In Rh(III) mediated α-alkyl diazoester's carbonyl ylide cycloaddition reaction, the *endo*-type transition state provides the *trans*-configuration product, due to the presence of the α-alkyl group.

(14) The cycloadduct **4g** could be trapped by **1a** in the condition of Ag(I) catalyst to give OH insertion product **4gs**. See the Supporting Information for the details.

(15) The asynchronous transition state was first proposed in Rh(III) mediated carbonyl ylide cycloaddition reaction; see ref 4b.

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