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Intermolecular domino Michael/aldol reactions of α,β-unsaturated esters, aromatic aldehydes, and various nucleophiles promoted with a catalytic amount of a guanidine base in DMSO

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ABSTRACT

In DMSO, a catalytic amount of Barton's base (2-*t*-butyl-1,1,3,3-tetramethylguanidine, BTMG) effectively catalyzed intermolecular three-component reactions of α,β-unsaturated esters, aldehydes, and carbon-, sulfur-, or nitrogen-pronucleophiles to give three-component addition products with the formation of two new σ-bonds: pronucleophiles and aldehydes reacted with α,β-unsaturated esters at their β-positions and α-positions, respectively. Mechanism studies suggested that these reactions proceeded by the first intermolecular Michael addition of anionic nucleophiles that were formed from pronucleophiles with a catalytic amount of BTMG, followed by intermolecular aldol reactions of transient ester enolates even in the presence of more than stoichiometric amounts of acidic pronucleophiles. High nucleophilicity over Brønsted basicity of transient enolates in polar solvents was observed for transient ester enolates rather than ketone enolates.

1. Introduction

Multicomponent reactions (MCRs) are valuable synthetic tools for the preparation of structurally diverse compounds and for efficient synthesis of target molecules [1]. They are especially useful for building chemical libraries in drug discovery [2]. We have been interested in MCRs for the synthesis of a variety of β-hydroxy carboxylates **4** composed of three reactants including α,β-unsaturated carbonyl compounds **1**, acidic pronucleophiles **2**, and aldehydes **3** since β-hydroxy carbonyl compounds **4** are important synthetic intermediates in the synthesis of pharmaceuticals and bioactive compounds [3] (Scheme 1a).

To achieve the intermolecular three-component synthesis of **4**, sequential Michael/aldol reactions have been developed by stoichiometric pretreatment of pronucleophiles HX into anionic nucleophiles MX (M including Li [4], SiR_3 [5], etc.). Thus, a proton source from HX has been deprotonated in advance by using a stoichiometric amount of a base to avoid termination of the sequential reaction at the first Michael addition. Exceptions are domino Michael/*intramolecular* aldol reactions that were promoted with a catalytic amount of a base [6]. A more facile intramolecular aldol reaction rather than intermolecular protonation to Michael adducts enabled the catalytic use of a base for domino Michael/*intramolecular* aldol reactions. Organocatalytic asymmetric Michael/aldol reactions involving *intramolecular* aldol reactions have also been reported recently [7]. However, only a few examples of catalytic *intermolecular* three-component reactions of **1**–**3** to **4** have been reported.

A catalytic MCR to **4** without stoichiometric pretreatment of HX was achieved by tandem Baylis-Hillman/Michael reactions using a catalytic amount of a phosphine, ethyl acrylate **1**, sulfonamides as a pronucleophile **2**, and aldehydes **3** (Scheme 1b) [8]. However, Baylis-Hillman reactions to **6** have a limitation for substrates: it was pointed out that Baylis-Hillman reaction of β-substituted acrylates including alkyl crotonate, cinnamate, and 3,3-dimethylacrylate occurred sluggishly [9]. Also, Baylis-Hillman reaction inherently does not proceed with α-substituted acrylates such as methacrylates.

We focused on a *catalytic* domino Michael/*intermolecular* aldol reaction to **4** expecting broader substrate scope (Scheme 1c). The difficulty of this method had been pointed out by Wang's group [9]. They reported that mixing methyl acrylate and 2-nitropropane first with a stoichiometric amount of DBU followed by addition of

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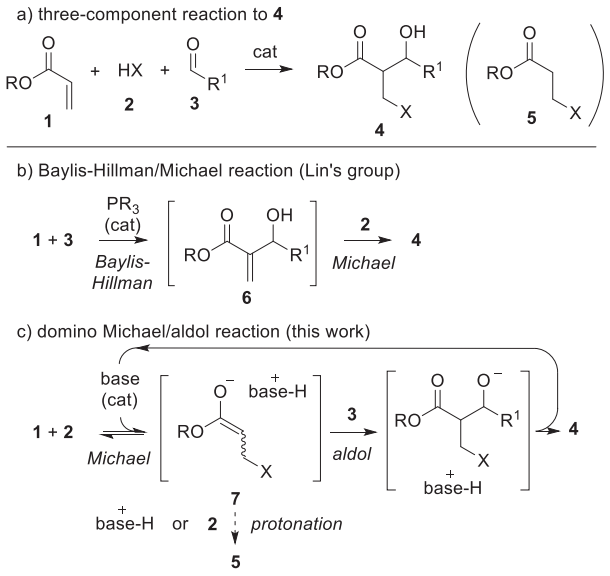


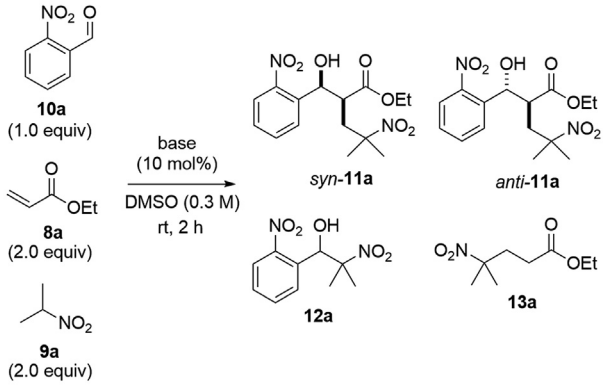
Scheme 1. Three-component reaction of acrylates **1**, acidic pronucleophiles **2**, and aldehydes **3** with a catalytic amount of a base.

benzaldehyde gave a Michael/aldol product **4** in less than 5% yield but afforded a Michael adduct **5** as the major product. Thus, three-component adduct **4** was not formed efficiently even with the use of a stoichiometric amount of DBU. The challenging point of our strategy was reaction selectivity between the intermolecular aldol reaction to **4** of catalytically formed transient ester enolates **7** and protonation with more than a stoichiometric amount of HX **2** to a Michael adduct **5**. Since the ester enolate **7** was sufficiently basic, protonation from an acidic nucleophile HX **2** or/and from a counter cation R_3NH^+ in **7** was suspected, especially in the reaction with a catalytic amount of a base. There have been only two reports of domino Michael/intermolecular aldol reactions using a catalytic amount of a base. Shibasaki reported catalytic asymmetric Michael/aldol reaction of enone, malonate, and aldehyde by using an AlLi-BINOL catalyst, and they reported that the formation of Michael adducts was inhibited as much as possible [10]. They proposed a slow protonation of an in-situ formed aluminum ketone enolate on the basis of the electronegativity of aluminium. Recently, we reported KOH-catalyzed intermolecular three-component reactions of acrylamides, nitroalkanes, and aldehydes to afford β′-hydroxy-γ-nitro amides [11]. Catalytic Michael/aldol reactions of acrylamides took place only with nitroalkanes due to the low electrophilicity of acrylamides. It was thus expected that the higher electrophilicity of alkyl acrylates would enable three-component reactions with various pronucleophiles other than nitroalkanes. However, it was also thought that the lower reactivity of transient ester enolates than that of amide enolates might influence the reaction selectivity between aldolization and protonation. Thus, we were interested in whether the difference of parent carbonyl compounds would affect Brønsted basicity and nucleophilicity of transient enolates. In this paper, we report details of domino intermolecular Michael/aldol reactions of various nucleophiles including nitroalkanes, malonates, sulfonamides, and thiols using a catalytic amount of a base in DMSO. We also report here the differences in nucleophilicity and Brønsted basicity of some kinds of catalytically formed transient enolates including esters, nitriles, and ketones.

2. Results and discussion

First, a suitable base was explored in an MCR of ethyl acrylate (**8a**), 2-nitropropane (**9a**), and 2-nitrobenzaldehyde (**10a**) by adding a solution of **9a** (2.0 equiv) and 10 mol% of a base in DMSO to a solution of acrylate **8a** (2.0 equiv) and aldehyde **10a** (1.0 equiv) in DMSO (Table 1, entries 1–8). It was found that strongly basic catalysts (pK_{BH+} >23 (CH_3CN) [12]) promoted the MCR smoothly, and 2-*tert*-butyl-1,1,3,3-tetramethylguanidine (BTMG) catalyzed the reaction most efficiently to afford the desired three-component adduct **11a** in 94% isolated yield as a mixture of *syn*- and *anti*-isomers (*syn*/*anti* = 55:45) (entry 3). In this case, the Michael adduct **13a** was also isolated in a mol ratio of **13a**/**11a** = 0.67, but the Henry adduct **12a** was not detected. Less basic catalysts including Et_3N and 2-phenyl-1,1,3,3-tetramethylguanidine (PhTMG) afforded the Henry adduct **12a** as the major product (entries 1 and 2). DBU and 1,5,7-triazabicyclo[4.4.0]dec-5-ene (TBD) worked effectively as BTMG (entries 4 and 5). Potassium *tert*-butoxide and potassium hydroxide promoted the three-component reaction smoothly, but the use of LHMDS gave the three-component adduct **11a** in only 14% yield along with the Michael adduct **13a** as the major product (entries 6–8). Thus, potassium ion was superior to lithium ion for the counter cation of a strong base, and this result implied naked anionic species would be suitable for the present intermolecular MCR. It was found that the diastereomeric ratios of **11a** were not drastically changed by the choice of bases. The stereochemistry of **11a** was determined by similarity of ^{1}H NMR spectra of *syn*-[13a] and *anti*-[13a]**11e** of which stereochemistries were determined by reductive removal of the nitro group of the minor diastereomer of **11e** into a stereochemically defined compound [13c]. The solvent

Table 1
Optimization of the reaction conditions.



entry	base[a]	Solvent	11a[b]	*syn*/*anti* of 11a[c]	12a[d]	13a/11a[e]
1	Et_3N (18.83)	DMSO	7	56:44	50	0
2	PhTMG (20.85)	DMSO	9	57:43	53	0.22
3	BTMG (23.56)	DMSO	94	55:45	0	0.67
4	DBU (24.31)	DMSO	91	56:44	trace	1.11
5	TBD (26.02)	DMSO	88	56:44	0	0.74
6	LHMDS	DMSO	14	50:50	0	7.36
7	KO*t*Bu	DMSO	67	53:47	0	1.33
8	KOH	DMSO	76	56:44	7	0.66
9	BTMG	CH_3CN	58	54:46	0	2.34
10	BTMG	THF	23	58:42	4	5.30
11	BTMG	CH_2Cl_2	23	57:43	0	6.17
12	BTMG	Toluene	13	57:43	4	6.31

[a] Numbers in parentheses are pK_{BH+} values in acetonitrile. PhTMG: 2-phenyl-1,1,3,3-tetramethylguanidine. BTMG: 2-*tert*-butyl-1,1,3,3-tetramehylguanidine. TBD: 1,5,7-Triazabicyclo[4.4.0]dec-5-ene.
[b] Isolated yield (%).
[c] *Syn*/*anti* ratio that was determined by ^{1}H NMR analysis.
[d] Yield (%) that was determined by ^{1}H NMR analysis of a mixture of **10a** and **12a**.
[e] Mol ratio.

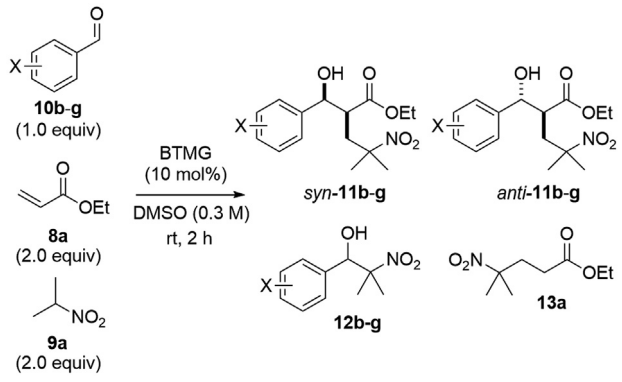
effects of DMSO were critical for the MCR since the use of less polar aprotic solvents including acetonitrile, THF, dichloromethane, and toluene gave lower yields of the desired product **11a** (entries 9–12). Judging from the ratio of **13a**/**11a** in various solvents, Michael adduct **13a** was found to form preferentially in less polar aprotic solvents.

The MCRs of benzaldehyde derivatives having electron-withdrawing groups including 4-nitro, 4-cyano, 4-bromo groups gave the corresponding desired products **11b-d** in good to high yields (Table 2, entries 1–3), while those of non-substituted and electron-releasing group-substituted benzaldehydes proceeded to afford the three-component adducts **11e-g** in moderate to low yields (entries 4–6). The ratios of **13a**/**11** suggested that the reactions of lower electrophilic aldehydes [14] tended to provide the Michael adduct **13**. Lower electrophilic aldehydes caused protonation of *in-situ* formed enolates to **13a** rather than aldol reactions to **11**. The reaction of pivalaldehyde, acrylate **8a**, and nitroalkane **9a** did not give the desired three-component adduct probably due to the low electrophilicity of aliphatic aldehydes.

Reactions of secondary nitroalkanes including nitrocyclopentane and nitrocyclohexane proceeded smoothly (Table 3, entries 1 and 2). However, the reaction with nitromethane gave the desired MCR adduct **11j** in 23% yield along with a Henry adduct **12j** in 60% yield (entry 3).

MCRs with some electrophilic alkenes were investigated. It should be noted that ethyl methacrylate reacted with 2-nitrobenzaldehyde and 2-nitropropane to give the MCR adduct **11k** in 67% yield as a mixture of diastereomers (*syn*/*anti* = 57:43) (entry 4). The stereochemistry of the minor diastereomer of **11k** was determined by X-ray crystallography of the similar compound. This result suggested that the present MCR did not proceed by the tandem Baylis-Hillman/Michael reaction [8] since the Baylis-Hillman reaction of methacrylates did not take place inherently. It was also found that BTMG was superior to DBU in the reaction with ethyl methacrylate by comparing the use of these two bases in

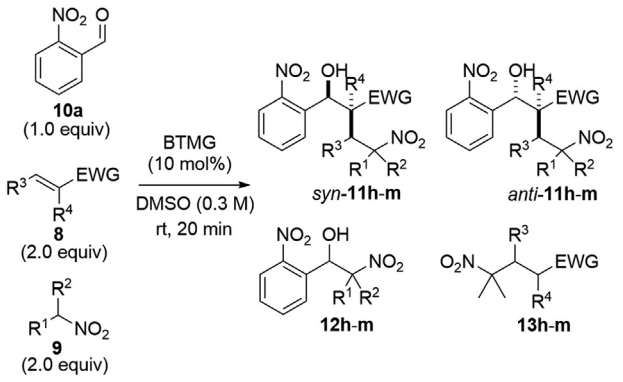
Table 2
Substrate scope of the various aromatic aldehydes.

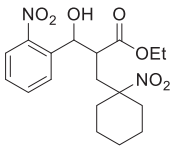
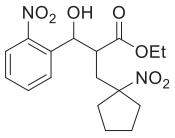
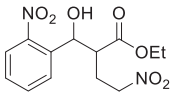
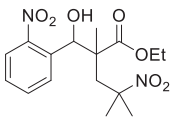
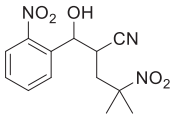
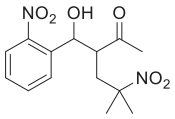


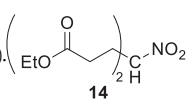
entry	X	11[a]	*syn*/*anti*[b]	12[c]	13a/11[d]
1	4-NO_2 (**10b**)	92	57:43	3	0.99
2	4-CN (**10c**)	85	57:43	4	1.06
3	4-Br (**10d**)	74	56:44	0	1.70
4	H (**10e**)	55	58:42	5	2.16
5	4-Me (**10f**)	32	50:50	0	3.63
6	4-MeO (**10g**)	26	53:47	0	5.62

[a] Isolated yield (%).
[b] *Syn*/*anti* ratio of **11** that was determined by ^{1}H NMR analysis.
[c] Yield (%) that was determined by ^{1}H NMR analysis of a mixture of **10** and **12**.
[d] Mol ratio.

Table 3
Substrate scope of the various α,β-unsaturated carbonyl compounds.



entry	11	11 (%)[a]	*syn*/*anti*[b]	12 (%)[c]	13/11[d]
1	 **11h**	92	55:45	0	1.05
2	 **11i**	89	56:44	trace	0.96
3	 **11j**	23	69:31	60	1.52[e]
4[f]	 **11k**	67 (40)[g]	57:43 (56:44)[g]	16 (37)[g]	0.87 (1.30)[g]
5	 **11l**	72	50:50	0	1.22
6[f]	 **11m**	24	54:46	0	5.83

[a] Isolated yield (%).
[b] *Syn*/*anti* ratio of **11** that was determined by ^{1}H NMR analysis.
[c] Yield (%) that was determined by H NMR analysis of a mixture of **10** and **12**. .
[d] Mol ratio.
[e] Compound **14** was formed (**14**/**11j**[d] = 1.87).

14
[f] Reaction time: 2 h.
[g] DBU was used in place of BTMG.

DMSO (entry 4). The reaction with ethyl crotonate by the use of a catalytic amount of BTMG in DMSO did not give the desired three-component adduct, and the Henry adduct **12** was obtained as the major product. Thus, substitution on the β-position of an unsaturated ester substantially influenced the reaction efficiency. The three-component reaction with acrylonitrile also proceeded smoothly to afford the corresponding product **11l** in 72% yield (entry 5), whereas the reaction with methyl vinyl ketone gave the desired product **11m** in only 24% yield (entry 6). In the case of methyl vinyl ketone, a Michael adduct **13m** was obtained as the major product.

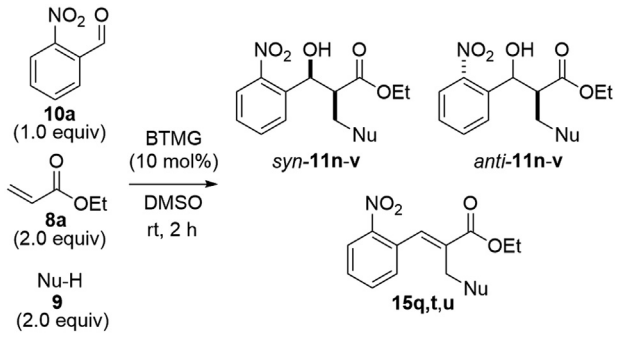
Reactions of various nucleophiles other than nitroalkanes were investigated using *o*-nitrobenzaldehyde (**10a**) and ethyl acrylate (**8a**) (Table 4). As a carbon nucleophile, we used diethyl malonate and diethyl methylmalonate (entries 1 and 2). The use of diethyl malonate afforded the desired compound **11n** in 41% yield, whereas the use of diethyl methylmalonate gave **11o** in a good yield (75%). In the case of diethyl malonate, base-catalyzed aldol condensation of diethyl malonate with **10a** might cause a decrease in the efficiency. Next, we studied the reactions of nitrogen nucleophiles using phthalimide and *N*-methyl-*p*-toluenesulfonamide (entries 3 and 4). Both nitrogen nucleophiles afforded the corresponding three-component adducts **11p,q** in moderate yields. In the case of *N*-methyl-*p*-toluenesulfonamide, elimination products **15q** and **16** were also obtained in 2% and 23% yields, respectively (entry 4).

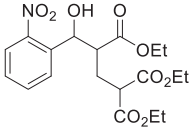
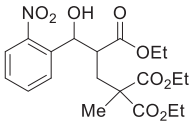
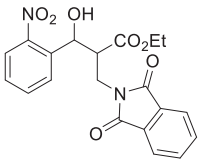
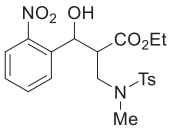
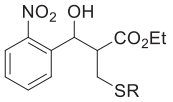
Finally, various thiols were used as pronucleophiles (entries 5–9). Optimization of the reaction conditions revealed that the use of aldehyde (5.0 equiv), thiol (1.0 equiv), and acylate (1.2 equiv) effectively promoted the three-component reactions. The results suggested that sterically hindered alkanethiols tended to give the desired products more efficiently (entries 5–8). Steric hindrance of alkanethiols might suppress the addition of alkanethiols to aldehydes to form the corresponding hemithioacetals [15]. When triphenylmethanethiol and 1-methyl-1-phenylethanethiol were used, low yields of dehydrated products **15t,u** accompanied by the desired products **11t**,**u** were obtained (entries 7 and 8). The reaction of benzenethiol gave the desired product **11v** in a low yield (entry 9). The higher acidity of benzenethiol might result in preferential formation of the Michael adduct.

In order to study the reaction mechanism, ethyl α-D-acrylate (**8a-D**, 92% D) was used for the MCR (Scheme 2a). ^{1}H NMR analysis of the product **11a** revealed that the D content of the carbonyl α-position of **11a-D** remained at 92%, indicating that the reaction did not proceed by Bailys-Hillman/Michael reaction [8] but proceeded by the domino Michael/Aldol reaction. Attempted aldol reaction of 2-nitrobenzaldehyde (**10a**) and an equimolar amount of Michael adduct **13a** with a catalytic amount (10 mol%) of BTMG in DMSO under identical conditions to those of the three-component reaction (Table 1, entry 3) gave the aldol product **11a** in only 4% yield (Scheme 2b). Therefore, the three-component reaction of acrylate, aldehyde, and nitroalkane took place mainly by the aldol reaction of transient ester enolates **7** that were formed by Michael addition of nitronates to acrylates (Scheme 1c). A reaction of Henry adduct **12a** with ethyl acrylate **8a** in the presence of 10 mol% of BTMG gave the three-component adduct **11a** in 47% yield along with the Michael adduct **13a** in 48% yield (Scheme 2c). This result suggested that retro-Henry reaction of **12a** followed by the three-component reaction took place. It was also suggested that the use of Et_3N and PhTMG as a catalyst for the three-component reaction did not promote the retro-Henry reaction (Table 1, entries 1 and 2). As described in the results for solvent effects (Table 1, entries 3 and 9–12), protonation of the transient ester enolate to the Michael adduct **13a** tended to proceed feasibly in less polar solvents. It was also assumed that retro-Henry reaction took place slowly in the case of the Henry adduct **12j** that was formed from nitromethane because of the less steric hindrance of **12j** (Table 3, entry 3).

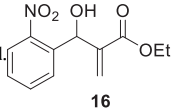
In ^{1}H NMR reaction monitoring of the BTMG-catalyzed reaction of acrylate **8a**, nitroalkane **9a**, and aldehyde **10a** in DMSO-d_6 at room temperature, the Henry adduct **12a** was not detected even in the early stage (7 min). This result was different from the three-

Table 4
Reactions of various nucleophiles.



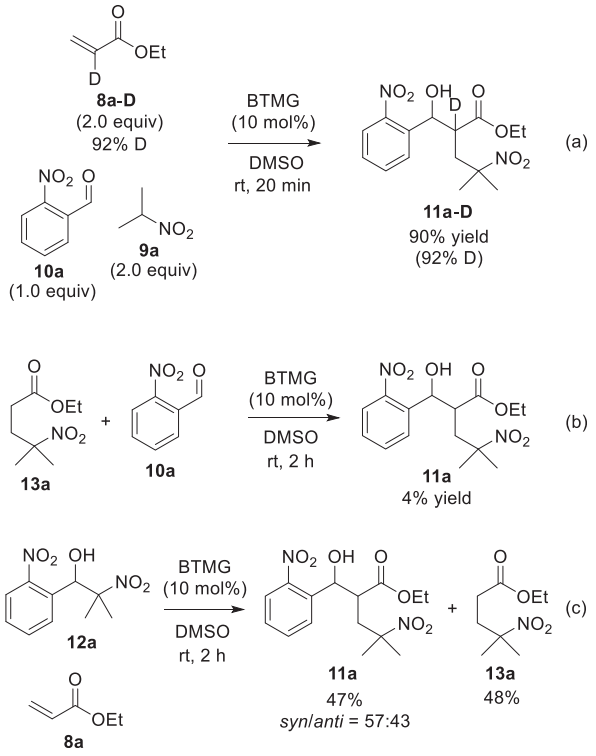
entry	11	11 (%)[a]	*syn*/*anti*[b]	15 (%)[a]
1[c]	 **11n**	41	64:36	0
2[c]	 **11o**	75	50:50	0
3[d]	 **11p**	55	56:44	0
4	 **11q**	59[e]	59:41	2
5[f]	 **11r**: R = *n*Hex	46	71:29	0
6[f]	**11s**: R = Bn	69	55:45	0
7[f]	**11t**: R = Ph_3C	69	68:32	11
8[f]	**11u**: R = $PhMe_2C$	79	56:44	5
9[f]	**11v**: R = Ph	37	54:46	0

[a] Isolated yield based on the aldehyde.
[b] The ratio was determined by ^{1}H NMR.
[c] Reaction time: 0.5 h.
[d] Reaction time: 60 h.
[e] Compound **16** (27%) was obtained.



16

[f] Aldehyde (5.0 equiv), thiol (1.0 equiv), and acrylate (1.2 equiv) were used.



Scheme 2. Mechanism study.

component reactions using acrylamide that showed a rapid generation of the corresponding Henry adduct followed by the appearance of the three-component adduct with the gradual disappearance of the Henry adduct [11]. Almost equimolar amounts of the three-component adduct **11a** and Michael adduct **13a** were detected in the early stage (7 min), and prolonged reaction times (2 h) did not change the yields of **11a** and **13a**. Also, the diastereomeric (*syn*/*anti*) ratios of the three-component adduct **11a** did not change from the beginning to the last stage of the reaction. The Henry adduct **12a** was not detected by the NMR monitoring because of the higher electrophilicity of ethyl acrylate than that of acrylamide, but **12a** might have formed just after addition of the catalyst.

As described for the three-component reaction with methyl vinyl ketone (Table 3, entry 6), Brønsted basicity of a transient ketone enolate was superior to its nucleophilicity to an aldehyde even in DMSO.

3. Conclusions

In conclusion, we have established intermolecular three-component reactions of acrylates, aromatic aldehydes, and various carbon-, nitrogen-, and sulfur-nucleophiles to β-hydroxy carbonyl compounds in the presence of a catalytic amount of BTMG in DMSO. Mechanistic studies revealed that the MCRs proceeded by domino Michael/aldol reactions. The present method provided the desired three-component adducts in shorter reaction times with broader substrate scopes than catalytic Baylis-Hillman/Michael reactions [8], and a variety of linear β-hydroxy esters were prepared directly from three components. It should be noted that catalytic intermolecular aldol reactions proceeded in the presence of protic pronucleophiles. We clarified that nucleophilicity for aldolization over Brønsted basicity of transient enolates was obvious in the reactions of transient ester enolates in DMSO, whereas transient ketone enolates showed less nucleophilicity compared with their Brønsted basicity. In addition, higher nucleophilicity of transient enolates was observed in more polar aprotic solvents. The utilization of high nucleophilicity of transient enolates would enable other types of MCRs by using catalytic amounts of bases.

4. Experimental

4.1. General

All melting points were determined on Yanagimoto micro melting point apparatus and were not corrected. Infrared spectra (IR) were recorded on Horiba IR-710. ^{1}H NMR spectra were recorded on a JEOL JNM ECA600 (600 MHz) or a JEOL JNM ECS400 (400 MHz) spectrometer at room temperature; chemical shifts (δ) are reported in parts per million relative to tetramethylsilane. Splitting patterns are designated as s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad. ^{13}C NMR spectra were recorded on a JEOL JNM ECA600 (150 MHz) or a JEOL JNM ECS400 (100 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in parts per million relative to tetramethylsilane with the solvent resonance as the internal standard $CDCl_3$. HRMS data were recorded on JEOL JMS-T100TD. Analytical TLC was performed on Merck precoated TLC plates (silica gel 60 GF254, 0.25 mm). Silica gel column chromatography was carried out on silica gel 60 N (Kanto Kagaku Co., Ltd., spherical, neutral, 63−210 μm). All reactions were carried out under nitrogen atmosphere in a dried glassware with magnetic stirring. DMSO was distilled from CaH_2. DMSO-d_6 was dried with MS4A. Ph Me_2CSH [16], nitrocyclopentane [17], and nitrocyclohexane [17] were prepared by the reported procedures.

4.2. Synthesis of ethyl α-D-acrylate (8a-D)

A mixture of ethyl acrylate (1.06 mL, 9.2 mmol) and DABCO (500 mg, 4.6 mmol) in D_2O (2.2 ml) was stirred at room temperature for 11 h. The reaction mixture was extracted, and the combined organic extracts were dried over anhydrous Na_2SO_4, filtrated to afford ethyl α-D-acrylate (**8a-D**) (90 mg, 10%). Its D-content (92%D) was determined by ^{1}H NMR.

4.3. General procedure of domino Michael/aldol reaction of nitroalkanes, acrylates, and aldehydes

To a mixture of ethyl acrylate (0.60 mmol) and aldehyde (0.30 mmol) in DMSO (0.50 mL), a solution of nitroalkane (0.60 mmol) and BTMG (0.03 mmol) in DMSO (0.50 mL) was added. The reaction mixture was stirred at room temperature until aldehyde was not detected by TLC analysis. The reaction mixture was quenched by adding saturated aqueous solution of NH_4Cl, and the aqueous layer was extracted with ethyl acetate. The combined organic extracts were washed with brine and dried over Na_2SO_4. The filtrate was concentrated under reduced pressure, and the residue was purified by column chromatography on silica gel (hexanes/ethyl acetate) to afford β′-hydroxy-γ-nitro carbonyl compounds **11**.

4.4. Three-component adducts

Ethyl (*R)-2-[(*R**)-hydroxy-(2-nitrophenyl)methyl]-4-methyl-4-nitropentanoate (*syn*-11a).** Yellow sticky oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.02 (1H, d, J = 7.8 Hz), 7.83 (1H, d, J = 8.0 Hz), 7.69 (1H, dd, J = 7.4, 8.0 Hz), 7.50 (1H, dd, J = 7.4, 7.8 Hz), 5.53 (1H, dd, J = 3.6, 4.4 Hz), 4.07 (2H, q, J = 7.2 Hz), 3.40 (1H, brs), 2.92 (1H, ddd, J = 1.8, 4.4, 9.8 Hz), 2.55 (1H, dd, J = 9.8, 15.2 Hz), 2.25 (1H, dd,

J = 1.8, 15.2 Hz), 1.46 (3H, s), 1.45 (3H, s), 1.16 (3H, t, J = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 174.2, 147.7, 135.5, 133.6, 129.5, 129.0, 125.1, 87.1, 70.2, 61.5, 46.3, 36.7, 26.0, 25.8, 13.7; IR ($CHCl_3$, cm^{-1}): 3597, 3030, 2987, 1728, 1539, 1527, 1348, 1190; HRMS (DART+) (m/z) calcd for $C_{15}H_{21}N_2O_7$ [$(M + H)^+$]: 341.13488, found 341.13473.

Ethyl (*R)-2-[(*S**)-hydroxy-(2-nitrophenyl)methyl]-4-methyl-4-nitropentanoate (*anti*-11a).** Yellow sticky oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.04 (1H, d, J = 8.4 Hz), 7.66−7.62 (2H, m), 7.51−7.46 (1H, m), 5.43 (1H, dd, J = 4.3, 8.3 Hz), 4.02−3.94 (2H, m), 3.87 (1H, d, J = 8.3 Hz), 3.05 (1H, ddd, J = 1.9, 4.3, 10.4 Hz), 2.78 (1H, dd, J = 10.4, 15.1 Hz), 2.24 (1H, dd, J = 1.9, 15.1 Hz), 1.62 (3H, s), 1.60 (3H, s), 1.05 (3H, t, J = 7.4 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 174.1, 137.2, 133.6, 128.9, 128.1, 125.0, 87.1, 71.9, 61.3, 46.7, 41.0, 26.5, 25.7, 13.7; IR ($CHCl_3$, cm^{-1}): 3597, 2987, 2929, 1730, 1707, 1541, 1527, 1346, 1265, 1188; HRMS (DART+) (m/z) calcd for $C_{15}H_{21}N_2O_7$ [$(M + H)^+$]: 341.13488, found 341.13473.

Ethyl (*R)-2-[(*R**)-hydroxy-(4-nitrophenyl)methyl]-4-methyl-4-nitropentanoate (*syn*-11b).** Yellow sticky oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.24 (2H, d, J = 8.6 Hz), 7.55 (2H, d, J = 8.6 Hz), 5.07 (1H, brs), 4.13−4.06 (2H, m), 2.99 (1H, d, J = 2.4 Hz), 2.72 (1H, dd, J = 4.8, 10.1 Hz), 2.53 (1H, dd, J = 10.1, 15.3 Hz), 2.12 (1H, d, J = 15.3 Hz), 1.48 (3H, s), 1.46 (3H, s), 1.09 (3H, t, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 173.9, 147.6, 127.0, 123.6, 87.0, 73.3, 61.6, 61.5, 48.3, 36.7, 26.1, 25.9, 21.4, 13.8; IR ($CHCl_3$, cm^{-1}): 3599, 3030, 2987, 1726, 1541, 1523, 1348, 1188; HRMS (DART+) (m/z) calcd for $C_{15}H_{21}N_2O_7$ [$(M + H)^+$]: 341.13488, found 341.13504.

Ethyl (*R)-2-[(*S**)-hydroxy-(4-nitrophenyl)methyl]-4-methyl-4-nitropentanoate (*anti*-11b).** Yellow sticky oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.23 (2H, d, J = 8.8 Hz), 7.49 (2H, d, J = 8.8 Hz), 4.92 (1H, dd, J = 6.0, 6.8 Hz), 4.03 (2H, q, J = 7.1 Hz), 3.22 (1H, d, J = 6.8 Hz), 2.82 (1H, ddd, J = 1.8, 6.0, 9.8 Hz), 2.50 (1H, dd, J = 9.8, 15.1 Hz), 2.25 (1H, dd, J = 1.8, 15.1 Hz), 1.60 (3H, s), 1.53 (3H, s), 1.09 (3H, t, J = 7.1 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 173.7, 148.2, 127.0, 127.0, 123.7, 87.2, 75.1, 61.5, 48.3, 39.7, 27.0, 25.2, 13.8; IR ($CHCl_3$, cm^{-1}): 3597, 3028, 2989. 1728, 1541, 1523, 1348, 1188; HRMS (DART+) (m/z) calcd for $C_{15}H_{21}N_2O_7$ [$(M + H)^+$]: 341.13488, found 341.13627.

Ethyl (*R)-2-[(*R**)-(4-cyanophenyl)hydroxymethyl]-4-methyl-4-nitropentanoate (*syn*-11c).** Colorless crystal; mp: 92.0−92.5 °C (recryst. from $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.67 (2H, d, J = 8.3 Hz), 7.48 (2H, d, J = 8.3 Hz), 5.00 (1H, dd, J = 2.4, 4.3 Hz), 4.07 (2H, dq, J = 2.0, 7.0 Hz), 2.90 (1H, d, J = 2.4 Hz), 2.69 (1H, dd, J = 4.3, 10.3 Hz), 2.51 (1H, dd, J = 10.3, 15.2 Hz), 2.14 (1H, d, J = 15.2 Hz), 1.48 (3H, s), 1.46 (3H, s), 1.16 (3H, t, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 173.9, 145.6, 132.3, 126.9, 111.9, 87.0, 73.4, 61.6, 48.4, 36.8, 26.0, 25.9, 13.8; IR ($CHCl_3$, cm^{-1}): 3599, 3028, 2231, 1726, 1541, 1188; HRMS (DART+) (m/z) calcd for $C_{16}H_{21}N_2O_5$ [$(M + H)^+$]: 321.14505, found 321.14619.

Ethyl (*R)-2-[(*S**)-(4-cyanophenyl)hydroxymethyl]-4-methyl-4-nitropentanoate (*anti*-11c).** Colorless crystal; mp: 97.0−98.0 °C (recryst. from $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.67 (2H, d, J = 8.6 Hz), 7.43 (2H, d, J = 8.6 Hz), 4.86 (1H, dd, J = 6.0, 6.8 Hz), 4.02 (2H, q, J = 7.2 Hz), 3.15 (1H, d, J = 6.8 Hz), 2.78 (1H, ddd, J = 1.9, 6.0, 9.9 Hz), 2.49 (1H, dd, J = 9.9, 15.2 Hz), 2.23 (1H, dd, J = 1.9, 15.2 Hz), 1.59 (3H, s), 1.52 (3H, s), 1.09 (3H, t, J = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 173.7, 146.3, 132.3, 126.8, 118.5, 87.2, 75.3, 61.4, 48.2, 39.8, 27.0, 25.2, 13.8; IR ($CHCl_3$, cm^{-1}): 3597, 3030, 2989, 2231, 1728, 1541; HRMS (DART+) (m/z) calcd for $C_{16}H_{21}N_2O_5$ [$(M + H)^+$]: 321.14505, found 321.14438.

Ethyl (*R)-2-[(*R**)-(4-bromophenyl)hydroxymethyl]-4-methyl-4-nitropentanoate (*syn*-11d).** Slight yellow sticky oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.49 (2H, d, J = 8.0 Hz), 7.22 (2H, d, J = 8.0 Hz), 4.87 (1H, brs), 4.02 (2H, q, J = 7.1 Hz), 2.78 (1H, brs), 2.66 (1H, ddd, J = 1.4, 5.4, 10.2 Hz), 2.50 (1H, dd, J = 10.2, 15.1 Hz), 2.22 (1H, d, J = 15.1 Hz), 1.49 (3H, s), 1.46 (3H, s), 1.13 (3H, t, J = 7.1 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 173.9, 139.5, 131.6, 127.9, 122.0, 87.1, 73.6, 61.3, 48.8, 37.1, 26.1, 25.8, 13.8; IR ($CHCl_3$, cm^{-1}): 3600, 2987, 1726, 1541, 1188; HRMS (DART+) (m/z) calcd for $C_{15}H_{21}NO_5{}^{81}Br$ [$(M + H)^+$]: 376.05826, found 376.05722.

Ethyl (*R)-2-[(*S**)-(4-bromophenyl)hydroxymethyl]-4-methyl-4-nitropentanoate (*anti*-11d).** Colorless crystal; mp: 87.0−88.0 °C (recryst. from $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.49 (2H, d, J = 8.2 Hz), 7.18 (2H, d, J = 8.2 Hz), 4.75 (1H, dd, J = 6.4, 6.6 Hz), 4.07 (2H, q, J = 7.3 Hz), 2.89 (1H, d, J = 6.4 Hz), 2.75 (1H, ddd, J = 1.6, 6.6, 10.1 Hz), 2.45 (1H, dd, J = 10.1, 15.3 Hz), 2.06 (1H, d, J = 15.3 Hz), 1.54 (3H, s), 1.49 (3H, s), 1.15 (3H, t, J = 7.3 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 174.0, 139.9, 131.7, 127.9, 122.2, 87.2, 75.4, 61.3, 48.6, 39.6, 26.6, 25.5, 13.8; IR ($CHCl_3$, cm^{-1}): 3599, 2987, 1728, 1541, 1265, 1186; HRMS (DART+) (m/z) calcd for $C_{15}H_{21}NO_5{}^{81}Br$ [$(M + H)^+$]: 376.05826, found 376.05722.

Ethyl (*R)-2-[(*R**)-hydroxy(phenyl)methyl]-4-methyl-4-nitropentanoate (*syn*-11e).** Yellow sticky oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.38−7.27 (5H, m), 4.90 (1H, dd, J = 2.9, 5.4 Hz), 4.00 (2H, q, J = 7.0 Hz), 2.70 (1H, ddd, J = 1.7, 5.4, 10.2 Hz), 2.63 (1H, d, J = 2.9 Hz), 2.53 (1H, dd, J = 10.2, 14.9 Hz), 2.23 (1H, dd, J = 1.7, 14.9 Hz), 1.48 (3H, s), 1.45 (3H, s), 1.09 (3H, t, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 174.0, 140.5, 128.4, 128.1, 126.1, 87.3, 74.3, 61.1, 49.1, 37.3, 26.1, 25.7, 13.8; IR ($CHCl_3$, cm^{-1}): 3599, 3030, 2987, 1722, 1541, 1188; HRMS (DART+) (m/z) calcd for $C_{15}H_{22}NO_5$ [$(M + H)^+$]: 296.14980, found 296.15219.

Ethyl (*R)-2-[(*S**)-hydroxy(phenyl)methyl]-4-methyl-4-nitropentanoate (*anti*-11e).** Colorless crystal; mp: 48.0−49.0 °C (recryst. from $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.39−7.29 (5H, m), 4.77 (1H, dd, J = 6.4, 6.4 Hz), 4.09 (2H, q, J = 7.2 Hz), 2.81−2.75 (2H, m), 2.46 (1H, dd, J = 10.4, 15.1 Hz), 2.02 (1H, d, J = 15.1 Hz), 1.51 (3H, s), 1.47 (3H, s), 1.15 (3H, t, J = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 174.2, 140.8, 128.6, 128.4, 126.3, 87.3, 76.1, 61.2, 48.9, 39.6, 26.4, 25.5, 13.8; IR ($CHCl_3$, cm^{-1}): 3599, 3032, 2989, 1728, 1541, 1184; HRMS (DART+) (m/z) calcd for $C_{15}H_{22}NO_5$ [$(M + H)^+$]: 296.14980, found 296.14958.

Ethyl (*R)-2-[(*R**)-hydroxy-(4-methylphenyl)methyl]-4-methyl-4-nitropentanoate (*syn*-11f).** Yellow sticky oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.21 (2H, d, J = 8.2 Hz), 7.15 (2H, d, J = 8.2 Hz), 4.86 (1H, d, J = 5.6 Hz), 4.00 (2H, q, J = 7.0 Hz), 2.69 (1H, ddd, J = 1.9, 5.6, 10.1 Hz), 2.52 (1H, dd, J = 10.1, 15.1 Hz), 2.34 (4H, s), 2.30 (1H, dd, J = 1.9, 15.1 Hz), 1.48 (3H, s), 1.46 (3H, s), 1.10 (3H, t, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 174.0, 137.8, 137.5, 129.1, 126.0, 87.3, 74.2, 61.1, 49.1, 37.3, 26.1, 25.7, 21.1, 13.8; IR ($CHCl_3$, cm^{-1}): 3521, 3030, 2987, 1726, 1541, 1376, 1348, 1188; HRMS (DART+) (m/z) calcd for $C_{16}H_{22}NO_4$ [$(M - OH)^+$]: 292.15488, found 292.15505.

Ethyl (*R)-2-[(*S**)-hydroxy-(4-methylphenyl)methyl]-4-methyl-4-nitropentanoate (*anti*-11f).** Yellow sticky oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.20−7.15 (4H, m), 4.72 (1H, brs), 4.11 (2H, q, J = 7.1 Hz), 2.78 (1H, ddd, J = 1.9, 8.0, 10.5 Hz), 2.61 (1H, brs), 2.44 (1H, dd, J = 10.5, 14.9 Hz), 2.35 (3H, s), 1.96 (1H, dd, J = 1.9, 14.9 Hz), 1.50 (3H, s), 1.47 (3H, s), 1.19 (3H, t, J = 7.1 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 174.3, 138.2, 137.8, 129.3, 126.3, 92.4, 87.2, 76.1, 61.1, 48.9, 39.6, 26.3, 25.6, 21.1, 13.9; IR ($CHCl_3$, cm^{-1}): 3512, 3030, 2987, 1728, 1541, 1377, 1186; HRMS (DART+) (m/z) calcd for $C_{16}H_{24}NO_5$ [$(M + H)^+$]: 310.16545, found 310.16468.

Ethyl (*R)-2-[(*R**)-hydroxy-(4-methoxyphenyl)methyl]-4-methyl-4-nitropentanoate (*syn*-11g).** Colorless sticky oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.25 (2H, d, J = 8.8 Hz), 6.88 (2H, d, J = 8.8 Hz), 4.82 (1H, d, J = 6.0 Hz), 3.99 (2H, q, J = 7.6 Hz), 3.80 (3H, s), 2.68 (1H, ddd, J = 1.9, 6.0, 9.9 Hz), 2.52 (1H, brs), 2.51 (1H, dd, J = 9.9, 15.0 Hz), 2.33 (1H, dd, J = 1.9, 15.0 Hz), 1.49 (3H, s), 1.47 (3H, s), 1.09 (3H, t, J = 7.6 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 173.9, 159.4, 132.6, 127.4, 113.8, 87.3, 74.1, 61.0, 55.3, 49.3, 37.6, 26.1, 25.8, 13.8; IR ($CHCl_3$, cm^{-1}): 3600, 3024, 2987, 1724, 1539, 1265, 1178; HRMS (DART+) (m/z) calcd for $C_{16}H_{22}NO_5$ [$(M - OH)^+$]: 308.14980, found

308.15054.

Ethyl (*R)-2-[(*S**)-hydroxy-(4-methoxyphenyl)methyl]-4-methyl-4-nitropentanoate (*anti*-11g).** Colorless crystal; mp: 78.0–78.5 °C (recryst. from $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz): δ 7.23 (2H. d. $J = 8.8$ Hz), 6.89 (2H, d, $J = 8.8$ Hz), 4.71 (1H, dd, $J = 5.4$, 7.6 Hz), 4.12 (2H, q, $J = 7.2$ Hz), 3.81 (3H, s), 2.76 (1H, ddd, $J = 1.8$, 7.6, 10.6 Hz), 2.53 (1H, d, $J = 5.4$ Hz), 2.43 (1H, dd, $J = 10.6$, 15.1 Hz), 1.94 (1H, dd, $J = 1.8$, 15.1 Hz), 1.50 (3H, s), 1.47 (3H, s), 1.21 (3H, t, $J = 7.2$ Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 174.3, 159.7, 132.9, 127.7, 114.1, 87.3, 75.9, 61.2, 55.3, 49.1, 39.6, 26.3, 25.6, 13.9; IR ($CHCl_3$, cm^{-1}): 3599, 2987, 1726, 1541, 1265; HRMS (DART+) (*m/z*) calcd for $C_{16}H_{22}NO_5$ [(M − OH)$^+$]: 308.14980, found 308.15054.

Ethyl (*R)-2-[(*R**)-hydroxy-(2-nirophenyl)methyl]-3-cyclohexylnitromethylpropanoate (*syn*-11h).** Orange sticky oil; ^1H NMR ($CDCl_3$, 600 MHz): δ 8.03 (1H, d, $J = 8.1$ Hz), 8.02 (1H, d, $J = 7.5$ Hz), 7.69 (1H, ddd, $J = 1.2$, 7.5, 7.8 Hz), 7.50 (1H, ddd, $J = 1.2$, 7.8, 8.1 Hz), 5.51 (1H, dd, $J = 4.2$, 4.8 Hz), 4.07 (2H, q, $J = 7.1$ Hz), 3.23 (1H, dd, $J = 4.2$, 4.2 Hz), 4.07 (2H, q, $J = 7.1$ Hz), 2.95 (1H, ddd, $J = 1.8$, 4.5, 9.8 Hz), 2.44 (1H, dd, $J = 9.8$, 15.5 Hz), 2.28–2.22 (2H, m), 2.20 (1H, dd, $J = 1.8$, 15.5 Hz), 1.57–1.22 (8H, m), 1.17 (3H, t, $J = 7.1$ Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 174.1, 174.7, 135.5, 133.6, 129.5, 129.1, 125.2, 90.4, 70.4, 61.5, 45.4, 36.3, 34.1, 33.8, 24.5, 22.2, 22.1, 13.8; IR ($CHCl_3$, cm^{-1}): 3597, 2943, 1728, 1535, 1346, 1186; HRMS (DART+) (*m/z*) calcd for $C_{18}H_{25}N_2O_7$ [(M + H)$^+$]: 381.16618, found 381.16601.

Ethyl (*R)-2-[(*S**)-hydroxy-(2-nirophenyl)methyl]-3-cyclohexylnitromethylpropanoate (*anti*-11h).** Yellow sticky oil; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.04 (1H, dd, $J = 1.3$, 7.9 Hz), 7.65 (1H, ddd, $J = 1.3$, 7.8, 7.9 Hz), 7.59 (1H, dd, $J = 1.6$, 7.8 Hz), 7.48 (1H, ddd, $J = 1.6$, 7.6, 7.9 Hz), 5.40 (1H, dd, $J = 4.6$, 8.1 Hz), 3.99 (2H, q, $J = 6.9$ Hz), 3.66 (1H, d, $J = 8.1$ Hz), 3.05 (1H, ddd, $J = 1.9$, 4.6, 10.6 Hz), 2.68 (1H, dd, $J = 10.6$, 15.2 Hz), 2.41–2.32 (2H, m), 2.17 (1H, dd, $J = 1.9$, 15.2 Hz), 1.71–1.32 (8H, m), 1.06 (3H, t, $J = 6.9$ Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 173.9, 147.6, 137.1, 133.6, 128.9, 128.0, 125.0, 90.3, 71.8, 61.3, 46.0, 34.3, 33.8, 29.7, 24.6, 22.2, 22.1, 13.7; IR ($CHCl_3$, cm^{-1}): 2941, 1716, 1537, 1346; HRMS (DART+) (*m/z*) calcd for $C_{18}H_{25}N_2O_7$ [(M + H)$^+$]: 381.16618, found 381.16605.

Ethyl (*R)-2-[(*R**)-hydroxy-(2-nirophenyl)methyl]-3-cyclopentylnitromethylpropanoate (*syn*-11i).** Slight orange sticky oil; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.02 (1H, d, $J = 8.0$ Hz), 7.82 (1H, d, $J = 7.8$ Hz), 7.69 (1H, dd, $J = 7.6$, 7.8 Hz), 7.50 (1H, dd, $J = 7.6$, 8.0 Hz), 5.51 (1H, brs), 4.11–4.01 (2H, m), 3.45 (1H, brs), 2.90 (1H, dd, $J = 4.8$, 10.1 Hz), 2.61 (1H, dd, $J = 10.1$, 15.2 Hz), 2.48–2.38 (2H, m), 2.32 (1H, d, $J = 15.2$ Hz), 1.73–1.51 (6H, m), 1.17 (3H, t, $J = 7.0$ Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 174.3, 147.7, 135.5, 133.5, 129.4, 129.0, 125.2, 98.4, 70.1, 61.5, 46.8, 37.4, 37.4, 35.5, 24.1, 23.7, 13.7; IR ($CHCl_3$, cm^{-1}): 3591, 2983, 1728, 1535, 1348, 1265, 1190; HRMS (DART+) (*m/z*) calcd for $C_{17}H_{23}N_2O_7$ [(M + H)$^+$]: 367.15053, found 367.14863.

Ethyl (*R)-2-[(*S**)-hydroxy-(2-nirophenyl)methyl]-3-cyclopentylnitromethylpropanoate (*anti*-11i).** Yellow sticky oil; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.04 (1H, d, $J = 8.4$ Hz), 7.68–7.61 (2H, m), 7.48 (1H, dd, $J = 6.8$, 8.4 Hz), 5.42 (1H, dd, $J = 4.2$, 7.6 Hz), 4.01–3.95 (1H, m), 3.98 (2H, q, $J = 7.2$ Hz), 3.01 (1H, ddd, $J = 1.8$, 4.2, 10.2 Hz), 2.85 (1H, dd, $J = 10.2$, 15.2 Hz), 2.62–2.48 (2H, m), 2.33 (1H, dd, $J = 1.8$, 15.2 Hz), 1.88–1.77 (6H, m), 1.06 (3H, t, $J = 7.2$ Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 174.2, 147.6, 137.2, 133.6, 128.9, 128.1, 125.0, 98.4, 71.8, 61.3, 47.4, 39.8, 38.0, 37.4, 24.2, 24.0, 13.7; IR ($CHCl_3$, cm^{-1}): 3597, 2985, 1705, 1537, 1346, 1265; HRMS (DART+) (*m/z*) calcd for $C_{17}H_{23}N_2O_7$ [(M + H)$^+$]: 367.15053, found 367.15160.

Ethyl 2-[hydroxy(2-nitrophenyl)methyl]-4-nitrobutanoate (11j). Yellow sticky oil; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.11 (1H, dd, $J = 0.8$, 8.4 Hz, *anti*), 8.05 (1H, d, $J = 8.4$ Hz, *syn*), 7.93 (1H, d, $J = 8.0$ Hz, *anti*), 7.76–7.73 (1H, m, *anti*), 7.75–7.72 (2H, m, *syn*), 7.58–7.53 (1H, m, *syn*), 7.58–7.53 (1H, m, *anti*), 5.98 (1H, dd, $J = 3.2$, 4.0 Hz, *anti*), 5.73 (1H, dd, $J = 5.6$, 6.0 Hz, *syn*), 5.10–5.05 (1H, m, *syn*), 5.01 (1H, dt, $J = 3.2$, 10.4 Hz), 4.13 (2H, q, $J = 7.5$ Hz, *syn*), 4.06 (2H, q, $J = 7.4$ Hz, *anti*), 3.48 (1H, d, $J = 6.0$ Hz, *syn*), 3.42 (1H, d, $J = 4.0$ Hz, *anti*), 2.51–2.09 (5H, m, *syn*), 2.51–2.09 (5H, m, *anti*), 1.25 (3H, t, $J = 7.5$ Hz, *syn*), 1.19 (3H, t, $J = 7.4$ Hz, *anti*); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 171.9, 147.8, 147.3, 134.2, 134.0, 133.7, 129.7, 129.6, 129.2, 128.8, 125.4, 125.1, 125.4, 125.1, 91.2, 89.0, 69.9, 69.5, 61.1, 60.9, 30.1, 29.8, 25.3, 22.2, 14.1, 14.0; IR ($CHCl_3$, cm^{-1}): 3597, 3030, 2985, 1730, 1554, 1529, 1348, 1265; HRMS (DART+) (*m/z*) calcd for $C_{13}H_{17}N_2O_7$ [(M + H)$^+$]: 313.10358, found 313.10310.

Ethyl (*R)-2-[(*R**)-hydroxy-(2-nitrophenyl)methyl]-2,4-dimethyl-4-nitropentanoate (*syn*-11k).** Yellow sticky oil; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.82 (1H, d, $J = 8.0$ Hz), 7.78 (1H, d, $J = 8.2$ Hz), 7.64 (1H, dd, $J = 7.6$, 8.2 Hz), 7.46 (1H, dd, $J = 7.6$, 8.0 Hz), 5.68 (1H, d, $J = 3.2$ Hz), 4.05–3.97 (2H, m), 3.02 (1H, d, $J = 3.2$ Hz), 2.79 (1H, d, $J = 15.4$ Hz), 2.57 (1H, d, $J = 15.4$ Hz), 1.57 (3H, s), 1.49 (3H, s), 1.15 (3H, t, $J = 7.4$ Hz), 1.01 (3H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 175.1, 133.1, 132.3, 130.1, 129.0, 124.4, 86.7, 71.8, 61.8, 50.7, 43.3, 30.6, 23.6, 13.8, 13.7; IR ($CHCl_3$, cm^{-1}): 3599, 3030, 2931, 1720, 1541, 1352; HRMS (DART+) (*m/z*) calcd for $C_{16}H_{23}N_2O_7$ [(M + H)$^+$]: 355.15053, found 355.15057.

Ethyl (*R)-2-[(*S**)-hydroxy-(2-nitrophenyl)methyl]-2,4-dimethyl-4-nitropentanoate (*anti*-11k).** Slight yellow sticky oil; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.86 (1H, d, $J = 8.0$ Hz), 7.62–7.61 (2H, m), 7.50–7.46 (1H, m), 5.66 (1H, d, $J = 6.6$ Hz), 4.14 (2H, q, $J = 7.1$ Hz), 3.17 (1H, d, $J = 6.6$ Hz), 2.56 (1H, d, $J = 15.2$ Hz), 2.47 (1H, d, $J = 15.2$ Hz), 1.53 (3H, s), 1.48 (3H, s), 1.24 (3H, t, $J = 7.1$ Hz), 0.97 (3H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 175.4, 149.5, 134.1, 132.5, 129.1, 129.0, 124.3, 86.6, 73.2, 61.7, 50.8, 44.5, 30.9, 22.9, 13.9, 13.8; IR ($CHCl_3$, cm^{-1}): 3604, 3030, 2993, 1718, 1543, 1350; HRMS (DART+) (*m/z*) calcd for $C_{16}H_{23}N_2O_7$ [(M + H)$^+$]: 355.15053, found 355.14933.

(*R)-2-[(*R**)-Hydroxy-(2-nitrophenyl)methyl]-4-methyl-4-nitropentanenitrile (*syn*-11l).** Yellow sticky oil; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.10–8.07 (2H, m), 7.79 (1H, dd, $J = 7.4$, 8.0 Hz), 7.57 (1H, dd, $J = 7.4$, 8.0 Hz), 5.40 (1H, brs), 3.28 (1H, d, $J = 9.6$ Hz), 2.71 (1H, dd, $J = 10.2$, 15.1 Hz), 2.63 (1H, brs), 2.59 (1H, dd, $J = 2.8$, 15.1 Hz), 1.77 (3H, s), 1.74 (3H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 135.8, 134.4, 129.8, 129.0, 125.0, 118.3, 86.9, 70.0, 41.0, 35.9, 27.1, 25.2; IR ($CHCl_3$, cm^{-1}): 3602, 3357, 3028, 2247, 1543, 1527, 1346, 1265; HRMS (DART+) (*m/z*) calcd for $C_{13}H_{16}N_3O_5$ [(M + H)$^+$]: 294.10900, found 294.10887.

(*R)-2-[(*S**)-Hydroxy-(2-nitrophenyl)methyl]-4-methyl-4-nitropentanenitrile (*anti*-11l).** Yellow sticky oil; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.12 (1H, d, $J = 8.0$ Hz), 7.92 (1H, d, $J = 7.8$ Hz), 7.76 (1H, dd, $J = 7.4$, 7.8 Hz), 7.57 (1H, dd, $J = 7.4$, 8.0 Hz), 5.71 (1H, brs), 3.14–3.10 (1H, m), 3.07 (1H, brs), 2.45 (1H, dd, $J = 14.7$ Hz), 2.33 (1H, dd, $J = 10.6$, 14.7 Hz), 1.67 (3H, s), 1.62 (3H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 134.8, 134.1, 129.8, 129.0, 125.5, 119.9, 86.9, 69.7, 37.0, 34.2, 27.3, 24.8; IR ($CHCl_3$, cm^{-1}): 3608, 3350, 3028, 2247, 1543, 1529, 1346; HRMS (DART+) (*m/z*) calcd for $C_{13}H_{16}N_3O_5$ [(M + H)$^+$]: 294.10900, found 294.10975.

(*R)-3-[(*R**)-Hydroxy-(2-nitrophenyl)methyl]-5-methyl-5-nitrohexan-2-one (*syn*-11m).** Orange oil; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.01 (1H, dd, $J = 1.2$, 7.9 Hz), 7.69 (1H, ddd, $J = 1.2$, 7.5, 8.0 Hz), 7.57 (1H, dd, $J = 1.3$, 8.0 Hz), 7.51 (1H, ddd, $J = 1.3$, 7.5, 7.9 Hz), 5.30 (1H, dd, $J = 5.7$, 6.8 Hz), 3.43 (1H, d, $J = 6.8$ Hz), 3.31 (1H, ddd, $J = 2.0$, 5.7, 9.4 Hz), 2.61 (1H, dd, $J = 9.4$, 15.3 Hz), 2.05 (1H, dd, $J = 2.0$, 15.3 Hz), 1.99 (3H, s), 1.60 (3H, s), 1.53 (3H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 212.2, 136.5, 133.9, 129.2, 128.5, 125.0, 87.2, 72.1, 52.1, 40.8, 32.3, 26.5, 26.3; IR ($CHCl_3$, cm^{-1}): 3030, 1714, 1537, 1348; HRMS (DART+) (*m/z*) calcd for $C_{14}H_{19}N_2O_6$ [(M + H)$^+$]: 311.12431 found 311.12467.

(*R)-3-[(*S**)-Hydroxy-(2-nitrophenyl)methyl]-5-methyl-5-nitrohexan-2-one (*anti*-11m).** Orange oil; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.15 (1H, dd, $J = 0.8$, 8.1 Hz), 7.92 (1H, d, $J = 7.9$ Hz), 7.75

(1H, ddd, J = 1.7, 7.8, 7.9 Hz), 7.53 (1H, ddd, J = 1.7, 7.8, 8.1 Hz), 5.70 (1H, brs), 3.12 (1H, ddd, J = 1.6, 1.9, 9.0 Hz), 2.71 (1H, d, J = 1.6 Hz), 2.52 (1H, dd, J = 9.0, 15.7 Hz), 2.45 (3H, s), 1.97 (1H, dd, J = 1.9, 15.7 Hz), 1.35 (3H, s), 1.27 (3H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 210.9, 136.1, 133.9, 131.9, 129.0, 125.6, 123.7, 87.2, 68.7, 51.8, 34.7, 30.0, 26.4, 25.6; IR ($CHCl_3$, cm^{-1}): 3030, 1714, 1539, 1348; HRMS (DART+) (*m/z*) calcd for $C_{14}H_{19}N_2O_6$ [(M + H)$^+$]: 311.12431 found 311.12526.

Triethyl (*R)-1-[(*R**)-hydroxy-(2-nitrophenyl)methyl]-1,3,3-propanetricarboxylate (*syn*-11n).** Yellow sticky oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.01 (1H, dd, J = 1.0, 8.1 Hz), 7.89 (1H, dd, J = 0.9, 7.9 Hz), 7.68 (1H, ddd, J = 0.9, 7.6, 7.9 Hz), 7.47 (1H, ddd, J = 1.0, 7.6, 8.1 Hz), 5.70 (1H, d, J = 4.4 Hz), 4.18−4.12 (4H, m), 4.09 (2H, q, J = 7.2 Hz), 3.53 (1H, brs), 3.38 (1H, dd, J = 4.4, 4.7 Hz), 2.97 (1H, dt, J = 4.0, 10.1 Hz), 2.33 (1H, ddd, J = 4.7, 10.1, 14.5 Hz), 2.14 (1H, ddd, J = 4.4, 10.1, 14.5 Hz), 1.24 (3H, t, J = 6.8 Hz), 1.22 (3H, t, J = 6.6 Hz), 1.16 (3H, t, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 174.2, 169.0, 168.6, 147.5, 136.1, 133.5, 129.3, 128.6, 124.9, 69.3, 61.6, 61.4, 61.3, 49.8, 47.5, 25.2, 13.9, 13.9; IR ($CHCl_3$, cm^{-1}): 1730, 1527, 1348, 1221; HRMS (DART+) (*m/z*) calcd for $C_{19}H_{26}NO_9$ [(M + H)$^+$]: 412.16076, found 412.16027.

Triethyl (*R)-1-[(*S**)-hydroxy-(2-nitrophenyl)methyl]-1,3,3-propanetricarboxylate (*anti*-11n).** Yellow sticky oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.01 (1H, dd, J = 1.0, 8.0 Hz), 7.71 (1H, dd, J = 1.6, 7.8 Hz), 7.65 (1H, ddd, J = 1.0, 7.4, 7.8 Hz), 7.46 (1H, ddd, J = 1.6, 7.4, 8.0 Hz), 5.48 (1H, dd, J = 4.2, 8.0 Hz), 4.25−4.17 (4H, m), 4.10−4.01 (2H, m), 3.92 (1H, d, J = 8.0 Hz), 3.46 (1H, dd, J = 6.0, 6.4 Hz), 3.05 (1H, ddd, J = 4.2, 5.2, 5.4 Hz), 2.45−2.38 (1H, m), 2.33−2.26 (1H, m), 1.30−1.25 (6H, m), 1.10 (3H, t, J = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 173.9, 168.7, 147.8, 137.3, 133.5, 128.7, 128.4, 124.9, 70.0, 61.7, 61.7, 61.1, 49.6, 48.4, 28.7, 14.0, 14.0, 13.9; IR ($CHCl_3$, cm^{-1}): 3020, 1730, 1527, 1373, 1216; HRMS (DART+) (*m/z*) calcd for $C_{19}H_{26}NO_9$ [(M + H)$^+$]: 412.16076, found 412.16027.

Triethyl (*R)-1-[(*R**)-hydroxy-(2-nitrophenyl)methyl]-1,3,3-butanetricarboxylate (*syn*-11o).** Yellow sticky oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.97 (1H, d, J = 8.2 Hz), 7.82 (1H, d, J = 7.8 Hz), 7.66 (1H, dd, J = 7.2, 7.8 Hz), 7.46 (1H, dd, J = 7.2, 8.2 Hz), 5.44 (1H, dd, J = 4.2, 5.2 Hz), 4.14−3.97 (6H, m), 3.60 (1H, d, J = 4.2 Hz), 2.98 (1H, ddd, J = 1.3, 5.2, 9.6 Hz), 2.48 (1H, dd, J = 9.6, 14.7 Hz), 2.26 (1H, dd, J = 1.3, 14.7 Hz), 1.29 (3H, s), 1.21 (3H, t, J = 7.0 Hz), 1.16 (3H, t, J = 7.2 Hz), 1.12 (3H, t, J = 7.4 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 174.5, 171.8, 171.6, 147.9, 136.1, 133.3, 129.8, 128.7, 124.9, 71.0, 61.4, 61.1, 52.9, 47.0, 32.4, 19.8, 13.9, 13.8, 13.8; IR ($CHCl_3$, cm^{-1}): 2987, 2931, 1728, 1527, 1265; HRMS (DART+) (*m/z*) calcd for $C_{20}H_{28}NO_9$ [(M + H)$^+$]: 426.17641, found 426.17542.

Triethyl (*R)-1-[(*S**)-hydroxy-(2-nitrophenyl)methyl]-1,3,3-butanetricarboxylate (*anti*-11o).** Yellow sticky oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.03 (1H, d, J = 8.4 Hz), 7.66−7.62 (2H, m), 7.48−7.43 (1H, m), 5.48 (1H, dd, J = 3.9, 8.2 Hz), 4.26−4.14 (4H, m), 3.92 (2H, q, J = 7.2 Hz), 3.87 (1H, d, J = 8.2 Hz), 3.03 (1H, ddd, J = 2.4, 3.9, 10.1 Hz), 2.64 (1H, dd, J = 10.1, 14.7 Hz), 2.36 (1H, dd, J = 2.4, 14.7 Hz), 1.42 (3H, s), 1.26 (3H, t, J = 7.2 Hz), 1.24 (3H, t, J = 6.8 Hz), 0.99 (3H, t, J = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 174.4, 171.7, 171.6, 137.6, 133.4, 128.6, 128.2, 125.0, 72.0, 61.7, 61.5, 60.9, 53.1, 46.8, 36.0, 29.7, 19.6, 13.9, 13.7; IR ($CHCl_3$, cm^{-1}): 2985, 2929, 1728, 1527, 1265; HRMS (DART+) (*m/z*) calcd for $C_{20}H_{28}NO_9$ [(M + H)$^+$]: 426.17641, found 426.17586.

Ethyl (*R)-2-[(*R**)-hydroxy-(2-nitrophenyl)methyl]- 3-(1,3-dioxoisoindolin-2-yl)propanoate (*syn*-11p).** Yellow crystal; mp: 146.0−147.0 °C (recryst. from $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.99 (1H, d, J = 8.2 Hz), 7.88 (1H, d, J = 8.0 Hz), 7.82 (2H, dd, J = 3.1, 5.1 Hz), 7.72 (2H, dd, J = 3.1, 5.1 Hz), 7.64 (1H, dd, J = 7.6, 8.0 Hz), 7.44 (1H, dd, J = 7.6, 8.2 Hz). 5.75 (1H, dd, J = 4.3, 4.4 Hz), 4.25 (1H, dd, J = 8.6, 14.2 Hz), 4.05−3.99 (3H, m), 3.92 (1H, dd, J = 4.3, 14.2 Hz), 3.38−3.33 (1H, m), 1.01 (3H, t, J = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 172.7, 168.2, 135.6, 134.2, 133.4, 131.8, 128.8, 128.7, 125.0, 123.4, 67.6, 61.7, 48.9, 35.5, 29.7, 13.6; IR ($CHCl_3$, cm^{-1}): 2927, 1774, 1718, 1527, 1396, 1265; HRMS (DART+) (*m/z*) calcd for $C_{20}H_{19}N_2O_7$ [(M + H)$^+$]: 399.11923, found 399.11943.

Ethyl (*R)-2-[(*S**)-hydroxy-(2-nitrophenyl)methyl]- 3-(1,3-dioxoisoindolin-2-yl)propanoate (*anti*-11p).** Yellow sticky oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.04 (1H, d, J = 8.0 Hz), 7.89 (2H, dd, J = 3.0, 5.0 Hz), 7.85 (1H, d, J = 8.0 Hz), 7.75 (2H, dd, J = 3.0, 5.0 Hz), 7.66 (1H, dd, J = 7.2, 8.0 Hz), 7.44 (1H, dd, J = 7.2, 8.0 Hz), 5.57 (1H, dd, J = 3.4, 6.6 Hz), 4.25−4.20 (2H, m), 4.14 (1H, dd, J = 6.0, 14.4 Hz), 3.97 (2H, q, J = 7.1 Hz), 3.37−3.32 (1H, m), 0.97 (3H, t, J = 7.1 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 171.2, 168.5, 146.9, 137.4, 134.3, 133.5, 131.8, 128.7, 128.4, 124.9, 123.6, 67.6, 61.0, 49.3, 36.9, 29.7, 13.7; IR ($CHCl_3$, cm^{-1}): 3479, 2927, 1774, 1716, 1527, 1396, 1265, 1192; HRMS (DART+) (*m/z*) calcd for $C_{20}H_{19}N_2O_7$ [(M + H)$^+$]: 399.11923, found 399.11943.

Ethyl (*R)-2-[(*R**)-hydroxy-(2-nitrophenyl)methyl]-3-[(*N*,4-dimethylphenylsulfonamido)methyl]propanoate (*syn*-11q).** Yellow sticky oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.09 (1H, d, J = 8.4 Hz), 7.86 (1H, d, J = 7.8 Hz), 7.73 (2H, d, J = 8.0 Hz), 7.67 (1H, dd, J = 7.4, 7.8 Hz), 7.47 (1H, dd, J = 7.4, 8.4 Hz), 7.35 (2H, d, J = 8.0 Hz), 5.81 (1H, dd, J = 1.8, 6.3 Hz), 4.00−3.84 (2H, m), 3.76 (1H, dd, J = 9.0, 14.1 Hz), 3.32−3.27 (1H, m), 3.12 (1H, dd, J = 6.8, 14.1 Hz), 2.91 (3H, s), 2.45 (3H, s), 0.95 (3H, t, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 171.4, 146.8, 143.8, 137.8, 134.0, 133.6, 129.9, 128.7, 128.3, 127.4, 124.9, 67.2, 60.8, 49.5, 48.4, 35.8, 21.5, 13.8; IR ($CHCl_3$, cm^{-1}): 3525, 3032, 1728, 1527, 1346, 1161; HRMS (DART+) (*m/z*) calcd for $C_{20}H_{25}N_2O_7S$ [(M + H)$^+$]: 437.13825, found 437.13900.

Ethyl (*R)-2-[(*S**)-hydroxy-(2-nitrophenyl)methyl]-3-[(*N*,4-dimethylphenylsulfonamido)methyl]propanoate (*anti*-11q).** Yellow sticky oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.00 (1H, d, J = 8.0 Hz), 7.83 (1H, d, J = 7.8 Hz), 7.67 (1H, dd, J = 7.4, 7.8 Hz), 7.55 (2H, d, J = 7.8 Hz), 7.49 (1H, dd, J = 7.4, 8.0 Hz), 7.29 (2H, d, J = 7.8 Hz), 5.64 (1H, dd, J = 4.4, 4.8 Hz), 4.12 (2H, q, J = 7.1 Hz), 3.60−3.55 (1H, m), 3.59 (1H, d, J = 4.8 Hz), 3.31−3.27 (1H, m), 3.19 (1H, dd, J = 4.2, 13.4 Hz), 2.66 (3H, s), 2.43 (3H, s), 1.18 (3H, t, J = 7.1 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 172.9, 147.9, 143.6, 135.8, 133.9, 133.4, 129.7, 129.2, 128.9, 127.5, 125.0, 68.7, 61.5, 49.8, 48.6, 36.2, 21.5, 13.9; IR ($CHCl_3$, cm^{-1}): 3032, 1730, 1527, 1346, 1217, 1161; HRMS (DART+) (*m/z*) calcd for $C_{20}H_{25}N_2O_7S$ [(M + H)$^+$]: 437.13825, found 437.13874.

Ethyl (*R)-2-[(*R**)-hydroxy-(2-nitrophenyl)methyl]-3-(hexylthio)propanoate (*syn*-11r).** Yellow sticky oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.00 (1H, dd, J = 1.2, 8.1 Hz), 7.86 (1H, dd, J = 1.3, 7.8 Hz), 7.67 (1H, ddd, J = 1.2, 7.6, 7.8 Hz), 7.48 (1H, ddd, J = 1.3, 7.6, 8.1 Hz), 5.63 (1H, dd, J = 3.2, 4.4 Hz), 4.16 (2H, dq, J = 2.7, 7.2 Hz), 3.61 (1H, dd, J = 3.2 Hz), 3.21−3.16 (1H, m), 2.90 (1H, dd, J = 9.2, 13.5 Hz), 2.77 (1H, dd, J = 4.6, 13.5 Hz), 2.42 (2H, dt, J = 3.0, 7.2 Hz), 1.47−1.42 (2H, m), 1.32−1.20 (6H, m), 1.22 (3H, t, J = 7.2 Hz), 0.87 (3H, t, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 173.8, 147.8, 135.9, 133.5, 129.4, 128.8, 124.9, 69.6, 61.3, 50.4, 32.5, 31.3, 29.2, 29.0, 28.4, 22.5, 14.0, 14.0; IR ($CHCl_3$, cm^{-1}): 2929, 1726, 1527, 1348, 1200; HRMS (DART+) (*m/z*) calcd for $C_{18}H_{28}NO_5S$ [(M + H)$^+$]: 370.16882, found 370.16815.

Ethyl (*R)-2-[(*R**)-hydroxy-(2-nitrophenyl)methyl]-3-(hexylthio)propanoate (*anti*-11r).** Slight orange sticky oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.02 (1H, dd, J = 1.3, 7.7 Hz), 7.70 (1H, dd, J = 1.7, 7.9 Hz), 7.64 (1H, ddd, J = 1.3, 7.0, 7.9 Hz), 7.46 (1H, ddd, J = 1.7, 7.0, 7.7 Hz), 5.62 (1H, dd, J = 3.4, 8.0 Hz), 4.10−4.01 (2H, m), 3.98 (1H, d, J = 8.0 Hz), 3.19 (1H, ddd, J = 3.4, 6.1, 9.3 Hz), 3.00 (1H, dd, J = 9.3, 13.5 Hz), 2.92 (1H, dd, J = 6.1, 13.5 Hz), 2.60−2.50 (2H, m), 1.60−1.54 (2H, m), 1.39−1.26 (6H, m), 1.08 (3H, t, J = 7.2 Hz), 0.89 (3H, t, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 173.7, 147.5, 137.8, 133.5, 128.6, 128.1, 124.9, 69.8, 61.1, 50.6, 32.2, 32.0, 31.4, 29.2, 28.5, 22.5, 14.0, 14.0; IR ($CHCl_3$, cm^{-1}): 2929, 1728, 1705, 1527, 1346, 1196;

HRMS (DART+) (*m/z*) calcd for $C_{18}H_{28}NO_5S$ [(M + H)$^+$]: 370.16882, found 370.16815.

Ethyl (*R)-2-[(*R**)-hydroxy-(2-nitrophenyl)methyl]-3-(benzylthio)propanoate (*syn*-11s).** Yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.01 (1H, d, *J* = 7.8 Hz), 7.76 (1H, d, *J* = 7.6 Hz), 7.60 (1H, dd, *J* = 7.6, 7.6 Hz), 7.46 (1H, dd, *J* = 7.6, 7.8 Hz), 7.19–7.16 (3H, m), 7.13–7.11 (2H, m), 5.61 (1H, dd, *J* = 3.2, 3.6 Hz), 4.18 (2H, dq, *J* = 2.4, 6.9 Hz), 3.60 (2H, s), 3.53 (1H, d, *J* = 3.2 Hz), 3.17–3.12 (1H, m), 2.81 (1H, dd, *J* = 9.8, 13.5 Hz), 2.54 (1H, dd, *J* = 4.4, 13.5 Hz), 1.25 (3H, t, *J* = 6.9 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 173.9, 137.6, 135.8, 133.5, 129.3, 128.7, 128.7, 128.4, 127.0, 124.9, 69.6, 69.3, 61.4, 49.7, 36.1, 27.4, 14.1; IR ($CHCl_3$, cm^{-1}): 3030, 1716, 1527, 1348, 1198; HRMS (DART+) (*m/z*) calcd for $C_{19}H_{22}NO_5S$ [(M + H)$^+$]: 376.12187, found 376.12029.

Ethyl (*R)-2-[(*S**)-hydroxy-(2-nitrophenyl)methyl]-3-(benzylthio)propanoate (*anti*-11s).** Yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.02 (1H, d, *J* = 8.0 Hz), 7.66–7.60 (2H, m), 7.48–7.44 (1H, m), 7.32–7.11 (5H, m), 5.61–5.59 (1H, m), 4.05 (2H, q, *J* = 6.9 Hz), 3.90 (1H, d, *J* = 8.4 Hz), 3.76 (2H, s), 3.22–3.19 (1H, m), 2.87 (1H, dd, *J* = 8.8, 14.0 Hz), 2.70 (1H, dd, *J* = 6.8, 14.0 Hz), 1.08 (3H, t, *J* = 7.1 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 173.6, 137.7, 137.6, 133.5, 129.0, 128.6, 128.5, 128.4, 128.2, 127.1, 124.9, 69.6, 61.1, 50.2, 35.9, 30.6, 14.0; IR ($CHCl_3$, cm^{-1}): 3032, 1703, 1527, 1346, 1213, 1196; HRMS (DART+) (*m/z*) calcd for $C_{19}H_{22}NO_5S$ [(M + H)$^+$]: 376.12187, found 376.12261.

Ethyl (*R)-2-[(*R**)-hydroxy-(2-nitrophenyl)methyl]-3-[(triphenylmethyl)thio]propanoate (*syn*-11t).** Yellow crystal; mp: 60.0–61.0 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.96 (1H, d, *J* = 8.0 Hz), 7.58 (1H, d, *J* = 7.6 Hz), 7.53 (1H, dd, *J* = 7.2, 7.6 Hz), 7.40 (1H, dd, *J* = 7.2, 8.0 Hz), 7.30 (6H, d, *J* = 7.6 Hz), 7,21–7.15 (9H, m), 5.49 (1H, dd, *J* = 3.2, 3.6 Hz), 4.17 (2H, q, *J* = 6.9 Hz), 3.15 (1H, d, *J* = 3.2 Hz), 2.83–2.78 (1H, m), 2.72 (1H, dd, *J* = 9.6, 12.2 Hz), 2.22 (1H, dd, *J* = 3.6, 12.2 Hz), 1.24 (3H, t, *J* = 6.9 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 173.5, 147.3, 144.4, 135.9, 133.3, 129.5, 129.2, 128.5, 127.8, 126.6, 124.9, 69.3, 61.3, 49.7, 29.7, 28.4, 14.1; IR ($CHCl_3$, cm^{-1}): 3589, 3010, 1728, 1527, 1346; HRMS (DART+) (*m/z*) calcd for $C_{31}H_{30}NO_5S$ [(M + H)$^+$]: 528.18447, found 528.18263.

Ethyl (*R)-2-[(*S**)-hydroxy-(2-nitrophenyl)methyl]-3-[(triphenylmethyl)thio]propanoate (*anti*-11t).** Yellow sticky oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.94 (1H, d, *J* = 8.0 Hz), 7.56–7.51 (2H, m), 7.45–7.20 (16H, m), 5.37 (1H, dd, *J* = 4.4, 7.8 Hz), 4.03 (2H, q, *J* = 7.3 Hz), 3.54 (1H, d, *J* = 7.8 Hz), 2.89–2.84 (1H, m), 2.65 (1H, dd, *J* = 9.6, 11.7 Hz), 2.41 (1H, dd, *J* = 5.4, 11.7 Hz), 1.08 (3H, t, *J* = 7.3 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 173.1, 147.6, 144.3, 136.9, 133.2, 129.5, 128.5, 128.3, 127.9, 126.7, 124.8, 69.8, 67.0, 61.1, 50.3, 31.4, 14.0; IR ($CHCl_3$, cm^{-1}): 3589, 3008, 1728, 1527, 1348, 1192; HRMS (DART+) (*m/z*) calcd for $C_{31}H_{30}NO_5S$ [(M + H)$^+$]: 528.18447, found 528.17922.

Ethyl (*R)-2-[(*R**)-hydroxy-(2-nitrophenyl)methyl]-3-[(1-methyl-1-phenylethyl)thio]propanoate (*syn*-11u).** Yellow sticky oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.96 (1H, d, *J* = 8.0 Hz), 7.67 (1H, d, *J* = 8.0 Hz), 7.58 (1H, dd, *J* = 7.4, 8.0 Hz), 7.43 (1H, dd, *J* = 7.4, 8.0 Hz), 7.37 (1H, d, *J* = 7.8 Hz), 7.22 (1H, dd, *J* = 7.2, 7.8 Hz), 7.14 (1H, dd, *J* = 7.2, 7.2 Hz), 5.49 (1H, brs), 4.10 (2H, q, *J* = 7.2 Hz), 3.28 (1H, brs), 2.88–2.83 (1H, m), 2.63 (1H, dd, *J* = 9.4, 12.9 Hz), 2.37 (1H, dd, *J* = 4.0, 12.9 Hz), 1.61 (3H, s), 1.60 (3H, s), 1.19 (3H, t, *J* = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 173.5, 147.5, 145.8, 136.0, 133.3, 129.2, 128.5, 128.0, 126.5, 126.4, 124.8, 69.1, 61.2, 50.2, 48.0, 30.1, 29.9, 26.3, 14.0; IR ($CHCl_3$, cm^{-1}): 2985, 1726, 1527, 1346, 1199; HRMS (DART+) (*m/z*) calcd for $C_{21}H_{26}NO_5S$ [(M + H)$^+$]: 404.15317, found 404.15522.

Ethyl (*R)-2-[(*S**)-hydroxy-(2-nitrophenyl)methyl]-3-[(1-methyl-1-phenylethyl)thio]propanoate (*anti*-11u).** Yellow sticky oil; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.96 (1H, d, *J* = 7.5 Hz), 7.59–7.55 (2H, m), 7.50 (2H, d, *J* = 8.1 Hz), 7.42 (1H, dd, *J* = 6.6, 7.5 Hz), 7.30 (2H, dd, *J* = 7.5, 8.1 Hz), 7.20 (1H, dd, *J* = 7.5, 7.5 Hz), 5.41 (1H, dd, *J* = 4.2, 7.7 Hz), 4.06–3.95 (2H, m), 3.64 (1H, d, *J* = 7.7 Hz), 2.93–2.90 (1H, m), 2.68 (1H, dd, *J* = 9.3, 12.6 Hz), 2.52 (1H, dd, *J* = 5.7, 12.6 Hz), 1.70 (3H, s), 1.69 (3H, s), 1.06 (3H, t, *J* = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 173.2, 147.6, 145.9, 137.3, 133.3, 128.5, 128.2, 128.1, 126.6, 126.5, 124.8, 69.8, 61.0, 50.8, 48.2, 30.2, 29.9, 29.4, 14.0; IR ($CHCl_3$, cm^{-1}): 2985, 1728, 1705, 1527, 1346, 1217; HRMS (DART+) (*m/z*) calcd for $C_{21}H_{26}NO_5S$ [(M + H)$^+$]: 404.15317, found 404.15287.

Ethyl (*R)-2-[(*R**)-hydroxy-(2-nitrophenyl)methyl]-3-(phenylthio)propanoate (*syn*-11v).** Yellow sticky oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.00 (1H, dd, *J* = 1.3, 8.2 Hz), 7.87 (1H, d, *J* = 7.9 Hz), 7.68 (1H, ddd, *J* = 1.3, 7.5, 7.9 Hz), 7.49 (1H, ddd, *J* = 1.2, 7.5, 8.2 Hz), 7.21–7.16 (5H, m), 5.68 (1H, dd, *J* = 3.6, 4.4 Hz), 4.09 (2H, q, *J* = 7.1 Hz), 3.47 (1H, d, *J* = 3.6 Hz), 3.29 (1H, dd, *J* = 9.8, 13.4 Hz), 3.22–3.15 (2H, m), 1.18 (3H, t, *J* = 7.1 Hz); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 173.3, 147.5, 135.9, 135.3, 133.5, 129.7, 129.2, 128.9, 128.8, 126.5, 125.0, 69.4, 61.4, 50.2, 31.1, 13.9; IR ($CHCl_3$, cm^{-1}): 2933, 1726, 1527, 1348, 1201; HRMS (DART+) (*m/z*) calcd for $C_{18}H_{20}NO_5S$ [(M + H)$^+$]: 362.10622, found 362.10719.

Ethyl (*R)-2-[(*S**)-hydroxy-(2-nitrophenyl)methyl]-3-(phenylthio)propanoate (*anti*-11v).** Yellow sticky oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.99 (1H, d, *J* = 7.6 Hz), 7.62 (2H, d, *J* = 8.0 Hz), 7.47–7.43 (1H, m), 7.39–7.37 (2H, m), 7.30 (2H, dd, *J* = 7.2, 8.0 Hz), 7.23–7.18 (1H, m), 5.60 (1H, dd, *J* = 4.3, 7.9 Hz), 4.10–3.97 (2H, m), 3.92 (1H, d, *J* = 7.9 Hz), 3.39 (1H, dd, *J* = 9.6, 13.7 Hz), 3.32 (1H, dd, *J* = 5.3, 13.7 Hz), 3.20 (1H, ddd, *J* = 4.3, 5.3, 9.6 Hz), 1.07 (3H, t, *J* = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 173.3, 147.5, 137.4, 134.8, 133.4, 130.0, 129.0, 128.6, 128.0, 126.7, 124.9, 69.8, 61.2, 50.7, 34.0, 13.9; IR ($CHCl_3$, cm^{-1}): 2929, 1730, 1703, 1527, 1346, 1215; HRMS (DART+) (*m/z*) calcd for $C_{18}H_{20}NO_5S$ [(M + H)$^+$]: 362.10622, found 362.10719.

4.5. Reduction of the minor diastereomer of **11e** for determination of the stereochemistry.

To a solution of *minor*-**11e** (23.9 mg, 0.08 mmol) in benzene (2.0 mL), AIBN (13.3 mg, 0.08 mmol) and Bu_3SnH (0.11 mL, 0.40 mmol) were added. The reaction mixture was refluxed for 17 h. After cooling to room temperature, benzene was removed under reduced pressure, and the residue was purified by column chromatography on silica gel (hexanes/ethyl acetate = 2:1) to afford **11e'** (16.1 mg, 0.06 mmol, 80% yield). It's spectroscopic data accorded with the reported value of (2*R**,3*S**)-ethyl 3-hydroxy-2-(2-methylpropyl)benzenepropanoate [18].

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.tet.2021.132329.

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[13] (a) We employ the Masamune syn-anti system[13b] for the nomenclature of diastereomers. The main chain that was associated with the aldol reaction is drawn in the zig-zag fashion, and the two substituents on the same side are referred “syn”, and those which are not, “anti”;. (b) S. Masamune, Sk A. Ali, D.L. Snitman, D.S. Garvey, Angew. Chem., Int. Ed. Engl. 19 (1980) 557–558.(c) For details, see the Experimental section. **Ethyl-(*R**)-2-[(*S**)-hydroxy(phenyl) methyl]-2,4-dimethyl-4-nitropentanoate (*anti*-11w)**. Colorless crystal; mp: 104.0–105.0 °C (recryst. from $CHCl_3$); ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.35–7.31 (3H, m), 7.22–7.20 (2H, m), 4.62 (1H, d, J = 4.8 Hz), 4.20–4.09 (2H, m), 2.95 (1H, d, J = 4.8 Hz), 2.68 (1H, d, J = 15.6 Hz), 2.50 (1H, d, J = 15.6 Hz), 1.57 (3H, s), 1.52 (3H, s), 1.22 (3H, t, J = 7.2 Hz), 0.98 (3H, s); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 176.1, 139.4, 128.4, 128.1, 127.5, 87.0, 81.0, 61.4, 50.1, 45.5, 30.7, 23.2, 14.4, 13.8; IR ($CHCl_3$, cm^{-1}): 2995, 1714, 1543, 1348, 1232, 1155; HRMS (DART+) (m/z) calcd for $C_{16}H_{24}NO_5$ [$(M + H)^+$]: 310.16545, found 310.16458. Crystallographic data (excluding structure factors) for the structures in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication CCDC 2082465. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK, (or e-mail: deposit@ccdc.cam.ac.Uk). Deposited data may be accessed by the journal and checked as part of the refereeing process. If data are revised prior to publication, a replacement file should be sent to CCDC. For details, see ESI.
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