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Cascade reactions initiated by radical addition of tetrahydrofuran to β-bromonitrostyrenes†

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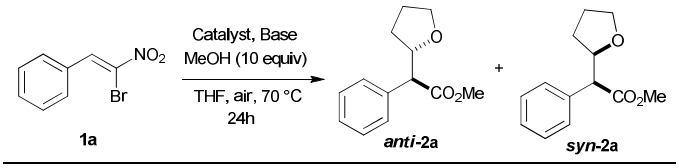
A silver(I) catalyzed addition of THF radical to β-bromonitrostyrenes under mild basic condition in the presence of air has been developed. Isotope labelling experiment $^{18}O_2$ was conducted and showed that dioxygen was involved in the mechanism to form the carbonyl group.

The addition of carbon radicals to alkenes is one of the most reliable and prominent approaches for forming C–C bonds in organic synthesis.[1] Among numerous reports, C–C bond formation by addition of alkenes to the unreactive α-C–H position of α-ethereal carbon radicals readily provides α-substituted cyclic ethers, which is also one of the most commonly found molecular architecture in bioactive molecules. A wide variety of strategies was reported for the generation of α-ethereal carbon radicals, which included usage of usual initiators such as peroxides, AIBN or Et_3B under heating or light irradiation conditions. However, most of the earlier reports described the addition of ether radicals to substituted alkenes such as α,β-unsaturated carbonyl compounds[2] and α,β-unsaturated sulfonyl compounds[3]. Consequently, addition of ether radicals to C=N bonds such as imines[4a-c], azirines[4d] and C=O bonds of aldehydes[5] have also been reported. Adding pace to this unique radical chemistry, for the first time herein, we described a THF radical addition to an activated alkene, the β-bromonitrostyrene, in the presence of air to furnish the dioxygen incoporated adduct.

The β-bromonitrostyrene, with β-position of the styrene disubstituted, exhibits peculiar properties compared to that of bromostyrenes and nitrostyrenes. Previous literature proved their versatile reactivity role as Michael acceptors,[6] dipolarophiles,[7] 1,3-dipoles,[8] dienophiles[9] and heterodienes[8]. When employed in Michael additions, β-bromonitrostyrenes were often shown to be effective dielectrophiles due to the presence of bromo and nitro functionalities on its scaffold. To investigate the prospect of addition of ether radicals to the β-bromonitrostyrenes, an initial attempt was conducted on β-bromonitrostyrene in THF with triethylborane-air[4b,5a] as radical initiator. However, no formation of desired THF adduct under these reaction conditions was observed. Other radical initiators such as dimethylzinc-air,[4b] N-hydroxyphthalimide-$Co(OAc)_2$-dioxygen,[2b] AIBN (reflux),[3a,b] benzoyl peroxide (reflux)[3c] and di-tert-butyl peroxide (heating),[5b] proved to be inefficient in obtaining the desired THF adduct as well. It is well known that, transition metals such as Mn(III), Ce(IV), Fe(III), V(V), Cu(II),

Table 1 Optimization of the reaction conditions[a]



1a anti-2a syn-2a

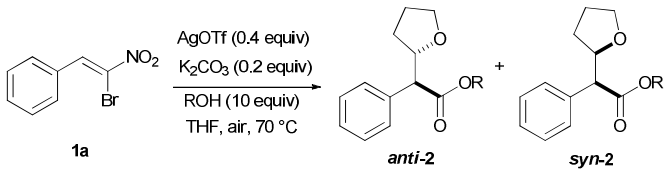
Entry	Catalyst (equiv)	Base (equiv)	Yield[b] (%)	*anti*:*syn*[c]
1	$AgNO_3$ (0.4)	K_2CO_3 (0.2)	50	1.3:1
2	AgOTf (0.4)	K_2CO_3 (0.2)	58	1.2:1
3	$AgSbF_6$ (0.4)	K_2CO_3 (0.2)	52	1.2:1
4	$AgPF_6$ (0.4)	K_2CO_3 (0.2)	51	1.1:1
5	$AgBF_4$ (0.4)	K_2CO_3 (0.2)	34	1.4:1
6	AgOAc (0.4)	K_2CO_3 (0.2)	22	2.5:1
7[d]	Ag_2O (0.4)	K_2CO_3 (0.2)	trace	-
8[d]	Ag_2CO_3 (0.4)	K_2CO_3 (0.2)	trace	-
9	Silver *p*-toluene sulfonate	K_2CO_3 (0.2)	29	1.5:1
10	AgOTf (0.4)	Na_2CO_3 (0.2)	52	1.2:1
11	AgOTf (0.4)	Cs_2CO_3 (0.2)	54	1.3:1
12[d]	AgOTf (0.4)	$KHCO_3$ (0.2)	42	1.3:1
13	AgOTf (0.4)	KOH (0.2)	12	1.6:1
14[d]	AgOTf (0.4)	DBU (0.2)	n.r.[e]	-
15[d]	AgOTf (0.4)	Et_3N (0.2)	n.r.[e]	-
16[d]	AgOTf (0.2)	K_2CO_3 (0.2)	45	1.3:1
17	AgOTf (0.6)	K_2CO_3 (0.2)	42	1.2:1
18	AgOTf (0.4)	K_2CO_3 (1.0)	57	1.2:1
19[f]	AgOTf (0.4)	K_2CO_3 (0.2)	48	1.3:1

[a] Reactions were performed using 0.2 mmol of **1a**. [b] Isolated yield. [c] The ratios of *anti*:*syn* isomers were determined by the crude ^1H NMR spectra. [d] The reaction time was 48 hr. [e] No reaction. [f] The reaction was carried out in O_2 atmosphere and finished in 10 hr.

Co(II)[10] and Ag(II)[11] are often used in oxidative radical formations, hence, the usage of such catalysts were explored. We found that the treatment of β-bromonitrostyrene with $AgNO_3$ and K_2CO_3 in THF-MeOH solution[12] under reflux and atmospheric air gave the desired methyl ester **2a**[13] in 50% yield (Table 1, entry 1). During this, Ag(I) was precipitated and we speculate that it facilitates the removal of bromide in the mixture and catalyse the reaction. Next, we examined the efficacy of various silver salts (Table 1). It was observed that most of the silver salts could catalyze this reaction and of which, AgOTf delivered the THF adduct in highest yield (Table 1, entry 2). Besides K_2CO_3, a series of bases were also screened. When Na_2CO_3, Cs_2CO_3, $KHCO_3$, KOH were used, the desired product has been formed albeit in lower yields (Table 1, entries 10-13). Notably, KOH was observed to give a much lower yield of 12% and we speculate that since KOH is hygroscopic, H_2O can quench the reactive intermediates. Interestingly, when DBU and Et_3N were used, no desired product was formed (Table 1, entries 14-15). The decreased silver(I) salt loading resulted in a slightly lower yield of product. However, longer reaction time (Table 1, entry 16) and increased catalyst loading had no effect on the yield (Table 1, entry 17). No significant difference was observed in the reaction yields when the amount of base was increased (Table 1, entry 18). Reaction was completed within a short period of time, when it was carried out under pure O_2 atmosphere instead of atmospheric air. However, this led to a decreased yield of product (Table 1, entry 19). No reaction was observed in the absence of either silver catalyst or base or oxygen in the reaction system. Since the β-bromonitrostyrene was a mixture of *Z*- and *E*-isomer, it is understandable that the product was a pair of *syn*- and *anti*-isomer.

Based on these results, we examined the scope of the reaction by replacing methanol with various alcohols (Table 2). When ethanol was used, the corresponding ethyl ester product was obtained in a much lower yield, while 1-propanol could give only 10% yield (Table 2, entries 2-3). Other alcohols were unable to afford the product.

Table 2 Radical reactions of β-bromonitrostyrene with various alcohols[a]

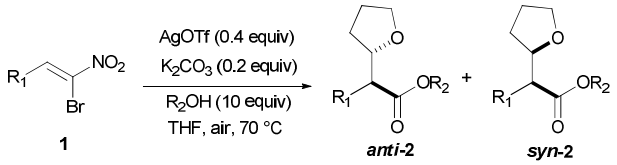


Entry	ROH	T (h)	Yield[b] (%)	*anti*:*syn*[c]
1	methanol	24	58	1.2:1
2	ethanol	48	39	1.5:1
3	1-propanol	48	10	2.2:1
4	2-propanol	48	trace	-
5	1-butanol	48	trace	-
6	*tert*-butanol	48	n.r.[d]	-

[a] Reactions were performed using 0.2 mmol of **1a**. [b] Isolated yield. [c] The ratios of *anti*:*syn* isomers were determined by the crude ^{1}H NMR spectra based on chemical shifts and coupling constant. [d] No reaction.

Next, we investigated the generality of this silver catalyzed radical reaction with various bromonitroalkenes. β-Bromonitrostyrenes bearing electron-withdrawing groups such as -F, -Cl, -Br on the phenyl ring generally gave good yields (Table 3, entries 2–7), while precursors with $-NO_2$ group gave lower yields (Table 3, entries 8 and 9). When the substituent of phenyl ring was changed to *p*-CH_2Br, the yields were moderate (Table 3, entry 10). In cases of electron-donating groups such as *p*-OMe on the phenyl ring or other aromatic systems with increased electron-density such as furan ring, there were no observed products (Table 3, entries 11 and 12). Lower reactivity was observed for the nonconjugated bromonitroalkene (Table 3, entry 13). There was no reaction when the alkyl substituent was used (Table 3, entry 14). When EtOH was used instead of MeOH, longer reaction times were required and yields were lower (Table 3, entries 15–19). Finally, 2-hydroxypyridine was attempted but no reaction was observed. This was likely due to strong coordinating effect of pyridine and silver.

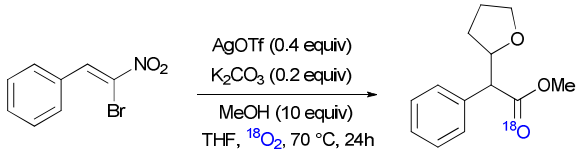
Table 3 Radical reactions of various β-bromonitrostyrenes[a]



Entry	R_1	R_2	T (h)	Product	Yield[b] (%)	*anti*:*syn*[c]
1	Ph	Me	24	**2a**	58	1.2:1
2	4-BrC_6H_4	Me	24	**2b**	69	1.3:1
3	3-BrC_6H_4	Me	24	**2c**	62	1.5:1
4	4-ClC_6H_4	Me	24	**2d**	68	1.2:1
5	3-ClC_6H_4	Me	24	**2e**	61	1.3:1
6	2-ClC_6H_4	Me	24	**2f**	59	1.4:1
7	4-FC_6H_4	Me	24	**2g**	60	1.3:1
8	4-$NO_2C_6H_4$	Me	48	**2h**	15	1.8:1
9	3-$NO_2C_6H_4$	Me	48	**2i**	37	1.5:1
10	4-$CH_2BrC_6H_4$	Me	24	**2j**	50	1.2:1
11	4-$OMeC_6H_4$	Me	48	**2k**	trace	-
12	2-Furyl	Me	48	**2l**	trace	-
13	$PhCH_2CH_2$	Me	24	**2m**	35	1.5:1
14	$(CH_3)_2CH$	Me	48	**2n**	n.r.[d]	-
15	Ph	Et	48	**2o**	39	1.5:1
16	4-BrC_6H_4	Et	48	**2p**	45	1.6:1
17	3-BrC_6H_4	Et	48	**2q**	40	1.8:1
18	4-ClC_6H_4	Et	48	**2r**	42	1.6:1
19	4-FC_6H_4	Et	48	**2s**	40	1.5:1
20	Ph	Py[e]	48	**2t**	n.r.[d]	-

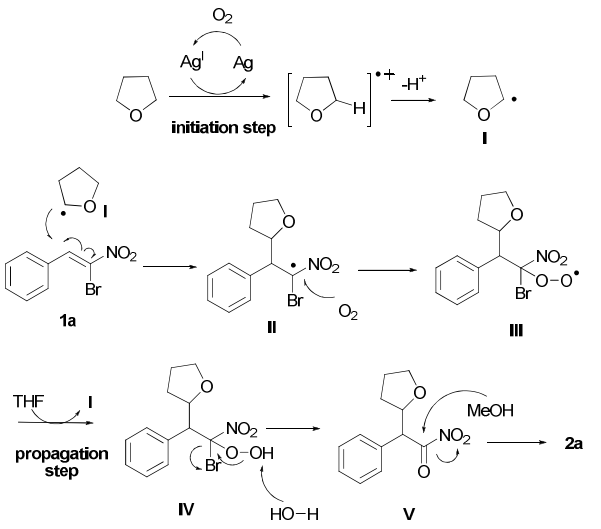
[a] Reactions were performed under standard procedures (see ESI†) using 0.5 mmol of **1**. [b] Isolated yield. [c] The ratios of *anti*:*syn* isomers were determined by the crude ^{1}H NMR spectra. [d] No reaction. [e]Py = 2-hydroxypyridine.

Reaction pathway for this radical reaction was meticulously investigated by conducting several reactions. When 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO) was added into the reaction system, no reaction was observed.[14] When the reaction was conducted in the absence of light, the product was obtained only in a trace amount. These evidences indicated that the reaction might proceed *via* a radical process. Through an isotope labelling experiment by using $^{18}O_2$ to replace air, it was shown that the molecular oxygen was incorporated into the carbonyl group (Scheme 1, also see ESI†).



Scheme 1 Isotope labelling experiment by $^{18}O_2$

A plausible mechanism for this reaction is shown in Scheme 2. Initially, THF radical **I** generates from THF and Ag(I) in the presence of oxygen adds to β-bromonitrostyrene **1a** to form an radical adduct **II**, which is trapped by dioxygen to give a peroxy radical **III**, followed by hydrogen abstraction from THF to generate a hydroperoxide **IV**. The O–O bond of hydroperoxide **IV** undergoes cleavage to form the intermediate **V** with the subsequent release of bromo group. Thereafter, intermediate **V** is subjected to nucleophilic attack by alcohols to give the desired ester **2a**. Since the intermediate **V** is less active than the acyl halide (the latter would be formed if the nitro group leaves first after the cleavage of the hydroperoxide), it is difficult for bulky alcohols to attack the intermediate **V** to form the corresponding ester. This clearly explains the low reactivity of bulky alcohols towards this reaction (Table 2). In addition, the base K_2CO_3 may serve to neutralize the acids generated from the reaction system. Lastly, since other free radical initiators such as triethylborane-air, dimethylzinc-air, N-hydroxyphthalimide-Co(OAc)$_2$-dioxygen, AIBN (reflux), benzoyl peroxide (reflux) or di-tert-butyl peroxide (heating) fail to initiate the reaction, we believe a strong affinity of Ag(I) towards Br plays a key role in this reaction.



Scheme 2 Plausible mechanism

Conclusions

In summary, a Ag(I) catalyzed addition of THF radical to β-bromonitrostyrenes under mild basic condition has been developed. This methodology utilized various β-bromonitrostyrenes as starting material in THF to synthesize the various α-substituted THF adduct cyclic ethers which is an useful synthetic tool for the preparation of various synthetic biological active cyclic ethers. Hence, this paves the way for further investigation into utilization of β-bromonitrostyrenes for α-substituted cyclic ethers. Further studies on reaction mechanism using isotope labelling experiment $^{18}O_2$ was conducted and showed that molecular oxygen was involved to form the carbonyl group.

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Experimental

^{1}H and ^{13}C nuclear magnetic resonance (NMR) spectra were recorded on Bruker AV400 (400 MHz) NMR spectrometer. ^{1}H and ^{13}C NMR spectra are reported in parts per million (ppm) downfield from an internal standard, tetramethylsilane (0 ppm) and $CHCl_3$ (77.0 ppm), respectively. IR spectra were recorded using FTIR Restige-21 (Shimadzu) and reported in cm-1. High-resolution mass spectra (HRMS) were obtained on a Finnigan/MAT LCQ quadrupole ion trap mass spectrometer, coupled with the TSP4000 HPLC system and the Crystal 310 CE system. Accurate masses are reported for the molecular ion [M+H]+ or a suitable fragment ion. X-ray crystallographic data was collected by using a Bruker X8Apex diffractometer with Mo K/α radiation (graphite monochromator). All reagents were purchased and used without further purification.All the solvents used are not anhydrous. All reactions were conducted under an atmosphere of air, unless otherwise indicated. Analytical thin-layer chromatography (TLC) was performed on Merck 60 F254 silica gel plates. Flash chromatography was performed on silica gel 60 (0.010 - 0.063 mm, Merck). The starting (E)-nitrostyrenes[15] and (Z)-β-bromonitrostyrenes[16] were prepared according to the literature procedure.

Synthesis of compound 2

Addition of THF radical to β-bromonitrostyrene: A mixture of the β-bromonitrostyrene (0.5 mmol, prepared as a mixture of *Z*- and *E*-isomer), silver triflate (51.4 mg, 0.2 mmol) and K_2CO_3 (13.8 mg, 0.1 mmol) in MeOH (0.2 mL, 5 mmol) and THF (2.5 mL) was heated at 70 °C with continuous air bubbling (flow rate; 0.5 mL/h).After the indicated period, the solvent was removed under reduced pressure, the residue was purified by silica-gel chromatography (hexane/EtOAc). Caution: THF tends to form highly-explosive peroxides in the presence of oxygen. Although we have never detected peroxides in this reaction, appropriate caution should always be paid when the reaction is carried out in a large scale. **Characterization of compounds 2a-2s**

2a: The diastereomer ratio was 1.2:1 (*anti:syn*). The diastereomers were separated by column chromatography (hexane/EtOAc= 10/1). The anti-isomer (**2a-1**) was obtained as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36-7.28 (m, 5H), 4.52 (dt, J = 10.0, 7.2 Hz, 1H), 3.92 (q, J = 6.8 Hz, 1H), 3.83 (q, J = 7.2 Hz, 1H), 3.70 (s, 3H), 3.53 (d, J = 10.0 Hz, 1H), 1.88-1.80 (m, 2H), 1.72-1.67 (m, 1H), 1.47-1.40 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.0, 135.9, 128.7, 128.4, 127.7, 80.6, 68.5, 57.6, 52.1, 29.5, 25.5; IR (neat) 3062, 3030, 2950, 2873, 1731, 1604, 1453, 1230, 1071, 736, 700 cm^{-1}; HRMS (ESI) Calcd for $C_{13}H_{17}O_3$ $[M+H]^+$ 221.1178, found 221.1177. The *syn*-isomer (**2a-2**) was obtained as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39-7.27 (m, 5H), 4.45 (dt, J = 8.0, 7.6 Hz, 1H), 3.80 (q, J = 7.2 Hz, 1H), 3.74-3.66 (m, 4H), 3.63 (d, J = 8.4 Hz, 1H), 2.16-2.06 (m, 1H), 1.91-1.84 (m, 2H), 1.70-1.64 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.6, 136.6, 128.6, 127.5, 80.0, 68.3, 56.8, 52.0, 30.1, 25.6; IR (neat) 3061, 3030,

2951, 2872, 1730, 1603, 1344, 1229, 1204, 1022, 735, 700 cm^{-1}; HRMS (ESI) Calcd for $C_{13}H_{17}O_3$ $[M+H]^+$ 221.1178, found 221.1171.

2b: The diastereomer ratio was 1.3:1 (*anti:syn*). The diastereomers were separated by column chromatography (hexane/EtOAc = 10/1). The *anti*-isomer (**2b-1**) was obtained as a colorless oil. ^1H NMR (400 MHz, $CDCl_3$): δ 7.45 (dd, J = 6.4, 1.6 Hz, 2H), 7.23 (dd, J = 6.4, 1.6 Hz, 2H), 4.45 (dt, J = 10.0, 7.2 Hz, 1H), 3.90 (q, J = 6.8 Hz, 1H), 3.82 (q, J = 6.8 Hz, 1H), 3.70 (s, 3H), 3.49 (d, J = 10.0 Hz, 1H), 1.88-1.81 (m, 2H), 1.74-1.66 (m, 1H), 1.45-1.36 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.6, 134.9, 131.9, 130.1, 121.8, 80.4, 68.5, 56.9, 52.2, 29.5, 25.4; IR (neat) 3009, 2971, 2870, 1734, 1489, 1409, 1300, 1204, 1012, 819, 765cm^{-1}; HRMS (ESI) Calcd for $C_{13}H_{16}O_3Br$ [M+H]+ 299.0283, found 299.0290. The *syn*-isomer (**2b-2**) was obtained as a colorless oil. ^1H NMR (400 MHz, $CDCl_3$): δ7.45 (d, J = 8.4 Hz, 2H), 7.25 (d, J = 8.4 Hz, 2H), 4.41 (q, J = 7.2 Hz, 1H), 3.81-3.73 (m, 1H), 3.72-3.67 (m, 4H), 3.57 (d, J = 8.4 Hz, 1H), 2.15-2.07 (m, 1H), 1.90-1.82 (m, 2H), 1.67-1.58 (m, 1H); ^{13}C NMR (100 MHz, CDCl3): δ 172.1, 135.6, 131.7, 130.4, 121.7, 79.8, 68.4, 56.3, 52.1, 30.2, 25.6; IR (neat) 3008, 2970, 2869, 1734, 1435, 1329, 1299, 1159, 1072, 819, 766 cm^{-1}; HRMS (ESI) Calcd for $C_{13}H_{16}O_3Br$ $[M+H]^+$ 299.0283, found 299.0279.

2c: The diastereomer ratio was 1.5:1 (*anti:syn*). The diastereomers were separated by column chromatography (hexane/EtOAc = 8/1). The *anti*-isomer (**2c-1**) was obtained as a colorless oil. ^1H NMR (400 MHz, $CDCl_3$): δ 7.51 (t, J = 1.6 Hz, 1H), 7.41 (dt, J = 8.0, 1.6 Hz, 1H), 7.27 (d, J = 7.6 Hz, 1H), 7.18 (t, J = 8.0 Hz, 1H), 4.46 (dt, J = 10.0, 7.2 Hz, 1H), 3.90 (q, J = 6.8 Hz, 1H), 3.82 (q, J = 6.8 Hz, 1H), 3.70 (s, 3H), 3.48 (d, J = 9.6 Hz, 1H), 1.89-1.81 (m, 2H), 1.75-1.67 (m, 1H), 1.44-1.39 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.5, 138.0, 131.4, 130.9, 130.3, 127.1, 122.8, 80.5, 68.6, 57.1, 52.3, 29.6, 25.5; IR (neat) 3010, 2972, 2865, 1735, 1480, 1406, 1302, 1204, 1015, 820, 752 cm^{-1}; HRMS (ESI) Calcd for $C_{13}H_{16}O_3Br$ $[M+H]^+$ 299.0283, found 299.0284. The *syn*-isomer (**2c-2**) was obtained as a colorless oil. ^1H NMR (400 MHz, $CDCl_3$): δ7.53 (t, J = 1.6 Hz, 1H), 7.41 (dt, J = 6.4, 1.2 Hz, 1H), 7.31 (d, J = 8.0 Hz, 1H), 7.20 (t, J = 8.0 Hz, 1H), 4.42 (dt, J = 8.4, 6.8 Hz, 1H), 3.79 (q, J = 6.8 Hz, 1H), 3.74-3.71 (m, 1H), 3.68 (s, 3H), 3.56 (d, J = 8.4 Hz, 1H), 2.16-2.08 (m, 1H), 1.92-1.87 (m, 2H), 1.67-1.58 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.0, 138.8, 131.7, 130.7, 130.0, 127.4, 122.6, 79.8, 68.4, 56.5, 52.2, 30.2, 25.6; IR (neat) 3010, 2973, 2870, 1735, 1482, 1405, 1301, 1205, 1012, 805, 761 cm^{-1}; HRMS (ESI) Calcd for $C_{13}H_{16}O_3Br$ $[M+H]^+$ 299.0283, found 299.0281.

2d: The diastereomer ratio was 1.2:1 (*anti:syn*). The diastereomers were separated by column chromatography (hexane/EtOAc = 15/1). The *anti*-isomer (**2d-1**) was obtained as a colorless oil. ^1H NMR (400 MHz, $CDCl_3$): δ 7.29 (s, 4H), 4.46 (dt, J = 9.6, 6.8 Hz, 1H), 3.90 (q, J = 6.8 Hz, 1H), 3.82 (q, J = 6.8 Hz, 1H), 3.70 (s, 3H), 3.50 (d, J = 9.6 Hz, 1H), 1.88-1.80 (m, 2H), 1.75-1.68 (m, 1H), 1.44-1.36 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.7, 134.4, 133.7, 129.8, 128.9, 80.5, 68.5, 56.8, 52.2, 29.5, 25.4; IR (neat) 3080, 3011, 2950, 2871, 1735, 1435, 1302, 1228, 1070, 816, 750 cm^{-1}; HRMS (ESI) Calcd for $C_{13}H_{16}O_3Cl$ $[M+H]^+$ 255.0788, found 255.0795. The *syn*-isomer (**2d-2**) was obtained as a colorless oil. ^1H NMR (400 MHz, $CDCl_3$): δ 7.31 (s, 4H), 4.41 (dt, J = 8.4, 7.2 Hz, 1H), 3.79 (q, J = 7.2 Hz, 1H), 3.74-3.68 (m, 4H), 3.58 (d, J = 8.4 Hz, 1H), 2.14-2.08 (m, 1H), 1.89-1.83 (m, 2H), 1.67- 1.63 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.2, 135.1, 133.5, 130.0, 128.7, 79.9, 68.4, 56.2, 52.2, 30.2, 25.6; IR (neat) 3080, 3012, 2949, 2870, 1734, 1435, 1333, 1302, 1227, 1070, 815, 750 cm^{-1}; HRMS (ESI) Calcd for $C_{13}H_{16}O_3Cl$ $[M+H]^+$ 255.0788, found 255.0795.

2e: The diastereomer ratio was 1.3:1 (*anti:syn*). The diastereomers were separated by column chromatography (hexane/EtOAc = 10/1). The *anti*-isomer (**2e-1**) was obtained as a colorless oil. ^1H NMR (400 MHz, $CDCl_3$): δ 7.36 (d, J = 1.6 Hz, 1H), 7.27-7.23 (m, 3H), 4.48 (dt, J = 9.6, 6.8 Hz, 1H), 3.90 (q, J = 6.8 Hz, 1H), 3.82 (q, J = 6.4 Hz, 1H), 3.71 (s, 3H), 3.50 (d, J = 10.0 Hz, 1H), 1.89-1.81 (m, 2H), 1.76-1.68 (m, 1H), 1.47-1.38 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.5, 137.8, 134.6, 130.0, 128.5, 128.0, 126.7, 80.4, 68.5, 57.1, 52.3, 29.6, 25.5; IR (neat) 2952, 2872, 1735, 1596, 1478, 1205,1162, 1070, 1021, 774 cm^{-1}; HRMS (ESI) Calcd for $C_{13}H_{16}O_3Cl$ $[M+H]^+$ 255.0788, found 255.0786. The *syn*-isomer (**2e-2**) was obtained as a colorless oil. ^1H NMR (400 MHz, $CDCl_3$): δ 7.38 (s, 1H), 7.27-7.24 (m, 3H), 4.42 (dt, J = 8.4, 7.2 Hz, 1H), 3.80 (q, J = 6.8 Hz, 1H), 3.71 (q, J = 6.8 Hz,1H), 3.69 (s, 3H), 3.58 (d, J = 8.4 Hz, 1H), 2.15-2.10 (m, 1H), 1.90-1.84 (m, 2H), 1.66-1.59 (m, 1H); 13C NMR (100 MHz, CDCl3): δ 172.0, 138.5, 134.3, 129.7, 128.8, 127.8, 126.9, 79.8, 68.4, 56.5, 52.2, 30.2, 25.6; IR (neat) 2951, 2872, 1734, 1597, 1477, 1433, 1161, 1070, 1001, 773 cm^{-1}; HRMS (ESI) Calcd for $C_{13}H_{16}O_3Cl$ $[M+H]^+$ 255.0788, found 255.0780.

2f: The diastereomer ratio was 1.4:1 (*anti:syn*). The diastereomers were separated by column chromatography (hexane/EtOAc = 10/1). The *anti*-isomer (**2f-1**) was obtained as a colorless oil. ^1H NMR (400 MHz, $CDCl_3$): δ 7.55 (d, J = 7.6 Hz, 1H), 7.40 (d, J = 7.6 Hz, 1H), 7.27-7.19 (m, 2H), 4.52 (dt, J = 9.6, 6.8 Hz, 1H), 4.29 (d, J = 9.6 Hz, 1H), 3.96 (q, J = 6.8 Hz, 1H), 3.85 (q, J = 6.8 Hz, 1H), 3.70 (s, 3H), 1.94-1.84 (m, 2H), 1.73-1.68 (m, 1H), 1.58-1.49 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.6, 134.2, 133.8, 129.8, 129.2, 128.7, 127.2, 81.0, 68.6, 52.2, 51.8, 28.9, 25.5; IR (neat) 3060, 2948, 2870, 1738, 1629, 1476, 1436, 1205, 1165, 1070, 752 cm^{-1}; HRMS (ESI) Calcd for $C_{13}H_{16}O_3Cl$ $[M+H]^+$ 255.0788, found 255.0780. The *syn*-isomer (**2f-2**) was obtained as a colorless oil. ^1H NMR (400 MHz, $CDCl_3$): δ 7.56 (d, J = 7.6 Hz, 1H), 7.38 (d, J = 7.6 Hz, 1H), 7.30-7.18 (m, 2H), 4.55 (dt, J = 7.6, 6.8 Hz, 1H), 4.33 (d, J = 8.0 Hz, 1H), 3.79-3.71 (m, 2H), 3.69 (s, 3H), 2.14-2.09 (m, 1H), 1.88-1.83 (m, 2H), 1.76-1.69 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.1, 134.7, 134.3, 129.9, 129.5, 128.5, 126.9, 79.5, 68.4, 52.2, 51.8, 30.1, 25.6; IR (neat) 3061, 2949, 2871, 1737, 1630, 1475, 1436, 1206, 1071, 751 cm^{-1}; HRMS (ESI) Calcd for $C_{13}H_{16}O_3Cl$ $[M+H]^+$ 255.0788, found 255.0786.

2g: The diastereomer ratio was 1.3:1 (*anti:syn*). The diastereomers were separated by column chromatography (hexane/EtOAc = 10/1). The *anti*-somer (**2g-1**) was obtained as

a colorless oil. 1H NMR (400 MHz, CDCl3): δ 7.34-7.30 (m, 2H), 7.04-6.99 (m, 2H), 4.46 (dt, J = 10.0, 7.2 Hz, 1H), 3.90 (q, J = 6.8 Hz, 1H), 3.83 (q, J = 7.2 Hz, 1H), 3.70 (s, 3H), 3.51 (d, J = 10.0 Hz, 1H), 1.89-1.81 (m, 2H), 1.74-1.66 (m, 1H), 1.45-1.38 (m, 1H); 13C NMR (100 MHz, CDCl3): δ 173.0, 131.7, 131.6, 130.0, 129.9, 115.7, 115.5, 80.6, 68.5, 56.7, 52.2, 29.5, 25.4; IR (neat) 2990, 2870, 1734, 1602, 1510, 1369, 1225, 1158, 1068, 839, 812 cm^{-1}; HRMS (ESI) Calcd for $C_{13}H_{16}O_3F$ $[M+H]^+$ 239.1083, found 239.1078. The *syn*-isomer (**2g-2**) was obtained as a colorless oil. ^1H NMR (400 MHz, $CDCl_3$): δ 7.37-7.32 (m, 2H), 7.05-7.00 (m, 2H), 4.42 (dt, J = 8.0, 7.2 Hz, 1H), 3.79 (q, J = 6.8 Hz, 1H), 3.71 (q, J = 7.2 Hz, 1H), 3.68 (s, 3H), 3.60 (d, J = 8.4 Hz, 1H), 2.14-2.07 (m, 1H), 1.89-1.83 (m, 2H), 1.67-1.62 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.4, 132.3, 130.3, 130.2, 115.5, 115.3, 79.9, 68.4, 56.0, 52.1, 30.1, 25.6; IR (neat) 2991, 2872, 1734, 1601, 1370, 1226, 1159, 1068, 840, 811 cm^{-1}; HRMS (ESI) Calcd for $C_{13}H_{16}O_3F$ $[M+H]^+$ 239.1083, found 239.1091.

2h: The diastereomer ratio was 1.8:1 (*anti:syn*). The diastereomers were separated by column chromatography (hexane/EtOAc = 10/1). The *anti*-isomer (**2h-1**) was obtained as a pale yellow solid. ^1H NMR (400 MHz, $CDCl_3$): δ 8.19 (d, J = 8.8 Hz, 2H), 7.55 (d, J = 8.8 Hz, 2H), 4.50 (dt, J = 9.6, 7.2 Hz, 1H), 3.91 (q, J = 6.8 Hz, 1H), 3.84 (q, J = 6.8 Hz, 1H), 3.71 (s, 3H), 3.68 (d, J = 9.6 Hz, 1H), 1.90-1.83 (m, 2H), 1.75-1.70 (m, 1H), 1.46-1.39 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.8, 147.6, 143.0, 129.5, 123.9, 80.4, 68.6, 57.2, 52.5, 29.6, 25.5; IR (neat) 2955, 2851, 1735, 1602, 1520, 1348, 1209, 1065, 841 cm^{-1}; HRMS (ESI) Calcd for $C_{13}H_{16}NO_5$ $[M+H]^+$ 266.1028, found 266.1033. The *syn*-isomer (**2h-2**) was obtained as a pale yellow oil. ^1H NMR (400 MHz, $CDCl_3$): δ 8.19 (d, J = 8.8 Hz, 2H), 7.56 (d, J = 8.8 Hz, 2H), 4.46 (dt, J = 8.0, 7.2 Hz, 1H), 3.79 (q, J = 7.2 Hz, 1H), 3.74-3.68 (m, 5H), 2.18-2.13 (m, 1H), 1.91-1.84 (m, 2H), 1.67-1.61 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.3, 147.4, 144.0, 129.8, 123.7, 79.8, 68.4, 56.7, 52.4, 30.3, 25.6; IR (neat) 2955, 2852, 1735, 1601, 1520, 1349, 1210, 1066, 841 cm^{-1}; HRMS (ESI) Calcd for $C_{13}H_{16}NO_5$ $[M+H]^+$ 266.1028, found 266.1021.

2i: The diastereomer ratio was 1.5:1 (*anti:syn*). The diastereomers were separated by column chromatography (hexane/EtOAc = 15/1). The *anti*-isomer (**2i-1**) was obtained as a colorless oil. ^1H NMR (400 MHz, $CDCl_3$): δ8.24 (t, J = 1.6 Hz, 1H), 8.16 (d, J = 8.0 Hz, 1H), 7.74 (d, J = 8.0 Hz, 1H), 7.52 (t, J = 8.0 Hz, 1H), 4.52 (dt, J = 9.2, 7.2 Hz, 1H), 3.92 (q, J = 6.8 Hz, 1H), 3.84 (q, J = 6.8 Hz, 1H), 3.72 (s, 3H), 3.68 (d, J = 9.6 Hz, 1H), 1.91-1.84 (m, 2H), 1.77-1.72 (m, 1H), 1.47-1.40 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.0, 148.4, 137.9, 134.6, 129.7, 123.6, 122.8, 80.4, 68.6, 57.0, 52.5, 29.6, 25.5; IR (neat) 2945, 2875, 1732, 1528, 1345, 1160, 1070, 736 cm^{-1}; HRMS (ESI) Calcd for $C_{13}H_{16}NO_5$ $[M+H]^+$ 266.1028, found 266.1016. The *syn*-isomer (**2i-2**) was obtained as a colorless oil. ^1H NMR (400 MHz, $CDCl_3$): δ8.26 (t, J = 2.0 Hz, 1H), 8.15 (d, J = 8.0 Hz, 1H), 7.74 (d, J = 8.0 Hz, 1H), 7.52 (t, J = 8.0 Hz, 1H), 4.48 (dt, J = 8.0, 7.2 Hz, 1H), 3.82-3.69 (m, 6H), 2.17-2.14 (m, 1H), 1.92-1.86 (m, 2H), 1.66-1.61 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.5, 138.6, 135.0, 129.4, 124.0, 123.7, 122.6, 79.7, 68.4, 56.5, 52.4, 30.3, 25.6; IR (neat) 2946, 2874, 1734, 1528, 1346, 1161, 1070, 735 cm^{-1}; HRMS (ESI) Calcd for $C_{13}H_{16}NO_5$ $[M+H]^+$ 266.1028, found 266.1036.

2j: The diastereomer ratio was 1.2:1 (*anti:syn*). The diastereomers were separated by column chromatography (hexane/EtOAc = 15/1). The *anti*-isomer (**2j-1**) was obtained as a colorless oil. ^1H NMR (400 MHz, $CDCl_3$): δ 7.36-7.31(m, 4H), 4.52-4.47 (m, 3H), 3.91 (q, J = 7.2 Hz, 1H), 3.82 (q, J = 7.6 Hz, 1H), 3.70 (s, 3H), 3.53 (d, J = 10.0 Hz, 1H), 1.89-1.80 (m, 2H), 1.75-1.68 (m, 1H), 1.46-1.41 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.8, 137.3, 136.1, 129.4, 128.9, 80.5, 68.5, 57.2, 52.2, 33.0, 29.6, 25.5; IR (neat) 2958, 2870, 1731, 1610, 1517, 1160, 1066, 736 cm^{-1}; HRMS (ESI) Calcd for $C_{14}H_{18}O_3Br$ [M + H]+ 313.0439, found 313.0440. The *syn*-isomer (**2j-2**) was obtained as a colorless oil. ^1H NMR (400 MHz, $CDCl_3$): δ 7.36 (s, 4H), 4.47 (s, 2H), 4.43 (dt, J = 8.0, 7.2 Hz, 1H), 3.79 (q, J = 7.2 Hz, 1H), 3.71 (q, J = 7.2 Hz, 1H), 3.69 (s, 3H), 3.62 (d, J = 8.8 Hz, 1H), 2.15-2.10 (m, 1H), 1.91-1.84 (m, 2H), 1.69-1.60 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.3, 137.0, 136.9, 129.3, 129.1, 79.9, 68.3, 56.6, 52.1, 33.2, 30.2, 25.6; IR (neat) 2959, 2871, 1732, 1610, 1518, 1160, 1067, 735 cm^{-1}; HRMS (ESI) Calcd for $C_{14}H_{18}O_3Br$ $[M+H]^+$ 313.0439, found 313.0427.

2m: The diastereomer ratio was 1.5:1 (*anti:syn*). The diastereomers were separated by column chromatography (hexane/EtOAc = 15/1). The *anti*-isomer (**2m-1**) was obtained as a colorless oil. ^1H NMR (400 MHz, $CDCl_3$): δ 7.30-7.26 (m, 2H), 7.21-7.16 (m, 3H), 3.99 (dt, J = 8.0, 7.2 Hz, 1H), 3.85 (q, J = 7.2 Hz, 1H), 3.75-3.70 (m, 4H), 2.64-2.45 (m, 3H), 2.01-1.95 (m, 2H), 1.89- 1.83 (m, 2H), 1.73-1.69 (m, 1H), 1.53-1.48 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.7, 141.4, 128.4, 126.0, 80.1, 68.1, 51.7, 51.3, 33.7, 31.0, 29.7, 25.5; IR (neat) 3050, 3030, 2950, 2868, 1736, 1455, 1205, 1161, 1067, 742, 700 cm^{-1}; HRMS (ESI) Calcd for $C_{15}H_{21}O_3$ $[M+H]^+$ 249.1491, found 249.1488. The *syn*-isomer (**2m-2**) was obtained as a colorless oil. ^1H NMR (400 MHz, $CDCl_3$): δ 7.30-7.25 (m, 2H), 7.19-7.17 (m, 3H), 3.96 (dt, J = 8.0, 7.2 Hz, 1H), 3.80-3.67 (m, 5H), 2.69-2.62 (m, 1H), 2.60-2.50 (m, 2H), 2.05-1.99 (m, 2H), 1.96-1.83 (m, 2H), 1.68-1.63 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.4, 141.5, 128.5, 128.3, 125.9, 79.6, 68.0, 51.6, 50.5, 33.7, 31.3, 29.3, 25.6; IR (neat) 3051, 3030, 2949, 2869, 1736, 1456, 1205, 1162, 1068, 742, 700 cm-1;HRMS (ESI) Calcd for $C_{15}H_{21}O_3$ $[M+H]^+$ 249.1491, found 249.1485.

2o: The diastereomer ratio was 1.5:1 (*anti:syn*). The diastereomers were separated by column chromatography (hexane/EtOAc = 12/1). The *anti*-isomer (**2o-1**) was obtained as a colorless oil. ^1H NMR (400 MHz, $CDCl_3$): δ 7.37-7.27 (m, 5H), 4.52 (dt, J = 10.0, 7.2 Hz, 1H), 4.22-4.16 (m, 1H), 4.15-4.10 (m, 1H), 3.93-3.89 (m, 1H), 3.86-3.82 (m, 1H), 3.50 (d, J = 10.0 Hz, 1H), 1.87-1.82 (m, 2H), 1.71-1.66 (m, 1H), 1.46-1.40 (m, 1H), 1.22 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.6, 136.1, 128.7, 128.4, 127.6, 80.7, 68.5, 60.9, 57.7, 29.5, 25.4, 14.1; IR (neat) 3060, 3028, 2975, 2862, 1738, 1549, 1453, 1372, 1158, 736, 698 cm^{-1}; HRMS (ESI) Calcd for $C_{14}H_{19}O_3$ $[M+H]^+$ 235.1334, found 235.1337. The *syn*-isomer (**2o-2**) was obtained as a colorless oil. ^1H NMR (400 MHz,

$CDCl_3$): δ7.40-7.27 (m, 5H), 4.44 (dt, J = 8.8, 7.2 Hz, 1H), 4.17-4.10 (m, 2H), 3.82-3.78 (m, 1H), 3.74-3.70 (m, 1H), 3.60 (d, J = 8.8 Hz, 1H), 2.15-2.11 (m, 1H), 1.90-1.85 (m, 2H), 1.71-1.66 (m, 1H), 1.22 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.1, 136.8, 128.6, 128.5, 127.4, 80.1, 68.3, 60.8, 57.1, 30.2, 25.6, 14.1; IR (neat) 3061, 3029, 2975, 2863, 1738, 1550, 1372, 1159, 736, 697 cm^{-1}; HRMS (ESI) Calcd for $C_{14}H_{19}O_3$ $[M+H]^+$ 235.1334, found 235.1339.

2p: The diastereomer ratio was 1.6:1 (*anti:syn*). The diastereomers were separated by column chromatography (hexane/EtOAc = 15/1). The *anti*-somer (**2p-1**) was obtained as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44 (dd, J = 6.4, 2.0 Hz, 2H), 7.25 (dd, J = 6.4, 2.0 Hz, 2H), 4.45 (dt, J = 9.6, 7.2 Hz, 1H), 4.16 (tq, J = 18.0, 3.6 Hz, 2H), 3.90 (q, J = 7.2 Hz, 1H), 3.82 (q, J = 7.2 Hz, 1H), 3.47 (d, J = 10.0 Hz, 1H), 1.88-1.81 (m, 2H), 1.72-1.67 (m, 1H), 1.42-1.37 (m, 1H), 1.22 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.2, 135.0, 131.8, 130.1, 121.8, 80.4, 68.5, 61.1, 57.0, 29.5, 25.4, 14.0; IR (neat) 2980, 2879, 1733, 1493, 1375, 1204, 1163, 1075, 1018, 824 cm^{-1}; HRMS (ESI) Calcd for $C_{14}H_{18}O_3Br$ $[M+H]^+$ 313.0439, found 313.0428. The *syn*-isomer (**2p-2**) was obtained as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ7.45 (dd, J = 6.4, 2.0 Hz, 2H), 7.27 (dd, J = 6.4, 2.0 Hz, 2H), 4.40 (dt, J = 8.4, 7.2 Hz, 1H), 4.18-4.09 (m, 2H), 3.79 (q, J = 6.8 Hz, 1H), 3.70 (q, J = 6.8 Hz, 1H), 3.54 (d, J = 8.8 Hz, 1H), 2.14-2.08 (m, 1H), 1.90-1.84 (m, 2H), 1.68-1.61 (m, 1H), 1.22 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.6, 135.8, 131.6, 130.4, 121.6, 79.9, 68.3, 61.0, 56.5, 30.2, 25.6, 14.1; IR (neat) 2982, 2880, 1732, 1528, 1492, 1374, 1308, 1074, 1018, 828 cm^{-1}; HRMS (ESI) Calcd for $C_{14}H_{18}O_3Br$ $[M+H]^+$ 313.0439, found 313.0449.

2q: The diastereomer ratio was 1.8:1 (*anti:syn*). The diastereomers were separated by column chromatography (hexane/EtOAc = 15/1). The *anti*-isomer (**2q-1**) was obtained as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.52 (t, J = 1.6 Hz, 1H), 7.41 (d, J = 8.0 Hz, 1H), 7.29 (t, J = 7.6 Hz, 1H), 7.19 (t, J = 7.6 Hz, 1H), 4.46 (dt, J = 4.4, 2.8 Hz, 1H), 4.23-4.11 (m, 2H), 3.90 (q, J = 6.8 Hz, 1H), 3.84 (q, J = 6.8 Hz, 1H), 3.46 (q, J = 10.0 Hz, 1H), 1.88-1.83 (m, 2H), 1.73-1.68 (m, 1H), 1.44-1.40 (m, 1H), 1.23 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.0, 138.2, 131.4, 130.9, 130.2, 127.1, 122.7, 80.5, 68.5, 61.2, 57.2, 29.5, 25.4, 14.1; IR (neat) 2970, 2870, 1736, 1568, 1475, 1162, 1071, 1032, 709 cm^{-1}; HRMS (ESI) Calcd for $C_{14}H_{18}O_3Br$ $[M+H]^+$ 313.0439, found 313.0436. The *syn*-isomer (**2q-2**) was obtained as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ7.54 (t, J = 1.6 Hz, 1H), 7.40 (d, J = 8.0 Hz, 1H), 7.32 (d, J = 8.0 Hz, 1H), 7.20 (t, J = 8.0 Hz, 1H), 4.41 (dt, J = 8.4, 6.8 Hz, 1H), 4.19-4.09 (m, 2H), 3.80 (q, J = 6.8 Hz, 1H), 3.71 (q, J = 6.8 Hz, 1H), 3.54 (d, J = 8.8 Hz, 1H), 2.14-2.09 (m, 1H), 1.90-1.85 (m, 2H), 1.67-1.62 (m, 1H), 1.23 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.5, 139.0, 131.7, 130.6, 130.0, 127.3, 122.6, 79.9, 68.4, 61.0, 56.7, 30.2, 25.6, 14.1; IR (neat) 2971, 2869, 1735, 1568, 1476, 1161, 1072, 1033, 710 cm^{-1}; HRMS (ESI) Calcd for $C_{14}H_{18}O_3Br$ $[M+H]^+$ 313.0439, found 313.0441.

2r: The diastereomer ratio was 1.6:1 (*anti:syn*). The diastereomers were separated by column chromatography (hexane/EtOAc = 15/1). The *anti*-isomer (**2r-1**) was obtained as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.29 (br s, 4H), 4.45 (dt, J = 10.0, 6.8 Hz, 1H), 4.22-4.10 (m, 2H), 3.90 (q, J = 7.2 Hz, 1H), 3.82 (q, J = 7.2 Hz, 1H), 3.49 (d, J = 10.0 Hz, 1H), 1.88-1.81 (m, 2H), 1.74-1.68 (m, 1H), 1.44-1.36 (m, 1H), 1.22 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.2, 134.5, 133.6, 129.8, 128.9, 80.5, 68.5, 61.1, 57.0, 29.5, 25.4, 14.1; IR (neat) 2969, 2868, 1738, 1490, 1160, 1090, 1066, 1017, 669 cm^{-1}; HRMS (ESI) Calcd for $C_{14}H_{18}O_3Cl$ $[M+H]^+$ 269.0944, found 269.0946. The *syn*-isomer (**2r-2**) was obtained as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34-7.28 (m, 4H), 4.40 (dt, J = 8.4, 6.8 Hz, 1H), 4.18-4.09 (m, 2H), 3.79 (q, J = 6.8 Hz, 1H), 3.71 (q, J = 6.8 Hz, 1H), 3.55 (d, J = 8.8 Hz, 1H), 2.15-2.08 (m, 1H), 1.91-1.84 (m, 2H), 1.68-1.62 (m, 1H), 1.22 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.7, 135.3, 133.4, 130.0, 128.7, 79.9, 68.3, 61.0, 56.5, 30.2, 25.6, 14.1; IR (neat) 2970, 2869, 1738, 1491, 1161, 1090, 1067, 1018, 670 cm^{-1}; HRMS (ESI) Calcd for $C_{14}H_{18}O_3Cl$ $[M+H]^+$ 269.0944, found 269.0945.

2s: The diastereomer ratio was 1.5:1 (*anti:syn*). The diastereomers were separated by column chromatography (hexane/EtOAc = 15/1). The *anti*-isomer (**2s-1**) was obtained as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35-7.31 (m, 2H), 7.03-6.98 (m, 2H), 4.46 (dt, J = 9.6, 6.8 Hz, 1H), 4.22-4.10 (m, 2H), 3.90 (q, J = 7.2 Hz, 1H), 3.84 (q, J = 7.2 Hz, 1H), 3.49 (d, J = 9.6 Hz, 1H), 1.87-1.82 (m, 2H), 1.72-1.67 (m, 1H), 1.43-1.38 (m, 1H), 1.22 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.5, 131.9, 131.8, 130.0, 129.9, 115.7, 115.5, 80.6, 68.5, 61.0, 56.8, 29.5, 25.4, 14.1; IR (neat) 2985, 2876, 1735, 1609, 1530, 1370, 1228, 1159, 1072, 840, 810 cm$_{-1}$; HRMS (ESI) Calcd for $C_{14}H_{18}O_3F$ $[M+H]^+$ 253.1240, found 253.1235. The *syn*-isomer (**2s-2**) was obtained as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37-7.34 (m, 2H), 7.04-7.00 (m, 2H), 4.40 (dt, J = 8.4, 6.8 Hz, 1H), 4.18-4.10 (m, 2H), 3.79 (q, J = 6.8 Hz, 1H), 3.71 (q, J = 6.8 Hz, 1H), 3.57 (d, J = 8.4 Hz, 1H), 2.13-2.10 (m, 1H), 1.90-1.86 (m, 2H), 1.67-1.62 (m, 1H), 1.22 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.9, 132.5, 130.2, 130.1, 115.5, 115.3, 80.0, 68.3, 60.9, 56.3, 30.2, 25.6, 14.1; IR (neat) 2984, 2876, 1734, 1608, 1530, 1371, 1228, 1158, 1071, 840, 809 cm^{-1}; HRMS (ESI) Calcd for $C_{14}H_{18}O_3F$ $[M+H]^+$ 253.1240, found 253.1237.

Notes and references

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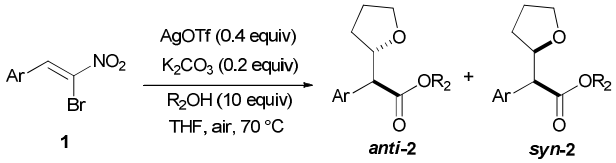
Graphical Abstract



Silver(I) catalyzed addition of THF radical to β-bromonitrostyrenes under mild basic condition in the presence of air has been developed.