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# Tandem $S_N2$-Michael addition to vinylogous carbonates for the stereoselective construction of 2,3,3,5-tetrasubstituted tetrahydrofurans

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ABSTRACT

A stereoselective method for the synthesis of substituted tetrahydrofuran derivatives employing a tandem alkylation-Michael addition sequence to vinylogous carbonates is developed. The method could be used to synthesize THFs bearing tertiary ethers. Further, the method is extended to the synthesis of adjacent bis-THFs.



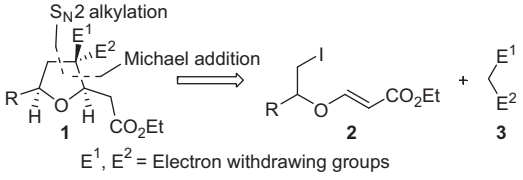
## 1. Introduction

The tetrahydrofuran (THF) moiety is present in a variety of natural products with important biological activity and this has provided impetus to the research directed at new methods for the synthesis of THF derivatives.[1] Vinylogous carbonates or β-(alkoxy)acrylates have been proven to be excellent radical acceptors. As a result, a large number of methods have been developed for the construction of THF derivatives using alkyl and acyl radical cyclization to vinylogous carbonates under a variety of conditions.[2] Recently, our group has utilized alkyl radical cyclization to vinylogous carbonates for the stereoselective synthesis of new oxa-cage compounds.[3] In contrast, vinylogous carbonates have been sparingly used for the synthesis of THFs under non-radical conditions. Recently, examples have shown that vinylogous carbonates participate in intramolecular Michael additions involving carbanion intermediates—most notable being the use of Stetter reaction for the synthesis of THFs.[4] We have developed a stereoselective intramolecular cyclopropanation of vinylogous carbonates using carbenes for the construction of donor–acceptor cyclopropafuranones which were converted into THF derivatives by opening the cyclopropane ring under radical conditions.[5] However, in general, the utility of vinylogous carbonates as Michael acceptors under non-radical conditions for the synthesis of THFs is still largely underdeveloped.

Over the years, tandem reactions have proved to be an effective tool in developing the environmentally benign processes since they generate several bonds in a 'single pot' operation thereby minimizing the amount of waste that is generated.[6] Recently, a stereoselective synthesis of 1,2,2-trisubstituted indane derivatives employing a tandem $S_N2$-Michael addition sequence was reported from our lab.[7] In a program directed at the synthesis of cyclic ethers using vinylogous carbonates, we used this tandem $S_N2$-alkylation-Michael addition to vinylogous carbonates for the stereoselective construction of THP derivatives.[8] Herein, we describe an extension of this approach to the stereoselective synthesis of 2,3,3,5-tetrasubstituted tetrahydrofurans.[9] This study further demonstrates that vinylogous carbonates are excellent acceptors in Michael addition even under non-radical conditions.

## 2. Results and discussion

It was envisaged that THF **1** can be assembled by reaction of the iodide **2** with the active methylene compound **3** in the presence of appropriate base via a tandem $S_N2$-Michael addition sequence (Scheme 1). The C3–C4 bond of the THF would be formed by alkylation reaction whereas the C2–C3 bond would




**Scheme 1.** Retrosynthesis for tetrasubstituted tetrahydrofurans.

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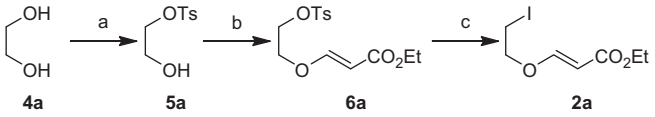
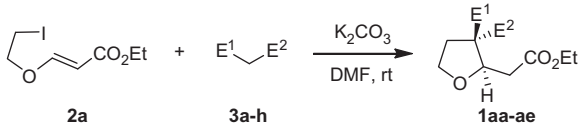



**Scheme 2.** Reagents, conditions, and yields: (a) TsCl, Py, $CH_2Cl_2$, 0 °C–rt, 12 h, 54%; (b) ethyl propiolate, NMM, $CH_2Cl_2$, rt, 3 h, 85%; (c) NaI, acetone, reflux, 12 h, 92%.

**Table 1**
Tandem alkylation-Michael addition for the synthesis of THFs: scope of the nucleophiles




| Entry | $E^1$ | $E^2$ | | Product | Time (h) | Yield (%) | dr[a] |
|---|---|---|---|---|---|---|---|
| 1 | CN | CN | **3a** | **1aa** | 3.5 | 79 | — |
| 2 | $CO_2Me$ | $CO_2Me$ | **3b** | **1ab** | 3.5 | 56 | — |
| 3 | CN | $CO_2Et$ | **3c** | **1ac** | 2.5 | 60 | 5:1 |
| 4 | CN | $SO_2Ph$ | **3d** | **1ad** | 12 | 71 | ⩾19:1 |
| 5 | $CO_2Me$ | $SO_2Ph$ | **3e** | **1ae** | 6.5 | 40 | ⩾19:1 |

[a] Determined on crude reaction mixtures by $^1H$ NMR.

be formed by the Michael addition of the active methylene moiety to the vinylogous carbonate.

To test the feasibility of the proposed THF synthesis, preparation of the iodide **2a** (R = H) was undertaken. Thus, ethylene glycol (**4a**) on monotosylation furnished the tosylate **5a** (Scheme 2). Michael addition of the alcohol **5a** to ethyl propiolate in the presence of *N*-methyl morpholine (NMM) resulted in the formation of the corresponding vinylogous carbonate **6a** in good yield. Displacement of tosyl group in the vinylogous carbonate **6a** with iodide using Finkelstein conditions resulted in the formation of the iodide **2a**.

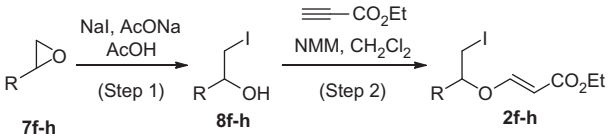
Having the requisite iodide **2a** in hand, attention was turned toward testing the feasibility of the proposed THF synthesis. Toward this end, the iodide **2a** was treated with malononitrile (**3a**) in DMF in the presence of $K_2CO_3$ at room temperature, which gratifyingly lead to the formation of 2,3,3-trisubstituted THF derivative **1aa** in excellent yield (Table 1, entry 1).[10,11] To study the scope of the nucleophiles, the reaction was carried out with a variety of active methylene compounds. The results are summarized in Table 1. Dimethyl malonate (**3b**) was also found to be a good nucleophile in this transformation leading to the formation of triester **1ab** in good yield (Table 1, entry 2). Even unsymmetrically substituted active methylene compounds could be used as nucleophiles for the synthesis of the THF derivatives. Thus, ethyl cyanoacetate (**3c**) on reaction with the iodide **2a** under optimized condition gave the THF **1ac** in good yield and moderate diastereoselectivity. On the other hand, when sulfone-nitrile **3d** and sulfone-ester **3e** were used as nucleophiles, the corresponding THF derivatives **1ad** and **1ae** were obtained in good yields with excellent diastereoselectivity.

The diastereoselectivity in these cases appears to be dependent on the relative bulk of the susbstituents on the active methylene compound—higher the difference in the relative bulk, higher the diastereoselectivity. The stereochemistry shown is on the basis that the bulkier substituents on the C2 and C3 would occupy the pseudo-equatorial orientation whereas the smaller substituents would occupy pseudo-axial positions.[7] It is also apparent that under the reaction conditions employed, the retro-oxy-Michael reaction is sufficiently slow allowing for the isolation of the THFs.

After establishing the scope of the reaction with different nucleophiles, we turned our attention to expand the scope of this strategy for the synthesis of 2,3,3,5-tetrasubstituted THF derivatives. The requisite iodides **2b–e** required for the study were prepared from the vicinal diols **4b–e** in a similar manner to that described for the iodide **2a**. Thus, monotosylation of the primary alcohols **4b–e** using tosyl chloride and catalytic dibutyltin oxide gave the tosylates **5b–e**, respectively, in good yields.[12] Reaction of the alcohols **5b–e** furnished the vinylogous carbonates **6b–e**, which upon displacement of tosyl group with iodide furnished the corresponding iodides **2b–e** in good overall yields. The reactions were uneventful and are summarized in the Table 2.

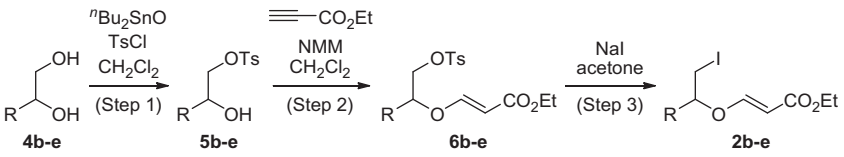
In another direction, the iodides **2f–h** were prepared from the epoxides **7f–h** by a shorter reaction sequence. In this strategy, the epoxides **7f–h** were opened with sodium iodide to the corresponding iodo-alcohols **8f–h** in acetic acid. The iodo-alcohols **8f–h** on reaction with ethyl propiolate in the presence of NMM furnished the corresponding vinylogous carbonates **2f–h** in excellent overall yields (Table 3).

**Table 3**
Synthesis of the iodide **2f–h** precursors from epoxides **7f–h**



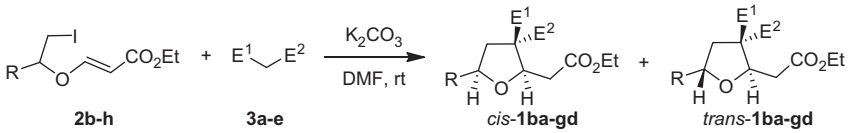

| Entry | R | | Yield (%) | |
|---|---|---|---|---|
| | | | Step 1 | Step 2 |
| 1 | Me | **f** | 73 | 72 |
| 2 | $BnOCH_2$ | **g** | 88 | 72 |
| 3 | Cy | **h** | 74 | 77 |

**Table 2**
Synthesis of the iodides **2b–e** from 1,2-diols **4b–e**




| Entry | R | | Yield (%) | | |
|---|---|---|---|---|---|
| | | | Step 1 | Step 2 | Step 3 |
| 1 | Et | **b** | 90 | 93 | 71 |
| 2 | $^i$Pr | **c** | 88 | 95 | 79 |
| 3 | Ph | **d** | 90 | 76 | 76 |
| 4 | *p*-Me-$C_6H_4$ | **e** | 76 | 90 | 68 |

**Table 4**
Tandem alkylation-Michael addition for the synthesis of 2,3,3,5-tetrasubstituted THFs: substrate scope




| Entry | R | | $E^1$ | $E^2$ | | Product | Time (h) | Yields[b] (%) | dr (*cis*:*trans*)[a] |
|---|---|---|---|---|---|---|---|---|---|
| 1 | Et | **2b** | CN | CN | **3a** | **1ba** | 3 | 79 | 2:1 |
| 2 | $^i$Pr | **2c** | CN | CN | **3a** | **1ca** | 2.5 | 67 | 2:1 |
| 3 | Ph | **2d** | CN | CN | **3a** | **1da** | 3.5 | 45 | 2.3:1 |
| 4 | *p*-Me-$C_6H_4$ | **2e** | CN | CN | **3a** | **1ea** | 5 | 47 | 2.1:1 |
| 5 | Me | **2f** | CN | CN | **3a** | **1fa** | 4 | 72 | 2.5:1 |
| 6 | $BnOCH_2$ | **2g** | CN | CN | **3a** | **1ga** | 5 | 61 | 2.4:1 |
| 7 | Cy | **2h** | CN | CN | **3a** | **1ha** | 3 | 69 | 2.4:1 |
| 8 | Me | **2f** | $CO_2Me$ | $CO_2Me$ | **3b** | **1fb** | 5 | 64 | 2.7:1 |
| 9 | $^i$Pr | **2c** | CN | $SO_2Ph$ | **3d** | **1cd** | 6 | 55 | 3:1 |
| 10 | Ph | **2d** | CN | $SO_2Ph$ | **3d** | **1dd** | 6 | 41 | 2.3:1 |
| 11 | Me | **2f** | CN | $SO_2Ph$ | **3d** | **1fd** | 10.5 | 51 | 2.8:1 |
| 12 | $BnOCH_2$ | **2g** | CN | $SO_2Ph$ | **3d** | **1gd** | 5 | 60 | 2:1 |

[a] Determined on crude reaction mixtures by $^1$H NMR.
[b] Isolated yields.

Table 4 outlines the scope of this tandem alkylation-Michael addition to vinylogous carbonates for the synthesis of 2,3,3,5-tetrasubstituted tetrahydrofurans. The iodides **2b–h** were subjected to the reaction with symmetrically substituted active methylene compounds like malononitrile (**3a**) and dimethyl malonate (**3b**) to furnish the corresponding THF derivatives **1ba–fb** (Table 4, entries 1–8). In all the cases, the product was formed in good to excellent yield albeit with moderate diastereoselectivity. With a view to improve the diastereoselectivity, unsymmetrically substituted active methylene compound sulfone nitrile **3d** was chosen as the nucleophile. It was reasoned that not only would it expand scope of the methodology by introducing an additional stereocenter, but it would lead to the tetrasubstituted THF derivatives with better diastereoselectivity owing to large difference in the relative bulk of the substituents on the active methylene compound. Thus, the iodides **2c–g** were subjected to reaction with sulfone nitrile **3d** to result in the THF derivatives **1cd–gd**, respectively, in good yields but with only marginal to moderate improvement in diastereoselectivity (Table 4, entries 9–12). This was in sharp contrast to what we had observed for the THP derivatives where the diastereoselectivities obtained with unsymmetrical active methylene compounds as nucleophiles were excellent.[8]

The low selectivity obtained in the case of THF derivatives can be attributed to the conformation of THF ring wherein there is no significant preference for the substituents to be in the pseudo-equatorial orientation unlike that for the THP derivatives. The stereochemistry of major isomer was assigned as *cis* on the basis of the NOE experiments. Further, the minor *trans* isomer of the nitrile **1da** was subjected to single-crystal X-ray diffraction studies to unambiguously ascertain the relative stereochemistry of the substituents in the THF derivatives.[13] These studies revealed that the substituents at C-2 and C-5 on the THF ring occupy the pseudo-equatorial and pseudo-axial positions, respectively (Fig. 1). In the other cases, the stereochemistry shown is by analogy to this example.

Synthesis of cyclic ethers with a tertiary ether is a challenging task. To highlight the utility of our strategy, it was decided to synthesize the cyclic ether **11** with carbethoxy group as the tertiary substitution. To this end, the mono-tosyl ethylene glycol (**5a**) was reacted with diethyl acetylene dicarboxylate in the presence of DABCO to furnish the ester **9** as a mixture of geometrical isomers. Displacement of the tosyl group of the ester **9** with sodium iodide in acetone furnished the requisite iodide precursor

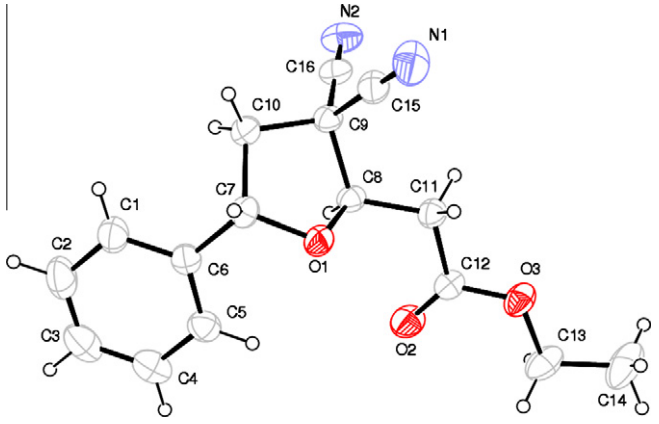
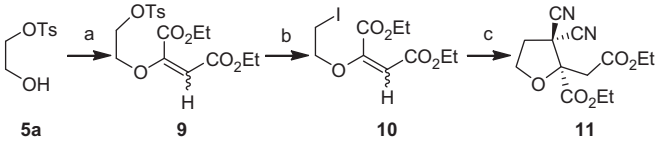


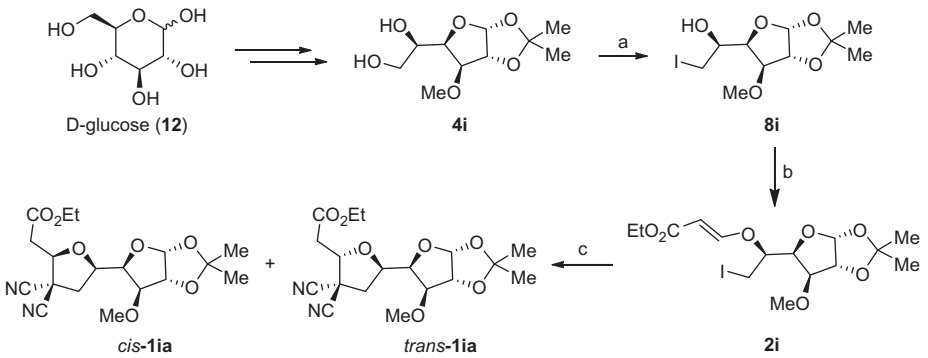

**Figure 1.** ORTEP diagram of the THF derivative *trans*-**1da**.




**Scheme 3.** Reagents, conditions, and yields: (a) diethyl acetylene dicarboxylate, DABCO, $CH_2Cl_2$, rt, 4 h, 85%; (b) NaI, acetone, reflux, 12 h, 92%; (c) $CH_2(CN)_2$, $K_2CO_3$, DMF, rt, 1 h, 62%.

**10**. Reaction of the iodide **10** with malononitrile (**3a**) in the presence of $K_2CO_3$ as base gave the THF derivative **11** with carbethoxy group as the tertiary substitution (Scheme 3). It is interesting to note here that the reaction proceeds through alkylation followed by 5-*exo* Michael addition to vinylogous carbonate rather than 6-*endo* Michael addition to α-alkoxy acrylate motif.

The adjacent bis-THF motif is present in a variety of natural products belonging to annonaceous acetogenin family.[14] We envisioned that synthesis of densely substituted adjacent bis-THF derivative would be challenging and thereby highlight the utility of the developed tandem alkylation-Michael reaction. Toward this end, the known[15] diol **4i**, prepared from D-glucose (**12**), was converted into the iodide **2i** following a sequence which is slightly different than that described for synthesis of the iodides **2**. Thus,




**Scheme 4.** Reagents, conditions, and yields: (a) $I_2$, $PPh_3$, DMF, 0 °C–rt, 12 h, 39%; (b) ethyl propiolate, NMM, $CH_2Cl_2$, rt, 7 h, 79%; (c) $CH_2(CN)_2$, $K_2CO_3$, DMF, rt, 3 h, 67%, dr 1.4:1 (*cis*:*trans*).

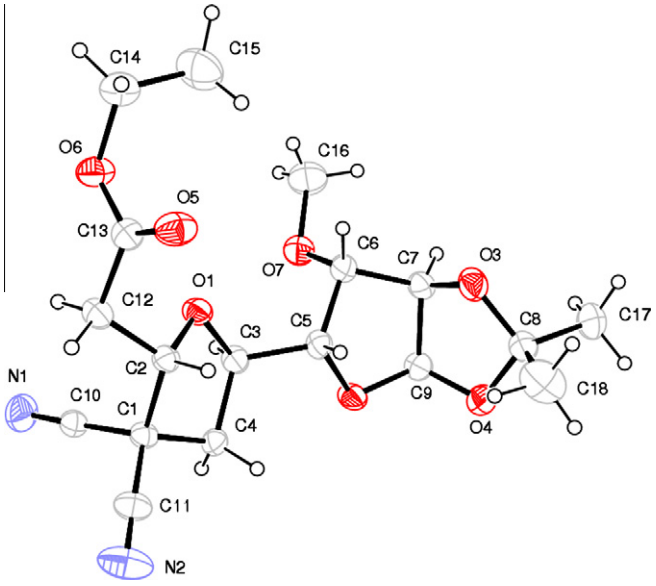



**Figure 2.** ORTEP diagram of the THF derivative *trans*-**1ia**.

selective monoiodination of the diol **4i** gave the iodo-alcohol **8i** which on reaction with ethyl propiolate yielded the requisite iodo-vinylogous carbonate **2i**. Gratifyingly, the reaction of this iodide **2i** under optimized conditions led to the formation of the adjacent bis-THF derivative **1ia** in good yields albeit with only moderate diastereoselectivity (Scheme 4). However, the two diastereomers could be readily separated by silica gel column chromatography.

The stereochemistry of *trans*-isomer *trans*-**1ia** was unambiguously established by single-crystal X-ray diffraction studies (Fig. 2). It is pertinent to mention here that the bis-THF derivative **1ia** contains an acetal linkage in one of the THF rings which could be further functionalized using Lewis acid mediated oxonium generation followed by trapping with various nucleophiles leading to C-alkyl/aryl substituted furanoside derivatives.

## 3. Conclusion

In conclusion, we have developed an efficient synthesis of the 2,3,3,5-tetrasubstituted THF derivatives employing tandem alkylation-Michael addition to vinylogous carbonates. This study showed that this method could be used for installing tertiary ether centre in THFs. Further, the utility of this strategy for the synthesis of adjacent bis-THF derivatives which are part structures of natural products has been highlighted. This study has further proved that reactivity of vinylogous carbonates are not limited to radical reactions but they are excellent Michael acceptors even under anionic conditions. Further efforts to expand the scope of the reaction and its application in target directed synthesis are underway in our laboratory and will be reported in due course.

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10. All the compounds exhibited spectral data consistent with their structures. Melting point, IR, NMR ($^1$H and $^{13}$C) and HRMS spectral data for some of the compounds are as follows: THF derivative **1aa**: IR (neat) 2983, 2931, 2183, 1732, 1625, 1450, 1401, 1384, 1369, 1315, 1186, 1147, 1083, 1025, 944, 857 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 4.47 (t, $J$ = 6.4, 1H), 4.30–4.15 (m, 1H), 3.99 (q, $J$ = 7.7 Hz, 1H), 2.94 (ABX, $J$ = 16.9, 7.1 Hz, 1H), 2.88 (ABX, $J$ = 16.9, 6.1 Hz, 1H), 2.79 (t, $J$ = 6.9 Hz, 2H), 1.33 (t, $J$ = 7.2 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$, DEPT) $\delta$ 168.68 (C), 114.15 (C), 113.35 (C), 82.18 (CH), 66.83 ($CH_2$), 61.75 ($CH_2$), 39.49 ($CH_2$), 38.30 (C), 36.82 ($CH_2$), 14.20 ($CH_3$); HRMS (ESI, M+Na$^+$) $m/z$ calcd. for $C_{10}H_{12}N_2O_3Na$ 231.0746, found 231.0750. THF derivative *cis*-**1da**: IR (neat) 2986, 2930, 2252, 1805, 1735, 1605, 1494, 1448, 1403, 1372, 1312, 1260, 1123, 1033, 850, 760, 701 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.45–7.30 (m, 5H), 5.07 (dd, J = 8.8, 6.8 Hz, 1H), 4.68 (t, $J$ = 6.8 Hz, 1H), 4.26 (q, $J$ = 7.2 Hz, 2H), 3.18 (ABX, $J$ = 14.0, 6.8 Hz, 1H), 3.14 (ABX, $J$ = 17.2, 6.8 Hz, 1H), 3.03 (ABX, $J$ = 17.2, 6.8 Hz, 1H), 2.67 (ABX, $J$ = 14.0, 8.8 Hz, 1H), 1.32 (t, $J$ = 7.2 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$, DEPT) $\delta$ 168.68 (C), 137.05 (C), 129.26 (CH), 129.11 (2 × CH), 126.27 (2 × CH), 114.57 (C), 113.77 (C), 81.94 (CH), 80.59 (CH), 61.86 ($CH_2$), 47.12 ($CH_2$), 38.50 (C), 36.88 ($CH_2$), 14.22 ($CH_3$); HRMS (ESI, M+Na$^+$) $m/z$ calcd. for $C_{16}H_{16}N_2O_3Na$ 307.1059, found 307.1056. THF derivative *trans*-**1da**: mp 76–78 °C; IR (neat) 2983, 2924, 2853, 2252, 1736, 1592, 1452, 1407, 1368, 1316, 1186, 1123, 1078, 1022, 764, 704 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.45–7.30 (m, 5H), 5.40 (dd, $J$ = 8.6, 6.6 Hz, 1H), 4.88 (dd, $J$ = 7.4, 5.8 Hz, 1H), 4.30–4.20 (m, 2H), 3.26 (ABX, $J$ = 13.4, 6.6 Hz, 1H), 3.04 (ABX, $J$ = 16.4, 7.5 Hz, 1H), 2.98 (ABX, $J$ = 16.4, 5.8 Hz, 1H), 2.74 (ABX, $J$ = 13.4, 8.8 Hz, 1H), 1.32 (t, $J$ = 7.1 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$, DEPT) $\delta$ 168.69 (C), 138.83 (C), 129.22 (2 × CH), 128.85 (CH), 125.26 (2 × CH), 113.21 (C), 112.99 (C), 81.15 (CH), 79.43 (CH), 61.81 ($CH_2$), 46.40 ($CH_2$), 39.62 (C), 37.06 ($CH_2$), 14.23 ($CH_3$); HRMS (ESI, M+Na$^+$) $m/z$ calcd. for $C_{16}H_{16}N_2O_3Na$ 307.1059, found 307.1056. THF derivative **11**: IR (neat) 2982, 2164, 1736, 1459, 1376, 1298, 1196, 1087, 1024, 855 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 4.42 (td, $J$ = 8.4, 5.2 Hz, 1H), 4.40–4.15 (m, 5H), 3.30 (AB, $J$ = 16.0 Hz, 1H), 3.08 (AB, $J$ = 16.0 Hz, 1H), 3.00–2.80 (m, 2H), 1.33 (t, $J$ = 7.2 Hz, 3H), 1.27 (t, $J$ = 7.2 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$, DEPT) $\delta$ 167.86 (C), 167.40 (C), 112.97 (C), 112.45 (C), 87.78 (C), 67.76 ($CH_2$), 63.35 ($CH_2$), 61.72 ($CH_2$), 42.09 (C), 40.47 ($CH_2$), 38.39 ($CH_2$), 14.10 ($CH_3$), 13.94 ($CH_3$). THF derivative *trans*-**1ia**: mp 82–84 °C; $[\alpha]_D^{30}$ −60.9 (*c* 1.0, $CHCl_3$); IR (neat) 2990, 2937, 2825, 2360, 2256, 1745, 1452, 1382, 1312, 1256, 1218, 1190, 1155, 1078, 1022, 882, 850, 645 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 5.92 (d, $J$ = 3.6 Hz, 1H), 4.69 (t, $J$ = 6.8 Hz, 1H), 4.59–4.50 (m, 2H), 4.37 (t, $J$ = 3.6 Hz, 1H), 4.30–4.15 (m, 2H), 3.75 (d, $J$ = 3.2 Hz, 1H), 3.38 (s, 3H), 3.00–2.80 (m, 4H), 1.50 (s, 3H), 1.32 (s, 3H), 1.30 (t, $J$ = 7.2 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$, DEPT) $\delta$ 168.50 (C), 113.54 (2 × C), 112.28 (C), 105.53 (CH), 84.38 (CH), 81.54 (CH), 81.27 (CH), 80.53 (CH), 76.08 (CH), 61.62 ($CH_2$), 57.97 ($CH_3$), 40.59 ($CH_2$), 39.28 (C), 36.97 ($CH_2$), 26.98 ($CH_3$), 26.36 ($CH_3$), 14.19 ($CH_3$). THF derivative *cis*-**1ia**: mp 92–94 °C; $[\alpha]_D^{23}$ −19.0 (*c* 1.0, $CHCl_3$); IR (neat) 2987, 2936, 2852, 2252, 1738, 1596, 1459, 1384, 1317, 1257, 1217, 1193, 1166, 1124, 1083, 1022, 889, 857 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 5.85 (d, $J$ = 3.6 Hz, 1H), 4.52 (d, $J$ = 4.0 Hz, 1H), 4.49 (d, $J$ = 6.4 Hz, 1H), 4.35 (td, $J$ = 7.2, 6.2 Hz, 1H), 4.24 (dd, $J$ = 5.6, 4.0 Hz, 1H), 4.23 (q, $J$ = 7.2 Hz, 2H), 3.73 (d, $J$ = 3.3 Hz, 1H), 3.40 (s, 3H), 2.96 (ABX, $J$ = 16.8, 7.2 Hz, 1H), 2.90 (ABX, $J$ = 13.6, 7.6 Hz, 1H), 2.89 (ABX, $J$ = 16.8, 6.0 Hz, 1H), 2.81 (ABX, $J$ = 13.6, 7.2 Hz, 1H), 1.48 (s, 3H), 1.32 (t, $J$ = 7.2 Hz, 3H), 1.31 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$, DEPT) $\delta$ 168.75 (C), 114.45 (C), 113.52 (C), 112.29 (CH), 105.35 (CH), 83.92 (CH), 81.40 (CH), 81.39 (CH), 80.21 (CH), 76.31 (CH), 61.71 ($CH_2$), 58.17 ($CH_3$), 41.07 ($CH_2$), 38.19 (C), 36.78 ($CH_2$), 26.97 ($CH_3$), 26.38 ($CH_3$), 14.23 ($CH_3$); HRMS (ESI, M+Na$^+$) $m/z$ calcd. for $C_{18}H_{24}N_2O_7Na$ 403.1481, found 403.1477.
11. *Representative experimental procedure*: To a 10 mL oven dried round bottom flask charged with $K_2CO_3$ (256 mg, 1.85 mmol) was added dry DMF (0.2 mL) followed by malononitrle (**3a**) (73.3 mg, 73 μL, 1.11 mmol) under nitrogen atmosphere and the mixture was allowed to stir for 15 min. A solution of the iodo-vinylogous carbonate **2a** (100 mg, 0.37 mmol) in dry DMF (0.3 mL) was added to the reaction mixture over a period of 15 min and allowed to stir at rt for 3.5 h (TLC control). Reaction mixture was diluted with diethyl ether (25 mL), washed with water (3 × 5 mL) and brine and the organic layer was dried (anhyd $Na_2SO_4$). Evaporation of the solvent and purification of the reisdue on a silica gel column using ethyl acetate/hexanes (1:12) as eluent furnished the THF derivative **1aa** (61 mg, 79%) as a colourless oil.
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13. Crystal data for THF derivative *trans*-**1da**: Formula: $C_{16}H_{16}N_2O_3$; Unit cell parameters: *a* 7.3930(3) *b* 10.1937(4) *c* 10.5704(5) $\alpha$ 75.305(2) $\beta$ 89.822(2) $\gamma$ 81.379(2) space group $P\bar{1}$; CCDC No. 787425. Crystal data for THF derivative *trans*-**1ia**: formula: $C_{18}H_{24}N_2O_7$ unit cell parameters: *a* 10.6929(12) *b* 8.5506(10) *c* 11.5532(15) $\beta$ 107.922(5) space group *P*21 CCDC No. 787426. CCDC Nos. 787425 and 787426 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
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