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Synthesis of 2,3-Dialkylated Tartaric Acid Esters via Visible Light Photoredox-Catalyzed Reductive Dimerization of α-Ketoesters

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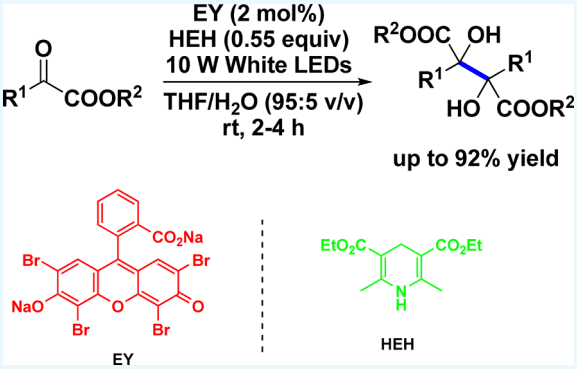
Supporting Information

ABSTRACT: A mild transition-metal-free protocol to prepare 2,3-dialkylated tartaric acid esters has been developed by taking advantage of a visible light photoredox-catalyzed reductive dimerization of α-ketoesters with a combination of an organic dye photocatalyst and a Hantzsch-type 1,4-dihydropyridine hydrogen donor. A broad range of functional groups including cyclopropane, alkene, alkyne, 4-methoxybenzyl ether, acetal, silyl ether, carbamate, cyclic ether, cyclic thioether, bromoalkane, and *N*-alkoxyphthalimide are well-compatible. By employing the visible light photoredox-catalyzed reductive coupling and the subsequent optical resolution, both enantioenriched diastereomers of 2,3-dialkylated tartaric acid could be acquired conveniently.



INTRODUCTION

Since the first isolation by Carl Wilhelm Scheele in 1769, tartaric acid and its derivatives have been applied widely in organic synthesis as resolving agents,[1] chiral auxiliaries,[2] and natural chiral pools.[3] Most importantly, an array of tartaric acid-derived compounds performed perfectly as privileged chiral ligands and catalysts in modern asymmetric synthesis, providing versatile opportunities to access optically active compounds in a catalytic fashion.[4−6] These chiral ligands and catalysts were mainly generated by specific modifications on either the existing carboxylic acid or alcohol functionalities of the naturally occurring (2*R*,3*R*)-dimethyl tartaric acid, while the modification of the C2 and C3 positions of the backbone was kept to be inconvenient (Figure 1). In some cases, a few alkyl substituents could be introduced to the C2 and C3 positions of the tartaric acid through alkylation of the corresponding enolates, in which multiple group protections and usage of strong bases are always required and competitive side reactions might be caused.[3a,e,f] Therefore, the development of more convenient and general approaches to 2,3-disubstituted tartaric acids together with their derivatives still remains in high demand. Such methodologies will not only expand the ligand framework diversity but also be helpful to acquire new insightful understandings on stereoselective transformations.

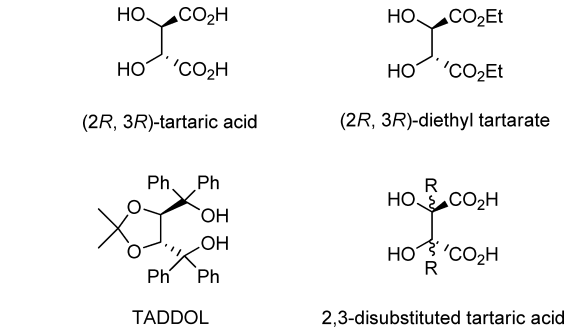


Figure 1. Tartaric acid and its derivatives.

Reductive dimerization of α-ketoesters makes 2,3-disubstituted tartaric acids available in a more straightforward manner, even though the bulky steric hindrance should be surmounted during the formation of two consecutive quaternary carbon centers. Actually, this kind of carbon−carbon bond formation based on the coupling of ketyl radicals has been carried out in a set of conditions in the past decades (Scheme 1), which involves the employment of stoichiometric amounts of one-electron-donating metal reagents [SmI_2, $TiCl_3$, and Mg(0)] and

Scheme 1. Reductive Coupling of α-Ketoester under Different Conditions

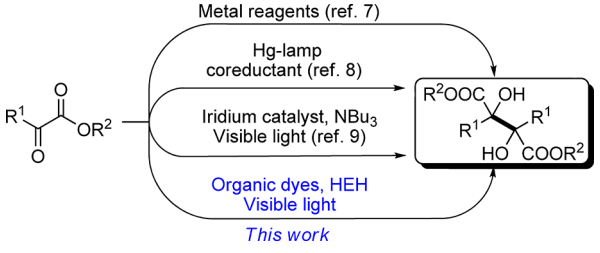


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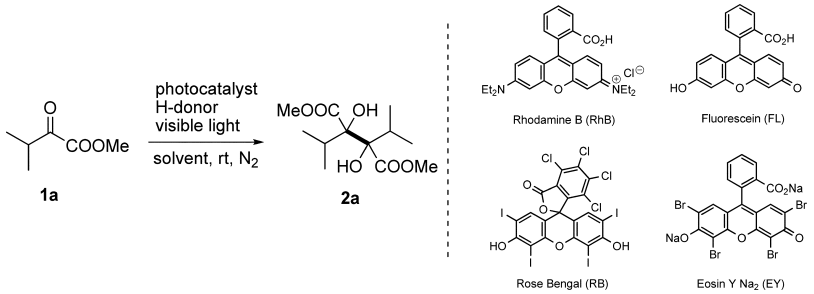
Table 1. Optimization Studies of Visible Light-Induced Reductive Coupling[a]



entry	light source	catalyst (mol %)	H donor (equiv)[b]	solvent[c]	time (h)	yield (%)[d]
1	23 W CFL	RhB (10%)	HEH (0.6)	DMF	63	61
2	23 W CFL	FL (10%)	HEH (0.6)	DMF	63	26
3	23 W CFL	RB (10%)	HEH (0.6)	DMF	63	39
4	23 W CFL	EY (10%)	HEH (0.6)	DMF	4	64
5	10 W white LEDs	EY (10%)	HEH (0.6)	DMF	3	64
6	10 W white LEDs	EY (10%)	HEH (0.6)	THF	6	70
7	10 W white LEDs	EY (10%)	HEH (0.6)	THF/H_2O	3	72
8	10 W white LEDs	EY (5%)	HEH (0.6)	THF/H_2O	4	78
9	10 W white LEDs	EY (2%)	HEH (0.6)	THF/H_2O	5	87
10	10 W white LEDs	EY (1%)	HEH (0.6)	THF/H_2O	12	83
11	10 W white LEDs	EY (2%)	BT (0.6)	THF/H_2O	12	51
12	10 W white LEDs	EY (2%)	DIPEA (0.6)	THF/H_2O	12	65
13	10 W white LEDs	EY (2%)	HEH (0.55)	THF/H_2O	5	87
14	10 W white LEDs	EY (2%)	HEH (0.5)	THF/H_2O	5	80
15[e]	10 W white LEDs	EY (2%)	HEH (0.55)	THF/H_2O	4	81
16[f]	10 W white LEDs	EY (2%)	HEH (0.55)	THF/H_2O	6	84
17	10 W white LEDs		HEH (0.55)	THF/H_2O	48	n. r.
18		EY (2%)	HEH (0.55)	THF/H_2O	48	n. r.

[a]Concentration is 0.05 M unless otherwise mentioned. [b]HEH = diethyl 2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate; BT = 2-phenyl-dihydrobenzothiazoline. [c]Ratio of THF/H_2O is 95:5 v/v. [d]Mixture of DL-, *meso*-**2a** with a ratio of about 1:1.07 was isolated by column chromatography, and the ratios were determined by the ^{1}H NMR method. [e]Concentration is 0.1 M. [f]Concentration is 0.025 M.

the utilization of high energetic UV light with coreductants.[7,8] A recent Rueping's work on visible light photoredox-catalyzed reductive coupling of ketones showed that two α-ketoester substrates were transformed to the corresponding 2,3-dialkylated tartaric acid esters in moderate yields under the catalysis of a polypyridyl−iridium complex.[9] Almost at that time, we launched a project on scalable synthesis of 2,3-disubstituted tartaric acids, in which a protocol based on organic dye catalysis[10] was envisioned with the consideration of obviation of transition metals and potential industrial applications. In this paper, we would like to report the developed transition-metal-free protocol, which features substantially mild condition and general functional group tolerance.

RESULTS AND DISCUSSION

This study was initiated by choosing α-ketoester **1a** as a model substrate, which contains a bulky isopropyl attached to the carbonyl group. An array of photocatalysts including rhodamine B (RhB), fluorescein (FL), rose bengal (RB), and Na_2-Eosin Y (EY) were examined first by establishing a Hantzsch-type 1,4-dihydropyridine as a hydrogen donor and a 23 W compact fluorescent lamp (CFL) as a light source (Table 1, entries 1−4). It was demonstrated that Na_2-EY exhibits the best catalytic efficiency in terms of yield and reaction time. Hence, in a degassed dimethylformamide (DMF) solution containing 10 mol % of Na_2-EY and 0.6 equiv of diethyl 2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate (HEH), **1a** was smoothly converted to dimethyl 2,3-diisopropyltartrate **2a** in 64% yield at room temperature after 4 h of irradiation. However, when the light source was changed to 10 W white light-emitting diodes (LEDs), the reaction was further accelerated even though the yield was kept the same (Table 1, entry 5). Under identical irradiation, solvent screening suggested that a mixture of tetrahydrofuran (THF) and water (95:5 v/v) is more favorable than either DMF or THF, giving **2a** in an increased isolated yield (Table 1, entries 6−7). The yield of product was improved to 87% when the amount of Na_2-EY was decreased from 5% to 2 mol % (Table 1, entries 8−9), while further reduction of the photocatalyst resulted in a prolonged reaction time (Table 1, entry 10). Other two types of hydrogen donors, 2-phenyl-dihydrobenzothiazoline (BT) and *N*,*N*-diisopropylethylamine (DIPEA), were also attempted to replace HEH; inferior results were afforded (Table 1, entries 11−12). Further fine-tuning of the condition parameters indicated that 0.55 equiv of HEH are preferred to assure the complete conversion of **1a** in a 0.05 M solution concentration (Table 1, entries 13−16). The control experiments also showed that no reaction occurred in the absence of either a photocatalyst or a light source (Table 1, entries 17−18). Accordingly, the optimal conditions for this metal-free reductive coupling were established as follows: 2 mol % of Na_2-EY as the catalyst, 0.55 equiv of HEH as the hydrogen donor, THF/H_2O (95:5 v/v) as the solvent, and 10 W white LEDs as the light source.

With the optimal reaction conditions in hand, the scope of the substrates was then explored (Table 2). Apart from **1a**, α-

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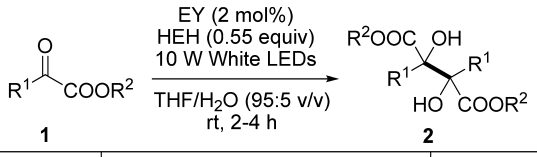
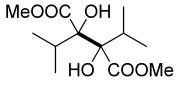
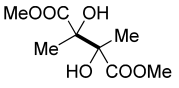
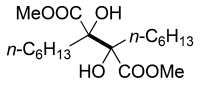
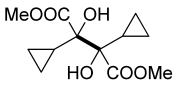
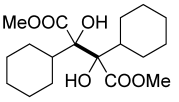
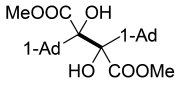
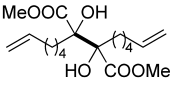
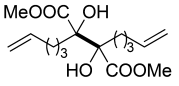
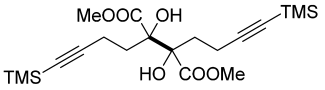
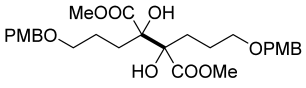
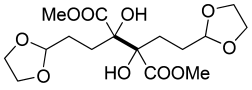
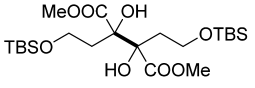
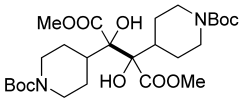
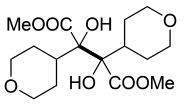
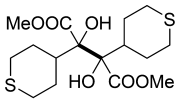
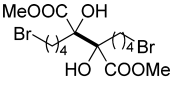
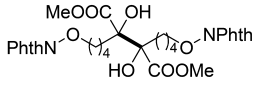
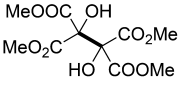
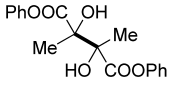
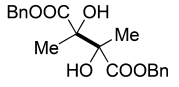
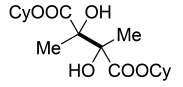
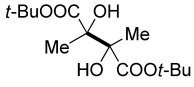
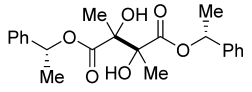
Table 2. Visible Light Photoredox-Catalyzed Reductive Coupling of α-Ketoesters[a]



1 2

 **2a**, 87%[b] *DL*: 42%, *meso*: 45%	 **2b**, 80% *DL*/*meso* = 1/1.05	 **2c**, 87% *DL*/*meso* = 1/1.1
 **2d**, 92%[b] *DL*: 44%, *meso*: 48%	 **2e**, 88%[b] *DL*: 42%, *meso*: 46%	 **2f**, 0%[c]
 **2g**, 80% *DL*/*meso* = 1/1	 **2h**, 72% *DL*/*meso* = 1/1	 **2i**, 70% *DL*/*meso* = 1/1
 **2j**, 83% *DL*/*meso* = 1/1	 **2k**, 78% *DL*/*meso* = 1/1	 **2l**, 78% *DL*/*meso* = 1/1
 **2m**, 83%[b] *DL*: 40%, *meso*: 43%	 **2n**, 83%[b] *DL*: 40%, *meso*: 43%	 **2o**, 81%[b] *DL*: 39%, *meso*: 42%
 **2p**, 85% *DL*/*meso* = 1/1	 **2q**, 40% *DL*/*meso* = 1/1.05	 **2r**, 0%[c]
 **2s**, 82%[b] *DL*: 40%, *meso*: 42%	 **2t**, 80%[b] *DL*: 40%, *meso*: 40%	 **2u**, 84%[b] *DL*: 40%, *meso*: 44%
 **2v**, 78%[b] *DL*: 38%, *meso*: 40%	 **2w**, 86% *DL*: 41%, *meso*: 45%	

[a]Reaction conditions: α-ketoester (0.3 mmol), HEH (0.165 mmol), Na_2-EY (2 mol %), THF/H_2O (6.0 mL, 95:5 v/v), room temperature, N_2, 10 W white LEDs, 2−4 h [monitored by thin-layer chromatography (TLC)]. [b]DL and meso compounds can be separated by column chromatography. [c]Alcohol product was isolated.

ketoesters **1b−1e** containing an acyclic primary alkyl substituent (Me, n-C_6H_{13}) or a cyclic secondary alkyl substituent (cyclopropyl, cyclohexyl) connected with a carbonyl group underwent the photoredox-catalyzed reductive coupling reaction smoothly, affording the corresponding dimethyl 2,3-dialkylated tartrates **2b−2e** in a yield ranging from 80 to 92%. To differentiate the ^{1}H NMR spectra of DL and meso forms of the products, we further confirmed the crystal structure of *meso*-**2e** diastereomer by using an X-ray diffraction technique (CCDC 1547831) (Figure 2). It is worthy to mention that the

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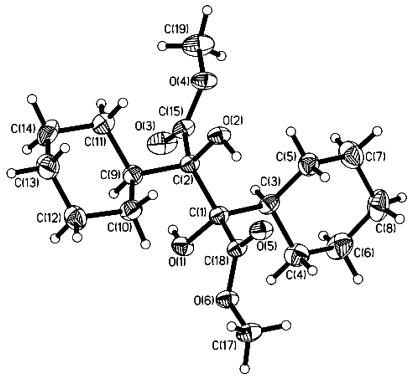
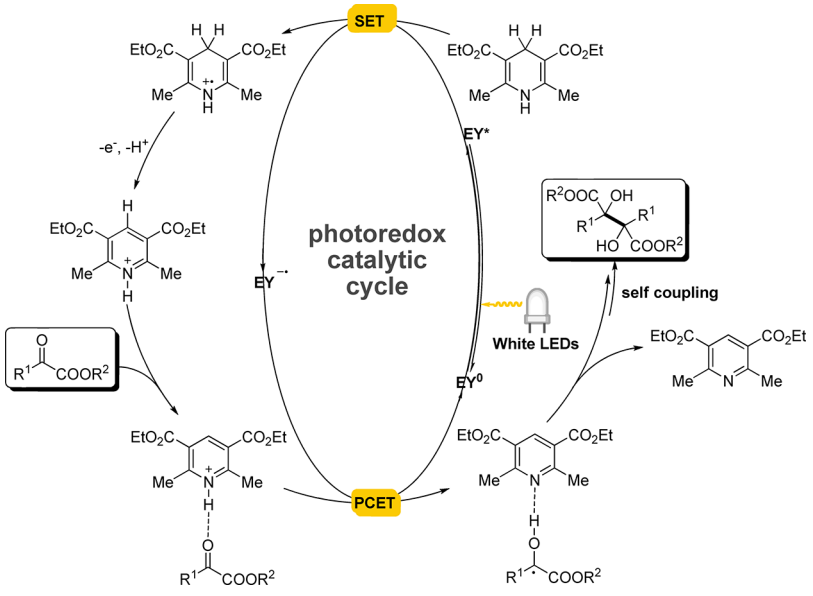


Figure 2. Thermal ellipsoid plot of *meso*-**2e** (30% probability levels).

cyclopropyl moiety was kept intact in this type of radical process. However, for α-ketoester **1f**, carbonyl reduction occurred instead of the expected coupling, suggesting that the bulky adamantyl substituent adjacent to the carbonyl group should inhibit the carbon−carbon bond formation of two ketyl radicals. For α-ketoesters **1g**−**1i** with an appendant terminal alkene or a silylated internal alkyne group, all photoredox-catalyzed reductive coupling reactions were performed well to give **2g**−**2i** in satisfactory yields (from 70 to 80%). The internal carbon−carbon π bonds remained untouched, and no cross-coupling between the carbon−carbon π bond and the carbonyl group was detected. A variety of α-ketoesters **1j**−**1q** with different heteroatom-containing groups involving 4-methoxybenzyl ether, aldehyde acetal, silyl ether, secondary amine carbamate, cyclic ether, cyclic thioether, bromoalkane, and *N*-alkoxyphthalimide were converted to **2j**−**2q** as expected in moderate to good yields, highlighting the general group tolerance of the conditions. Of note is the inertness of C−Br bond and N−O bond, both of which are prone to cleavage in the reductive conditions.[11,12] For **1r** bearing two electron-withdrawing groups (CO_2Me) attached to the same carbonyl group, no reductive coupling was captured and only carbonyl reduction was observed as the major reaction. To further detect the effect of ester group, α-ketoesters **1s**−**1v** with various alkoxy groups (PhO, BnO, cyclohexyloxy, and *tert*-butoxy) were then examined under the standard condition. However, **2s**−**2v** were generated in a comparative yield with a similar DL/meso ratio, indicating that the effect of ester moiety is not distinguished. In addition, the reaction of the substrate **1w** bearing a chiral moiety (*R*-1-phenylethyl ester) also afforded a mixture of two diastereomers **2w** (dr = 1:1.1 by ^{1}H NMR). This mentions that the stereogenic center of the substrate **1w** did not have much impact on the behaviors of the ketyl radical coupling as well as the stereochemical selectivity.

A mechanism involving proton-coupled electron transfer was proposed to account for the visible light photoredox-catalyzed reductive coupling (Scheme 2).[13] Initially, the excited-state EY* [$^*E^{red}_{1/2}$ = 0.83 V vs saturated calomel electrode (SCE)][14] is generated from Na_2-EY by irradiation of visible light. A single electron transfer from Hantzsch-type 1,4-dihydropyridine (HEH) to the excited-state EY* would afford radical anion $EY^{\bullet-}$ ($E^{ox}_{1/2}$ = −1.08 V vs SCE)[15] and a radical cation $HEH^{\bullet+}$.[16] After an electron transfer from radical anion $EY^{\bullet-}$ and a proton transfer from either radical cation $HEH^{\bullet+}$ or cation HEH^+, a neutral ketyl radical is formed from α-ketoester, which immediately undergoes dimerization to give 2,3-disubstituted tartaric acid ester. Owing to the high reduction potential of α-ketoester, as evidenced by **1a** ($E^{red}_{1/2}$ = −1.75 V vs SCE) (see Figure S1 in the Supporting Information for details), a transient hydrogen-bonded complex was supposed, which might facilitate the concurrent electron transfer from radical anion $EY^{\bullet-}$ to the carbonyl group. To confirm the radical pathway, two radical-trapping experiments were performed using 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) and 1,1-diphenylethylene as radical scavengers, respectively (Scheme 3). When 1 equiv of TEMPO was introduced to the standard reaction system, the visible light photoredox-catalyzed dimerization of **1b** was completely inhibited and no dimerized product was detected. Instead, a high yield of TEMPOH was provided. In the other parallel experiment using 5 equiv of 1,1-diphenylethylene, a competitive ketyl−olefin−ketyl coupling product **3** was isolated in 35% yield, along with the dimeric product **2b** (53% yield). These results mention that the ketyl radical species does play as the

Scheme 2. Proposed Mechanism



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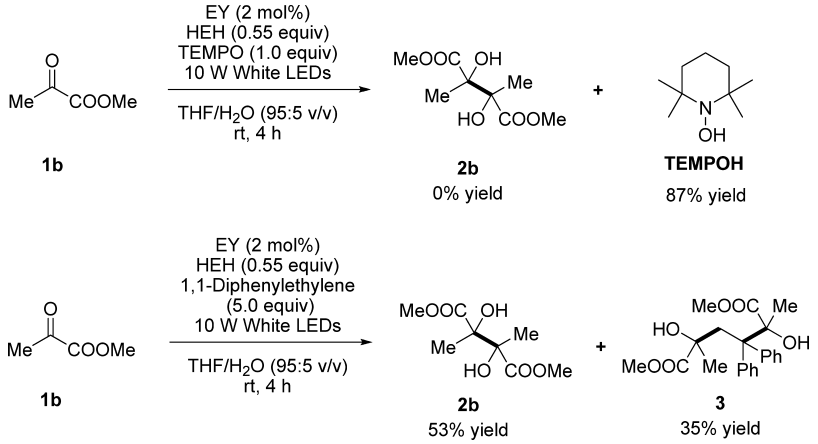
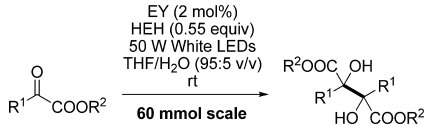
Scheme 3. Experiments of Trapping the Radical Intermediates



reactive intermediate in this type of visible light photoredox-catalyzed dimerization.

To test the practicality of the transition-metal-free protocol, the visible light photoredox-catalyzed reductive coupling reactions were carried out on a 60 mmol scale. By prolonging the reaction times, **1b**, **1e**, and **1t** were transformed to the desired products **2b**, **2e**, and **2t** without erosion of the yield, demonstrating that the new protocol is valuable for scale synthesis (Table 3).

Table 3. Gram-Scale Reactions[a]



entry	substrate	R^1	R^2	time (h)	**2**, yield (%)
1	**1a** (6.1 g)	Me	Me	22	**2a** (5.2 g), 84
2	**1e** (10.2 g)	Cy	Me	19	**2e** (9.2 g), 90
3	**1t** (10.7 g)	Me	Bn	15	**2t** (8.9 g), 83

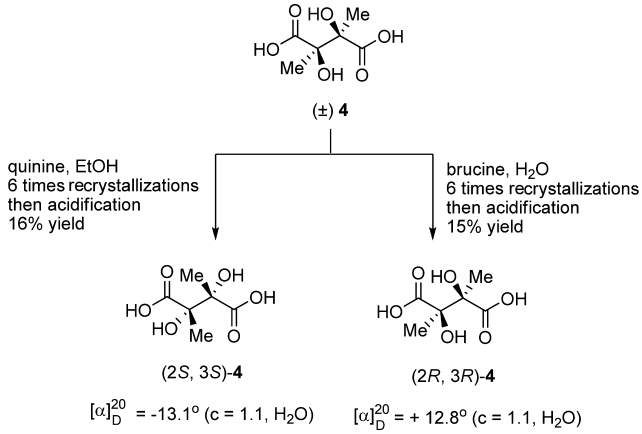
[a]Reaction conditions: α-ketoester (60 mmol), HEH (33 mmol), Na_2-EY (2 mol %), THF/H_2O (1200 mL, 95:5 v/v), room temperature, N_2, and 50 W white LEDs.

To get enantioenriched 2,3-dialkylated tartaric acids, two complementary optical resolution experiments were performed by using brucine and quinine as chiral-resolving reagents (Scheme 4).[17] As reported, the racemic 2,3-dimethyl tartaric acid **4** can be separated from its meso diastereomer in barium salt forms. By taking advantage of the different solubility of the diastereomers in water or ethanol, (2*S*,3*S*)-**4**·brucine and (2*R*,3*R*)-**4**·quinine can be purified by repetitive recrystallizations. After acidic dissociation of the salts, (2*S*,3*S*)-dimethyl tartaric acid or (2*R*,3*R*)-dimethyl tartaric acid could be obtained with the optical purity almost identical to the literature values $[[\alpha]_D^{20} = -13.2$ (c = 4.0, H_2O) and $[\alpha]_D^{20} = +13.2$ (c = 4.0, H_2O)].[17a]

CONCLUSIONS

A transition-metal-free protocol to prepare 2,3-dialkylated tartaric acid esters from α-ketoesters has been developed by means of a visible light photoredox-catalyzed reductive coupling, in which an organic dye Na_2-EY was used as the photocatalyst and a Hantzsch-type 1,4-dihydropyridine was used as the hydrogen donor. A range of functional groups such as cyclopropane, alkene, alkyne, 4-methoxybenzyl ether, aldehyde acetal, silyl ether, secondary amine carbamate, cyclic ether, cyclic thioether, bromoalkane, and *N*-alkoxyphthalimide can be well-tolerated under the optimal conditions. Optically pure 2,3-dialkylated tartaric acid diastereomers can be obtained by combining the photoredox-catalyzed reductive coupling and optical resolution.

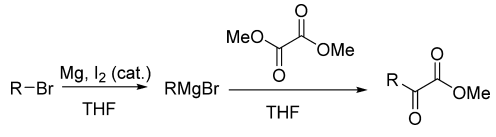
Scheme 4. Optical Resolution of *rac*-4



EXPERIMENTAL SECTION

General Information. All melting points were determined without correction. The ^1H NMR spectra were obtained at 400 MHz, and the ^{13}C NMR spectra were obtained at 100 MHz. The spectra were recorded in $CDCl_3$ and dimethyl sulfoxide-d_6 solution using the residual protonated solvent as the internal standard; J values were given in hertz. Mass spectra (ESI) were recorded on an LCQ Fleet spectrometer. High-resolution mass spectroscopy (HRMS) analyses were determined on a Q-TOF-MS spectrometer. α-Ketoester **1b** was purchased directly.

General Procedure for the Preparation of α-Ketoesters 1a, 1c−1e, and 1g−1k.[18]



To a stirred suspension of magnesium turnings (30 mmol, 1.5 equiv) in anhydrous THF (5 mL) was added a crystal of I_2 as

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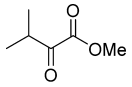
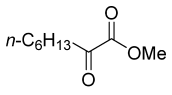
an activator. After stirring for 5 min, a solution of bromide (20 mmol, 1.0 equiv) in anhydrous THF (20 mL) was added dropwise (a water bath was used to control the temperature below 35 °C). The suspension was stirred for 1 h at room temperature, and the resulting Grignard reagent was used directly for the next step.

To a solution of dimethyl oxalate (20 mmol, 1.0 equiv) in anhydrous THF (30 mL) at −78 °C was added dropwise the Grignard reagents (commercially available or prepared as shown above) for more than 1 h. After stirring for 1 h at −78 °C, the mixture was warmed to room temperature, quenched with a saturated solution of NH_4Cl (30 mL), and extracted with Et_2O (3 × 20 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated in a rotary evaporator under vacuum. The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate, 30:1 v/v for **1c**, **1e**, **1g**−**1i**; 15:1 v/v for **1j** and **1k**) or distillation under vacuum (**1a**, **1d**) to afford pure α-ketoester.



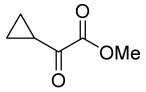
1a

*Methyl 3-Methyl-2-oxobutanoate (**1a**).*[19a] Pale yellow oil, 0.9 g, 35% yield; bp 71−73 °C/30 mm Hg; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.87 (s, 3H), 3.28 (hept, J = 7.0 Hz, 1H), 1.16 (d, J = 7.0 Hz, 6H); MS (ESI) m/z: 129 $[M - 1]^-$.



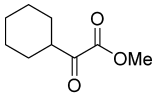
1c

*Methyl 2-Oxooctanoate (**1c**).*[19b] Pale yellow oil, 1.1 g, 31% yield; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.85 (s, 3H), 2.82 (t, J = 7.3 Hz, 2H), 1.62 (m, 2H), 1.34−1.24 (m, 6H), 0.87 (t, J = 6.8 Hz, 3H); MS (ESI) m/z: 171.15 $[M - 1]^-$.



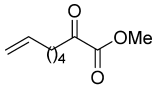
1d

*Methyl 2-Cyclopropyl-2-oxoacetate (**1d**).*[19c] Colorless oil, 0.95 g, 37% yield; bp 80−81 °C/30 mm Hg; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.89 (s, 3H), 2.80−2.68 (m, 1H), 1.28−1.22 (m, 2H), 1.15 (m, 2H); MS (ESI) m/z: 255 $[2M - 1]^-$, 279 $[2M + 23]^+$.



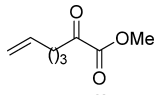
1e

*Methyl 2-Cyclohexyl-2-oxoacetate (**1e**).*[19d] Pale yellow oil, 1.1 g, 31% yield; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.85 (s, 3H), 3.07−3.00 (m, 1H), 1.94−1.84 (m, 2H), 1.84−1.74 (m, 2H), 1.72−1.64 (m, 1H), 1.42−1.27 (m, 4H), 1.27−1.15 (m, 1H); MS (ESI) m/z: 169 $[M - 1]^-$.



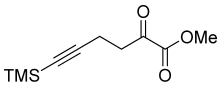
1g

*Methyl 2-Oxooct-7-enoate (**1g**).*[19e] Pale yellow oil, 1.2 g, 36% yield; ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.81−5.70 (m, 1H), 5.01−4.95 (m, 1H), 4.95−4.91 (m, 1H), 3.84 (s, 3H), 2.82 (t, J = 7.2 Hz, 2H), 2.05 (dd, J_1 = 14.3 Hz, J_2 = 7.2 Hz, 2H), 1.70−1.56 (m, 2H), 1.45−1.34 (m, 2H); MS (ESI) m/z: 169 $[M - 1]^-$.



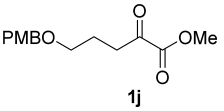
1h

*Methyl 2-Oxohept-6-enoate (**1h**).*[19e] Pale yellow oil, 1.3 g, 42% yield; ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.80−5.67 (m, 1H), 5.03−4.95 (m, 2H), 3.84 (s, 3H), 2.82 (dd, J_1 = 9.3 Hz, J_2 = 5.3 Hz, 2H), 2.14−2.00 (m, 2H), 1.78−1.65 (m, 2H); MS (ESI) m/z: 155 $[M - 1]^-$.



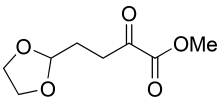
1i

*Methyl 2-Oxo-6-(trimethylsilyl)hex-5-enoate (**1i**).* Colorless oil, 0.6 g, 39% yield (7.5 mmol scale); ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.86 (s, 3H), 3.08 (t, J = 7.2 Hz, 2H), 2.53 (t, J = 7.2 Hz, 2H), 0.11 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.9, 160.9, 104.4, 85.8, 53.1, 38.7, 13.9, 0.0; IR (KBr) ν_{max}: 2960, 2178, 1736, 1252, 1081, 848 cm^{-1}; HRMS (ESI) m/z: calcd for $C_{10}H_{16}NaO_3Si$, 235.0761 $[M + Na]^+$; found, 235.0753.



1j

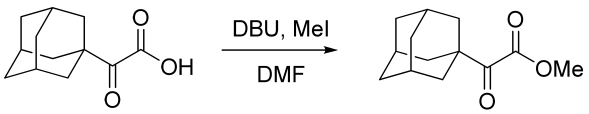
*Methyl 5-((4-Methoxybenzyl)oxy)-2-oxopentanoate (**1j**).* Pale yellow oil, 2.8 g, 50% yield; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.25−7.17 (m, 2H), 6.92−6.79 (m, 2H), 4.37 (s, 2H), 3.79 (s, 6H), 3.46 (t, J = 5.9 Hz, 2H), 2.92 (t, J = 7.0 Hz, 2H), 2.00−1.90 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 193.8, 161.4, 159.2, 130.2, 129.3, 113.8, 72.5, 68.5, 55.3, 52.8, 36.4, 24.0; IR (KBr) ν_{max}: 2949, 2859, 1733, 1614, 1514, 1448, 1249, 1178, 1101, 1040, 823 cm^{-1}; HRMS (ESI) m/z: calcd for $C_{14}H_{18}NaO_5$, 289.1064 $[M + Na]^+$; found, 289.1064.



1k

*Methyl 4-(1,3-Dioxolan-2-yl)-2-oxobutanoate (**1k**).* Colorless oil, 1.0 g, 27% yield; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.91 (t, J = 3.7 Hz, 1H), 3.90−3.85 (m, 2H), 3.82 (s, 3H), 3.81−3.76 (m, 2H), 2.87 (t, J = 7.0 Hz, 2H), 2.06 (td, J_1 = 7.0 Hz, J_1 = 3.7 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 193.2, 161.2, 102.6, 65.0, 52.8, 33.0, 27.6; IR (KBr) ν_{max}: 2954, 2887, 2537, 1730, 1546, 1401, 1247, 1134, 1088, 1031, 889 cm^{-1}; HRMS (ESI) m/z: calcd for $C_8H_{12}NaO_5$, 211.0577 $[M + Na]^+$; found, 211.0579.

Procedure for the Preparation of α-Ketoester 1f.[20,21]



1f

To a solution of 2-(adamantan-1-yl)-2-oxoacetic acid (5 mmol, 1.0 equiv) in DMF (5 mL) was added dropwise 1,8-diazabicyclo[5.4.0]undec-7-ene (5 mmol, 1.0 equiv) at 0 °C. The mixture was stirred at the same temperature for an hour, and then iodomethane (10 mmol, 2.0 equiv) was added dropwise to the solution at the same temperature. After stirring for 0.5 h, the reaction mixture was stirred at room temperature until the completion of the reaction (monitored by TLC),

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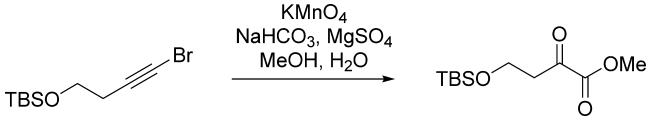
quenched with a saturated solution of NH_4Cl (5 mL), concentrated in a rotary evaporator under vacuum, and then extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with brine (20 mL), dried over Na_2SO_4, filtered, and concentrated in a rotary evaporator under vacuum. The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate, 50:1 v/v) to give **1f**.

*Methyl 2-(Adamantan-1-yl)-2-oxoacetate (**1f**).*[21] White solid, 0.87 g, 78% yield; mp 63−65 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.83 (s, 3H), 2.06 (s, 3H), 1.91 (d, J = 2.7 Hz, 6H), 1.73 (q, J = 12.3 Hz, 6H); MS (ESI) m/z: 245 $[M + 23]^+$.

Procedure for the Preparation of α-Ketoester 1l.[22]

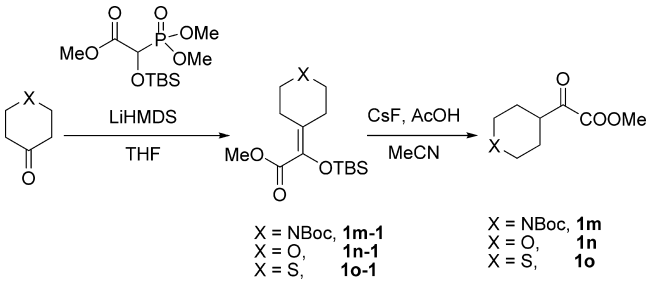


1l

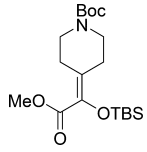
To a solution of ((4-bromobut-3-yn-1-yl)oxy)(*tert*-butyl)-dimethylsilane[23] (5 mmol, 1.0 equiv) in MeOH (75 mL) was added a solution of $NaHCO_3$ (3 mmol, 0.6 equiv) and $MgSO_4$ (10 mmol, 2.0 equiv) in water (75 mL) at 0 °C. The mixture was stirred for 10 min before $KMnO_4$ (12 mmol, 2.4 equiv) was added in portions. This mixture was then stirred at 0 °C until the completion of the reaction (monitored by TLC) and filtered through a Celite pad. The filter cake was washed with EtOAc (3 × 50 mL), and the filtrate was extracted with EtOAc (3 × 100 mL). The combined organic layers were washed with brine (100 mL), dried over Na_2SO_4, filtered, and concentrated in a rotary evaporator under vacuum. The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate, 30:1 v/v) to give **1l**.

*Methyl 4-((tert-Butyldimethylsilyl)oxy)-2-oxobutanoate (**1l**).*[22] Colorless oil, 0.92 g, 73% yield; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.97 (t, J = 6.2 Hz, 2H), 3.87 (s, 3H), 3.04 (t, J = 6.2 Hz, 2H), 0.86 (s, 9H), 0.05 (s, 6H); MS (ESI) m/z: 247 $[M + 1]^+$.

General Procedure for the Preparation of α-Ketoesters 1m−1o.[24]

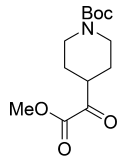


To a solution of methyl 2-((*tert*-butyldimethylsilyl)oxy)-2-(dimethoxyphosphoryl)acetate[24a] (11 mmol, 1.1 equiv) in THF (5 mL) was added dropwise a solution of LiHMDS (1 M solution in THF) (11 mmol, 1.1 equiv) at −78 °C under an N_2 atmosphere. After stirring for 30 min, a solution of ketone (10 mmol, 1.0 equiv) in THF (5 mL) was added dropwise over 15 min. The reaction mixture was stirred at −78 °C for 0.5 h, allowed to be stirred at room temperature until the completion of the reaction (monitored by TLC). The reaction was quenched with a saturated solution of NH_4Cl (20 mL) and extracted with Et_2O (3 × 20 mL). The combined organic layers were washed with brine (20 mL), dried over $MgSO_4$, filtered, and concentrated in a rotary evaporator under vacuum. The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate, 30:1 v/v) to give the corresponding silyl enol ether. To a solution of silyl enol ether (2 mmol, 1.0 equiv) and acetic acid (10 mmol, 5.0 equiv) in MeCN (20 mL) was added solid cesium fluoride (4 mmol, 2.0 equiv) in one portion at 0 °C. After stirring for 30 min, the mixture was allowed to be stirred at room temperature until the completion of the reaction (monitored by TLC). The reaction was quenched with a saturated solution of $NaHCO_3$ (20 mL) and extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with a saturated solution of $NaHCO_3$ (20 mL), brine (20 mL), dried over Na_2SO_4, filtered, and concentrated in a rotary evaporator under vacuum. The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate, 30:1 v/v) to give pure α-ketoester.



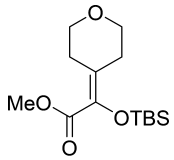
1m-1

*tert-Buty l4-(1-((tert-Butyldimethylsilyl)oxy)-2-methoxy-2-oxoethylidene)piperidine-1-carboxylate (**1m-1**).* Colorless oil, 3.4 g, 89% yield; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.73 (s, 3H), 3.49−3.32 (m, 4H), 2.69 (t, J = 6.1 Hz, 2H), 2.40 (t, J = 6.1 Hz, 2H), 1.45 (s, 9H), 0.93 (s, 9H), 0.07 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.4, 154.8, 135.0, 130.5, 79.6, 51.3, 43.7, 28.4, 27.9, 25.7, 18.4, −4.6; IR (KBr) ν_{max}: 2938, 2860, 2361, 1700, 1634, 1411, 1284, 1225, 1163, 1112, 1024, 841, 781 cm^{-1}; HRMS (ESI) m/z: calcd for $C_{19}H_{35}NNaO_5Si$, 408.2177 $[M + Na]^+$; found, 408.2177.



1m

*tert-Butyl 4-(2-Methoxy-2-oxoacetyl)piperidine-1-carboxylate (**1m**).* Colorless oil, 0.54 g, 98% yield; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.15−3.97 (m, 2H), 3.84 (s, 3H), 3.17 (tt, J_1 = 11.2 Hz, J_2 = 3.7 Hz, 1H), 2.83 (t, J = 12.0 Hz, 2H), 1.93−1.77 (m, 2H), 1.56−1.44 (m, 2H), 1.42 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 195.4, 161.5, 154.6, 79.8, 52.9, 44.4, 42.9, 28.4, 26.6; IR (KBr) ν_{max}: 2961, 2860, 1691, 1419, 1271, 1168, 1124, 1069, 1011 cm^{-1}; HRMS (ESI) m/z: calcd for $C_{13}H_{21}NNaO_5$, 294.1312 $[M + Na]^+$; found, 294.1313.



1n-1

*Methyl 2-((tert-Butyldimethylsilyl)oxy)-2-(tetrahydro-4H-pyran-4-ylidene)acetate (**1n-1**).* Colorless oil, 2.6 g, 92% yield; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.73 (s, 3H), 3.70 (t, J = 5.6 Hz, 2H), 3.67 (t, J = 5.5 Hz, 2H), 2.75 (t, J = 5.5 Hz, 2H), 2.44 (t, J = 5.6 Hz, 2H), 0.94 (s, 9H), 0.08 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.5, 134.5, 130.0, 68.5, 68.0, 51.3, 29.7, 29.2, 25.7, 18.4, −4.6; IR (KBr) ν_{max}: 2950, 2853, 1721, 1633, 1437, 1290, 1232, 1146, 1100, 1028, 844 cm^{-1}; HRMS (ESI) m/z: calcd for $C_{14}H_{26}NaO_4Si$, 309.1493 $[M + Na]^+$; found, 309.1487.

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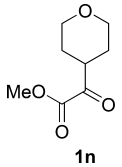
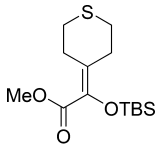


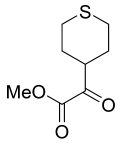
1n

*Methyl 2-Oxo-2-(tetrahydro-2H-pyran-4-yl)acetate (**1n**).* White solid, 0.29 g, 84% yield; mp 56−52 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.99 (dd, J_1 = 3.9 Hz, J_2 = 3.1 Hz, 1H), 3.97 (dd, J_1 = 3.9 Hz, J_2 = 3.1 Hz, 1H), 3.86 (s, 3H), 3.47 (td, J_1 = 11.5 Hz, J_2 = 2.4 Hz, 2H), 3.27 (tt, J_1 = 11.1 Hz, J_2 = 3.9 Hz, 1H), 1.86−1.78 (m, 2H), 1.74−1.63 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 195.1, 161.6, 66.8, 52.9, 43.5, 27.2; IR (KBr) ν_{max}: 2954, 2851, 1731, 1633, 1444, 1395, 1250, 1081, 1018 cm^{-1}; HRMS (ESI) *m*/*z*: calcd for $C_8H_{12}NaO_4$, 195.0628 [M + Na]$^+$; found, 195.0639.



1o-1

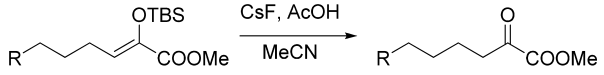
*Methyl 2-((tert-Butyldimethylsilyl)oxy)-2-(tetrahydro-4H-thiopyran-4-ylidene)acetate (**1o-1**).* Colorless oil, 2.8 g, 94% yield; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.73 (s, 3H), 2.86−2.89 (m, 2H), 2.71−2.64 (m, 6H), 0.94 (s, 9H), 0.08 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.6, 134.1, 129.7, 50.4, 29.7, 29.3, 28.9, 28.5, 24.7, 17.4, 0.0, −5.6; IR (KBr) ν_{max}: 2946, 2857, 2359, 1720, 1631, 1431, 1286, 1230, 1132, 1027, 835 cm^{-1}; HRMS (ESI) *m*/*z*: calcd for $C_{14}H_{26}NaO_3SSi$, 325.1264 [M + Na]$^+$; found, 325.1257.



1o

*Methyl 2-Oxo-2-(tetrahydro-2H-thiopyran-4-yl)acetate (**1o**).* Colorless oil, 0.36 g, 96% yield; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.85 (s, 3H), 3.12 (tt, J_1 = 11.1 Hz, J_2 = 3.2 Hz, 1H), 2.75−2.65 (m, 4H), 2.26−2.13 (m, 2H), 1.81−1.66 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 195.5, 161.7, 53.0, 45.6, 28.3, 27.6; IR (KBr) ν_{max}: 2914, 1728, 1433, 1261, 1190, 1071, 967 cm^{-1}; HRMS (ESI) *m*/*z*: calcd for $C_8H_{11}O_3S$, 187.0434 [M − H]$^-$; found, 187.0420.

General Procedure for the Preparation of α-Ketoesters 1p−1q.

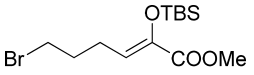


1p-1, 1q-1 1p, 1q

*Preparation of **1p-1**.* To a solution of methyl 2-((*tert*-butyldimethylsilyl)oxy)-6-hydroxyhex-2-enoate[24c] (5 mmol, 1.0 equiv) and CBr_4 (7.5 mmol, 1.5 equiv) in DCM (15 mL) was added dropwise a solution of PPh_3 (7.5 mmol, 1.5 equiv, in 5 mL DCM) at −30 °C under the N_2 atmosphere. After stirring for 2 h, the reaction mixture was allowed to be stirred at room temperature until the completion of the reaction (monitored by TLC). The reaction was concentrated in a rotary evaporator under vacuum. The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate, 50:1 v/v) to give **1p-1**.

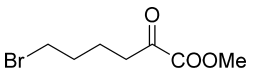
*Preparation of **1q-1**.* To a solution of methyl 2-((*tert*-butyldimethylsilyl)oxy)-6-hydroxyhex-2-enoate[20] (5 mmol, 1.0 equiv), *O*-phthalimide (6 mmol, 1.2 equiv), and PPh_3 (6 mmol, 1.2 equiv) in THF (15 mL) was added dropwise diisopropyl azodiformate (6 mmol, 1.2 equiv) at 0 °C under the N_2 atmosphere. After stirring for 0.5 h, the reaction mixture was allowed to be stirred at room temperature until the completion of the reaction (monitored by TLC). The reaction was concentrated in a rotary evaporator under vacuum. The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate, 10:1 v/v) to give **1q-1**.

*Procedure for the Preparation of **1p−1q**.* To a solution of silyl enol ether (2 mmol, 1.0 equiv) and acetic acid (10 mmol, 5.0 equiv) in MeCN (20 mL) was added solid cesium fluoride (4 mmol, 2.0 equiv) in one portion at 0 °C. After stirring for 30 min, the mixture was allowed to be stirred at room temperature until the completion of the reaction (monitored by TLC). The reaction was quenched with a saturated solution of $NaHCO_3$ (20 mL) and extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with a saturated solution of $NaHCO_3$ (20 mL), brine (20 mL), dried over Na_2SO_4, filtered, and concentrated in a rotary evaporator under vacuum. The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate, 30:1 v/v for **1p**, 10:1 v/v for **1q**) to give the corresponding α-ketoester.



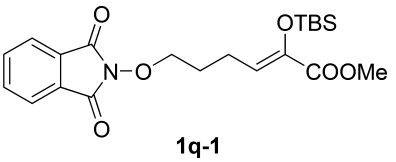
1p-1

*Methyl 6-Bromo-2-((tert-butyldimethylsilyl)oxy)hex-2-enoate (**1p-1**).* Colorless oil, 1.1 g, 65% yield; ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.46 (t, J = 8.1 Hz, 1H), 3.76 (s, 3H), 3.41 (t, J = 6.8 Hz, 2H), 2.61−2.56 (m, 2H), 2.03−1.90 (m, 2H), 0.93 (s, 9H), 0.12 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.0, 140.1, 122.1, 50.5, 32.0, 31.8, 24.8, 24.6, 17.2, −5.9; IR (KBr) ν_{max}: 2946, 2860, 1789, 1731, 1356, 1253, 1164, 986, 839 cm^{-1}; HRMS (ESI) *m*/*z*: calcd for $C_{13}H_{25}NaBrO_3Si$, 359.0649 [M + Na]$^+$; found, 359.0646.



1p

*Methyl 6-Bromo-2-oxohexanoate (**1p**).* Colorless oil, 0.27 g, 60% yield; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.86 (s, 3H), 3.41 (t, J = 6.5 Hz, 2H), 2.88 (t, J = 7.0 Hz, 2H), 1.95−1.85 (m, 2H), 1.84−1.74 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 193.5, 161.3, 53.0, 38.3, 32.9, 31.7, 21.5; IR (KBr) ν_{max}: 1731, 1399, 1253, 1075, 739 cm^{-1}; HRMS (ESI) *m*/*z*: calcd for $C_7H_{11}BrNaO_3$, 244.9784 [M + Na]$^+$; found, 244.9792.



1q-1

*Methyl 2-((tert-Butyldimethylsilyl)oxy)-6-((1,3-dioxoisoindolin-2-yl)oxy)hex-2-en-oate (**1q-1**).* Colorless oil, 2.0 g, 96% yield; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.83 (dd, J_1 = 5.5 Hz, J_2 = 3.0 Hz, 2H), 7.74 (dd, J_1 = 5.5 Hz, J_2 = 3.0 Hz, 2H), 5.56 (t, J = 8.1 Hz, 1H), 4.22 (t, J = 6.7 Hz, 2H), 3.75 (s, 3H), 2.69−2.62 (m, 2H), 2.07−1.80 (m, 2H), 0.93 (s, 9H), 0.12 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.0, 163.6, 140.9, 134.4, 129.0, 123.9, 123.5, 77.9, 51.5, 28.4, 25.6, 23.0,

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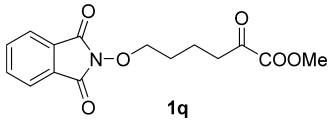
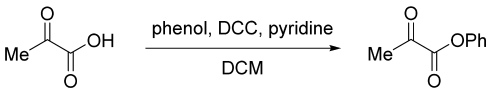
18.2, −4.9; IR (KBr) ν_{max}: 2947, 2886, 1784, 1650, 1462, 1394, 1184, 1125, 990 cm^{-1}; HRMS (ESI) m/z: calcd for $C_{21}H_{29}NNaO_6Si$, 442.1656 $[M + Na]^+$; found, 442.1654.



1q

*Methyl 6-((1,3-Dioxoisoindolin-2-yl)oxy)-2-oxohexanoate (**1q**).* White solid, 0.45 g, mp 128−130 °C; 73% yield; ^1H NMR (400 MHz, $CDCl_3$): δ 7.85−7.81 (m, 2H), 7.77−7.73 (m, 2H), 4.22 (t, J = 6.0 Hz, 2H), 3.87 (s, 3H), 2.99 (t, J = 6.9 Hz, 2H), 1.94−1.80 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 193.8, 163.6, 161.4, 134.5, 128.9, 123.5, 77.9, 53.0, 38.7, 27.3, 19.3; IR (KBr) ν_{max}: 2359, 1727, 1521, 1394, 1067, 696 cm^{-1}; HRMS (ESI) m/z: calcd for $C_{15}H_{15}NNaO_6$, 328.0792 $[M + Na]^+$; found, 328.0792.

Procedure for the Preparation of α-Ketoester 1s.[25]

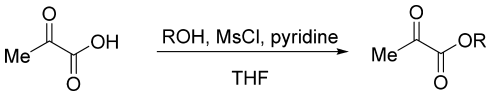


1s

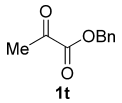
To a solution of pyruvic acid (10 mmol, 1.0 equiv), phenol (10 mmol, 1.0 equiv), and pyridine (10 mmol, 1.0 equiv) in DCM (30 mL) was added dropwise a solution of dicyclohexylcarbodiimide (11 mmol, 1.1 equiv) in DCM (10 mL) at 0 °C. After stirring for 30 min, the reaction mixture was allowed to be stirred at room temperature until the completion of the reaction (monitored by TLC). The reaction mixture was filtered, and the filter cake was washed with DCM (3 × 20 mL). The combined organic layers were washed with brine (50 mL), dried over Na_2SO_4, filtered, and concentrated in a rotary evaporator under vacuum. The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate, 20:1 v/v) to give **1s**.

*Phenyl Pyruvate (**1s**).*[25] White solid, 1.2 g, 70% yield; mp 63−67 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 7.47−7.39 (m, 2H), 7.33−7.27 (m, 1H), 7.21−7.14 (m, 2H), 2.60 (s, 3H); MS (ESI) m/z: 187 $[M + 23]^+$.

General Procedure for the Preparation of α-Ketoesters 1t−1v.[25]

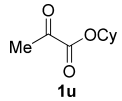


To a solution of pyruvic acid (10 mmol, 1.0 equiv), alcohol (20 mmol, 2.0 equiv), and pyridine (25 mmol, 2.5 equiv) in THF (10 mL) was added dropwise mesyl chloride (MsCl) (12 mmol, 1.2 equiv) at 0 °C. After stirring for 30 min, the reaction mixture was allowed to be stirred at room temperature until the completion of the reaction (monitored by TLC), quenched with water (20 mL), and then extracted with Et_2O (3 × 20 mL). The combined organic layers were then dried over Na_2SO_4, filtered, and concentrated in a rotary evaporator under vacuum. The resulting crude product was purified by silica gel flash column chromatography (petroleum ether/ethyl acetate, 20:1 v/v for **1t**, 40:1 v/v for **1u**, **1v**) to afford the desired α-ketoester.



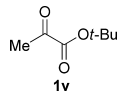
1t

*Benzyl Pyruvate (**1t**).*[25] Colorless oil, 1.1 g, 62% yield (20 mmol scale); ^1H NMR (400 MHz, $CDCl_3$): δ 7.46−7.33 (m, 5H), 5.28 (s, 2H), 2.47 (s, 3H); MS (ESI) m/z: 201 $[M + 23]^+$.



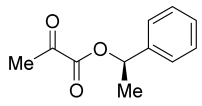
1u

*Cyclohexyl Pyruvate (**1u**).* Colorless oil, 0.9 g, 53% yield; ^1H NMR (400 MHz, $CDCl_3$): δ 4.93−4.83 (m, 1H), 2.45 (s, 3H), 1.94−1.87 (m, 2H), 1.80−1.72 (m, 2H), 1.59−1.50 (m, 3H), 1.44−1.28 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 192.5, 160.3, 75.5, 31.3, 26.7, 25.2, 23.7; IR (KBr) ν_{max}: 2932, 1726, 1401, 1268, 1128, 1013 cm^{-1}; HRMS (ESI) m/z: calcd for $C_9H_{14}NaO_3$, 193.0835 $[M + Na]^+$; found, 193.0830.



1v

*tert-Butyl Pyruvate (**1v**).* Colorless oil, 0.9 g, 62% yield; ^1H NMR (400 MHz, $CDCl_3$): δ 2.39 (s, 3H), 1.53 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 193.2, 160.3, 83.9, 27.8, 26.5; IR (KBr) ν_{max}: 2926, 1633, 1399, 1119, 909, 737 cm^{-1}; HRMS (ESI) m/z: calcd for $C_7H_{12}NaO_3$, 167.0679 $[M + Na]^+$; found, 167.0682.



1w

*(R)-1-Phenylethyl Pyruvate (**1w**).* Colorless oil, 1.2 g, 62% yield; ^1H NMR (400 MHz, $CDCl_3$): δ 7.46−7.28 (m, 1H), 5.98 (q, J = 6.6 Hz, 1H), 2.45 (s, 1H), 1.65 (d, J = 6.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 192.0, 160.1, 140.2, 128.7, 128.5, 126.3, 75.0, 26.7, 22.0; IR (KBr) ν_{max}: 3416, 2985, 1728, 1452, 1291, 1142, 699 cm^{-1}; HRMS (ESI) m/z: calcd for $C_{11}H_{12}NaO_3$, 215.0679 $[M + Na]^+$; found, 215.0682.

General Procedure for the Photoredox-Catalyzed Reductive Dimerization of α-Ketoesters. A solution of Na_2-EY (0.006 mmol), Hantzsch-type 1,4-dihydropyridine (0.165 mmol), and α-ketoester (0.3 mmol) in THF/H_2O (6.0 mL, 95:5 v/v, degassed) was stirred under the nitrogen atmosphere by irradiation of 10 W white LEDs at a distance of 5 cm at room temperature. The reaction mixture was concentrated in a rotary evaporator under vacuum upon the completion of the reaction (monitored by TLC). The residue was then purified by silica gel column chromatography (petroleum ether/ethyl acetate = 30:1 v/v for **2a−e**, **2g−i**, **2l−p**, **2s−t**; 20:1 v/v for **2j**, **2l**, **2u**, **2v**; 10:1 v/v for **2q**) to give pure 2,3-dialkylated tartaric acid esters.

*DL-Dimethyl 2,3-Diisopropyltartrate (DL-**2a**).* White solid, 16 mg, 42% yield; mp 46−51 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 3.80 (s, 6H), 3.77 (s, 2H), 2.18 (m, J = 6.7 Hz, 2H), 1.02 (d, J = 6.7 Hz, 6H), 0.82 (d, J = 6.7 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.9, 83.4, 52.6, 33.8, 19.1, 17.2; IR (KBr) ν_{max}: 2960, 1724, 1633, 1441, 1392, 1247, 1159, 1024, 763 cm^{-1}; HRMS (ESI) m/z: calcd for $C_{12}H_{22}NaO_6$, 285.1309 $[M + Na]^+$; found, 285.1308.

*meso-Dimethyl 2,3-Diisopropyltartrate (meso-**2a**).* White solid, 17.5 mg, 45% yield; mp 65−67 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 3.82 (s, 2H), 3.79 (s, 6H), 2.37 (m, J = 6.7 Hz, 2H), 1.01 (d, J = 6.7 Hz, 6H), 0.86 (d, J = 6.7 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.2, 83.6, 52.7, 34.0, 18.9, 17.4; IR (KBr) ν_{max}: 2959, 1732, 1454, 1249, 1145, 1019 cm^{-1}; HRMS

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(ESI) m/z: calcd for $C_{12}H_{22}NaO_6$, 285.1309 $[M + Na]^+$; found, 285.1310.

*DL,meso-Dimethyl 2,3-Dimethyltartrate (**2b**).* Colorless oil, 25 mg, 80% yield (DL/meso = 1/1.05); ^1H NMR (400 MHz, $CDCl_3$): δ 3.84 (s, 1H), 3.81 (s, 2.94H), 3.77 (s, 3.08H), 3.59 (s, 1H), 1.51 (s, 2.94H), 1.49 (s, 3.08H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.3, 174.7, 78.9, 78.8, 53.2, 53.0, 20.4, 20.3; IR (KBr) ν_{max}: 2952, 1735, 1446, 1377, 1258, 1155, 1091, 976, 762 cm^{-1}; HRMS (ESI) m/z: calcd for $C_8H_{14}NaO_6$, 229.0683 $[M + Na]^+$; found, 229.0681.

*DL,meso-Dimethyl 2,3-Dihexyltartrate (**2c**).* Colorless oil, 45 mg, 87% yield (DL/meso = 1/1.1); ^1H NMR (400 MHz, $CDCl_3$): δ 3.80 (s, 2.83H), 3.76 (s, 3.14H), 3.72 (s, 1H), 3.51 (s, 1H), 1.96−1.89 (m, 3H), 1.80−1.71 (m, 1H), 1.54−1.37 (m, 2H), 1.35−1.15 (m, 12H), 0.98−0.78 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.4, 174.3, 82.9, 82.4, 53.0, 52.8, 32.8, 32.7, 31.7, 31.7, 29.4, 29.4, 23.8, 23.6, 22.5, 14.0; IR (KBr) ν_{max}: 2928, 2859, 1733, 1447, 1239, 1145, 1084, 762 cm^{-1}; HRMS (ESI) m/z: calcd for $C_{18}H_{34}NaO_6$, 369.2248 $[M + Na]^+$; found, 369.2255.

*DL-Dimethyl 2,3-Dicyclopropyltartrate (DL-**2d**).* White solid, 17 mg, 44% yield; mp 94−96 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 3.81 (s, 6H), 3.32 (s, 2H), 1.66−1.59 (m, 2H), 0.71−0.64 (m, 2H), 0.53−0.41 (m, 2H), 0.37−0.23 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.5, 77.6, 51.6, 11.7, 0.0, −2.7; IR (KBr) ν_{max}: 3008, 2949, 1728, 1435, 1255, 1166, 1017, 892 cm^{-1}; HRMS (ESI) m/z: calcd for $C_{12}H_{18}NaO_6$, 281.0996 $[M + Na]^+$; found, 281.0993.

*meso-Dimethyl 2,3-Dicyclopropyltartrate (meso-**2d**).* White solid, 19 mg, 48% yield; mp 95−99 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 3.81 (s, 6H), 3.53 (s, 2H), 1.55−1.45 (m, 2H), 0.74−0.66 (m, 2H), 0.55−0.42 (m, 2H), 0.41−0.27 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.6, 79.4, 53.4, 13.0, 2.5, 0.0; IR (KBr) ν_{max}: 3009, 2953, 1728, 1437, 1260, 1163, 1018, 887 cm^{-1}; HRMS (ESI) m/z: calcd for $C_{12}H_{18}NaO_6$, 281.0996 $[M + Na]^+$; found, 281.0996.

*DL-Dimethyl 2,3-Dicyclohexyltartrate (DL-**2e**).* White solid, 21.5 mg, 42% yield; mp 98−100 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 3.79 (s, 2H), 3.79 (s, 6H), 2.10−1.97 (m, 2H), 1.90−1.79 (m, 2H), 1.79−1.66 (m, 4H), 1.60 (d, J = 10.5 Hz, 2H), 1.37 (d, J = 11.2 Hz, 2H), 1.28−1.05 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.2, 83.7, 52.6, 43.9, 28.5, 26.8, 26.5, 26.5, 26.0; IR (KBr) ν_{max}: 2926, 2853, 1726, 1633, 1445, 1236, 1149, 1110, 757 cm^{-1}; HRMS (ESI) m/z: calcd for $C_{18}H_{30}NaO_6$, 365.1935 $[M + Na]^+$; found, 365.1938.

*meso-Dimethyl 2,3-Dicyclohexyltartrate (meso-**2e**).* White solid, 23.5 mg, 46% yield; mp 106−108 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 3.96 (s, 2H), 3.78 (s, 6H), 2.03−1.89 (m, 4H), 1.81−1.66 (m, 4H), 1.62−1.56 (m, 2H), 1.50−1.43 (m, 2H), 1.28−1.14 (m, 6H), 1.13−0.95 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.3, 83.6, 52.6, 44.9, 28.0, 26.9, 26.5, 26.4, 26.0; IR (KBr) ν_{max}: 2926, 2853, 1730, 1637, 1444, 1239, 1114, 1022 cm^{-1}; HRMS (ESI) m/z: calcd for $C_{18}H_{30}NaO_6$, 365.1935 $[M + Na]^+$; found, 365.1936.

*DL,meso-Dimethyl 2,3-Di(hex-5-en-1-yl)tartrate (**2g**).* Colorless oil, 43 mg, 80% yield (DL/meso = 1/1); ^1H NMR (400 MHz, $CDCl_3$): δ 5.81−5.70 (m, 2H), 4.97 (dd, J_1 = 17.1 Hz, J_2 = 1.2 Hz, 2H), 4.92 (dd, J_1 = 10.2 Hz, J_2 = 0.9 Hz, 2H), 3.80 (s, 3H), 3.76 (s, 3H), 3.74 (s, 1H), 3.53 (s, 1H), 2.09−1.92 (m, 5H), 1.92−1.86 (m, 2H), 1.82−1.71 (m, 1H), 1.55−1.42 (m, 2H), 1.42−1.32 (m, 4H), 1.00−0.80 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.3, 174.2, 138.6, 138.6, 114.5, 82.8, 82.3, 53.1, 52.9, 33.6, 32.6, 32.5, 28.9, 28.9, 23.3, 23.1; IR (KBr) ν_{max}: 2925, 2856, 1731, 1637, 1440, 1238, 1167, 993, 906 cm^{-1}; HRMS (ESI) m/z: calcd for $C_{18}H_{30}NaO_6$, 365.1935 $[M + Na]^+$; found, 365.1936.

*DL,meso-Dimethyl 2,3-Di(pent-4-en-1-yl)tartrate (**2h**).* Colorless oil, 34 mg, 72% yield (DL/meso = 1/1); ^1H NMR (400 MHz, $CDCl_3$): δ 5.81−4.93 (m, 2H), 4.99 (d, J = 16.9 Hz, 2H), 4.94 (d, J = 10.2 Hz, 2H), 3.80 (s, 3H), 3.76 (s, 3H), 3.74 (s, 1H), 3.53 (d, J = 1.4 Hz, 1H), 2.10−1.97 (m, 5H), 1.96−1.90 (m, 2H), 1.82−1.71 (m, 1H), 1.65−1.52 (m, 2H), 1.11−0.90 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.2, 174.2, 138.2, 138.3, 114.8, 114.8, 82.8, 82.2, 53.1, 52.9, 33.7, 33.6, 32.2, 32.1, 23.1, 22.9; IR (KBr) ν_{max}: 2937, 174, 1639, 1442, 1246, 1150, 1092, 995, 910 cm^{-1}; HRMS (ESI) m/z: calcd for $C_{16}H_{26}O_6$, 337.1622 $[M + Na]^+$; found, 337.1622.

*DL,meso-Dimethyl 2,3-Bis(4-(trimethylsilyl)but-3-yn-1-yl)-tartrate (**2i**).* Colorless oil, 46 mg, 70% yield (DL/meso = 1/1); ^1H NMR (400 MHz, $CDCl_3$): δ 3.82 (s, 3H), 3.77 (s, 4H), 3.56 (s, 1H), 2.46−2.35 (m, 2H), 2.30−2.18 (m, 3H), 2.13−1.97 (m, 1H), 1.97−1.91 (m, 2H), 0.14 (s, 9H), 0.13 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.2, 173.2, 105.8, 105.8, 84.8, 84.8, 81.7, 81.0, 53.2, 53.0, 31.8, 31.6, 14.6, 14.5, 0.0, 0.0; IR (KBr) ν_{max}: 2957, 2858, 2174, 1738, 1633, 1444, 1399, 1253, 1114, 844, 649 cm^{-1}; HRMS (ESI) m/z: calcd for $C_{20}H_{34}NaO_6Si_2$, 449.1786 $[M + Na]^+$; found, 449.1786.

*DL,meso-Dimethyl 2,3-Bis(3-((4-methoxybenzyl)oxy)-propyl)tartrate (**2j**).* Colorless oil, 66.4 mg, 83% yield (DL/meso = 1/1); ^1H NMR (400 MHz, $CDCl_3$): δ 7.25 (dd, J_1 = 8.6 Hz, J_2 = 1.2 Hz, 4H), 6.87 (d, J = 8.3 Hz, 4H), 4.42 (s, 4H), 3.90 (s, 1H), 3.79 (s, 6H), 3.78 (s, 3H), 3.74 (s, 4H), 3.48−3.37 (m, 4H), 2.20−1.95 (m, 3H), 1.84−1.72 (m, 3H), 1.36−1.24 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.1, 174.0, 159.2, 130.5, 130.5, 129.3, 129.3, 113.8, 82.7, 82.1, 72.4, 72.4, 69.8, 55.3, 53.1, 52.9, 29.8, 29.7, 24.2, 24.1; IR (KBr) ν_{max}: 2944, 2855, 1735, 1512, 1450, 1246, 1090, 1031, 819 cm^{-1}; HRMS (ESI) m/z: calcd for $C_{28}H_{38}NaO_{10}$, 557.2357 $[M + Na]^+$; found, 557.2363.

*DL,meso-Dimethyl 2,3-Bis(2-(1,3-dioxolan-2-yl)ethyl)-tartrate (**2k**).* Colorless oil, 44.5 mg, 78% yield (DL/meso = 1/1); ^1H NMR (400 MHz, $CDCl_3$): δ 4.83 (q, J = 4.8 Hz, 2H), 3.95−3.91 (m, 4H), 3.85 (s, 1H), 3.84−3.80 (m, 4H), 3.79 (s, 3H), 3.74 (s, 3H), 3.68 (d, J = 0.9 Hz, 1H), 2.14−2.05 (m, 3H), 1.98−1.88 (m, 1H), 1.84−1.78 (m, 2H), 1.38−1.23 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.9, 173.8, 104.0, 104.0, 82.4, 81.8, 64.9, 53.2, 53.0, 28.4, 28.1, 27.2, 27.0; IR (KBr) ν_{max}: 2951, 1731, 1644, 1400, 1255, 1207, 1117, 1026, 803, 671 cm^{-1}; HRMS (ESI) m/z: calcd for $C_{16}H_{26}NaO_{10}$, 401.1418 $[M + Na]^+$; found, 401.1421.

*DL,meso-Dimethyl 2,3-Bis(2-((tert-butyldimethylsilyl)oxy)-ethyl)tartrate (**2l**).* Colorless oil, 58 mg, 78% yield (DL/meso = 1/1); ^1H NMR (400 MHz, $CDCl_3$): δ 4.08 (s, 1H), 4.00 (s, 1H), 3.77 (s, 3H), 3.75−3.66 (m, 7H), 2.34−2.26 (m, 2H), 2.24−2.16 (m, 1H), 2.08−2.02 (m, 1H), 0.86 (s, 18H), 0.02−0.00 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.8, 173.8, 81.2, 80.7, 59.4, 59.2, 52.7, 52.5, 34.9, 34.9, 25.9, 25.9, 18.4, 18.4, −5.5, −5.5, −5.6, −5.6; IR (KBr) ν_{max}: 3856, 3736, 2945, 2865, 1740, 1640, 1459, 1256, 1095, 834, 670 cm^{-1}; HRMS (ESI) m/z: calcd for $C_{22}H_{46}NaO_8Si_2$, 517.2623 $[M + Na]^+$; found, 517.2629.

*DL-Dimethyl 2,3-Bis(1-(tert-butoxycarbonyl)piperidin-4-yl)-tartrate (DL-**2m**).* White solid, 33 mg, 40% yield; mp 73−77 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 4.10 (s, 4H), 3.87 (s, 2H), 3.79 (s, 6H), 2.60 (s, 4H), 2.25−2.07 (m, 2H), 1.92 (d, J = 13.0 Hz, 2H), 1.77 (d, J = 11.0 Hz, 2H), 1.42 (s, 18H), 1.35−1.27 (m,

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4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.4, 154.6, 83.4, 79.5, 53.0, 43.7, 42.5, 28.4, 27.3, 26.3; IR (KBr) ν_{max}: 2963, 2854, 1688, 1417, 1257, 1149, 1092, 1020, 798 cm^{-1}; HRMS (ESI) m/z: calcd for $C_{26}H_{44}N_2NaO_{10}$, 567.2888 [M + Na]$^+$; found, 567.2892.

*meso-Dimethyl 2,3-Bis(1-(tert-butoxycarbonyl)piperidin-4-yl)tartrate (meso-**2m**).* White solid, 35 mg, 43% yield; mp 79−82 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.09 (s, 4H), 3.80 (s, 2H), 3.77 (s, 6H), 2.60 (d, J = 8.7 Hz, 4H), 2.09−2.00 (m, 2H), 1.96 (d, J = 13.2 Hz, 2H), 1.44 (s, 2H), 1.42 (s, 18H), 1.38−1.28 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.6, 154.6, 83.0, 79.4, 52.9, 43.7, 42.0, 28.4, 27.9, 26.5; IR (KBr) ν_{max}: 2961, 2855, 1735, 1688, 1414, 1251, 1093, 1022, 800 cm^{-1}; HRMS (ESI) m/z: calcd for $C_{26}H_{44}N_2NaO_{10}$, 567.2888 [M + Na]$^+$; found, 567.2893.

*DL-Dimethyl 2,3-Bis(tetrahydro-2H-pyran-4-yl)tartrate (DL-**2n**).* White solid, 21 mg, 40% yield; mp 127−129 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.98 (dd, J_1 = 11.6 Hz, J_2 = 3.9 Hz, 2H), 3.92 (dd, J_1 = 11.6 Hz, J_2 = 4.0 Hz, 2H), 3.81 (d, J = 5.8 Hz, 2H), 3.79 (s, 6H), 3.38−3.33 (m, 4H), 2.16 (tt, J_1 = 11.8 Hz, J_2 = 3.4 Hz, 2H), 1.87 (dd, J_1 = 13.3 Hz, J_2 = 2.4 Hz, 2H), 1.63−1.48 (m, 4H), 1.34 (dd, J_1 = 10.5 Hz, J_2 = 2.5 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.6, 82.9, 67.9, 67.7, 52.8, 41.0, 28.7, 27.4; IR (KBr) ν_{max}: 2956, 2841, 2358, 1734, 1630, 1440, 1240, 1091, 805 cm^{-1}; HRMS (ESI) m/z: calcd for $C_{16}H_{26}NaO_8$, 369.1520 [M + Na]$^+$; found, 369.1516.

*meso-Dimethyl 2,3-Bis(tetrahydro-2H-pyran-4-yl)tartrate (meso-**2n**).* White solid, 22 mg, 43% yield; mp 184−188 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.01−3.90 (m, 4H), 3.87 (s, 2H), 3.79 (s, 6H), 3.35−3.32 (m, 4H), 2.28 (tt, J_1 = 11.9 Hz, J_2 = 3.4 Hz, 2H), 1.83 (d, J = 13.2 Hz, 2H), 1.70−1.50 (m, 4H), 1.22−1.16 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.3, 83.4, 67.8, 67.7, 53.0, 41.4, 28.0, 27.3; IR (KBr) ν_{max}: 2954, 2843, 1734, 1636, 1443, 1243, 1093, 1024, 875 cm^{-1}; HRMS (ESI) m/z: calcd for $C_{16}H_{26}NaO_8$, 369.1520 [M + Na]$^+$; found, 369.1517.

*DL-Dimethyl 2,3-Bis(tetrahydro-2H-thiopyran-4-yl)tartrate (DL-**2o**).* White solid, 22 mg, 39% yield; mp 138−140 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.05 (s, 2H), 3.81 (s, 6H), 2.74−2.55 (m, 8H), 2.26 (d, J = 11.8 Hz, 2H), 1.97 (tt, J_1 = 11.8 Hz, J_2 = 2.6 Hz, 2H), 1.86 (d, J = 12.7 Hz, 2H), 1.70−1.57 (m, 2H), 1.41 (qd, J_1 = 11.9 Hz, J_2 = 4.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.5, 83.4, 53.0, 45.1, 29.4, 28.9, 28.3; IR (KBr) ν_{max}: 2946, 1728, 1634, 1435, 1247, 1118, 1020, 802 cm^{-1}; HRMS (ESI) m/z: calcd for $C_{16}H_{26}NaO_6S_2$, 401.1063 [M + Na]$^+$; found, 401.1061.

*meso-Dimethyl 2,3-Bis(tetrahydro-2H-thiopyran-4-yl)-tartrate (meso-**2o**).* White solid, 24 mg, 42% yield; mp 144−146 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.84 (s, 2H), 3.78 (s, 6H), 2.74−2.51 (m, 8H), 2.37 (d, J = 13.2 Hz, 2H), 1.98−1.83 (m, 4H), 1.61−1.45 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.7, 83.2, 52.9, 43.7, 30.2, 29.0, 28.9, 28.5; IR (KBr) ν_{max}: 2947, 1731, 1633, 1434, 1246, 1116, 1019, 801 cm^{-1}; HRMS (ESI) m/z: calcd for $C_{16}H_{26}NaO_6S_2$, 401.1063 [M + Na]$^+$; found, 401.1060.

*DL,meso-Dimethyl 2,3-Bis(4-bromobutyl)tartrate (**2p**).* Colorless oil, 57 mg, 85% yield (DL/meso = 1/1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.82 (s, 3H), 3.78 (s, 3H), 3.77 (s, 1H), 3.56 (d, J = 1.4 Hz, 1H), 3.37 (t, J = 6.8 Hz, 4H), 2.07−1.74 (m, 8H), 1.64−1.53 (m, 2H), 1.18−1.00 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.9, 173.9, 82.6, 82.1, 53.3, 53.1, 33.3, 32.7, 32.6, 31.8, 31.7, 22.5, 22.4; IR (KBr) ν_{max}: 2950, 1735, 1443, 1247, 1164, 1102, 810, 736 cm^{-1}; HRMS (ESI) m/z: calcd for $C_{14}H_{24}Br_2NaO_6$, 470.9811 [M + Na]$^+$; found, 470.9812.

*DL,meso-Dimethyl 2,3-Bis(4-((1,3-dioxoisoindolin-2-yl)-oxy)butyl)tartrate (**2q**).* Colorless oil, 37 mg, 40% yield (DL/meso = 1/1.05); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82 (dd, J_1 = 5.2 Hz, J_2 = 3.1 Hz, 4H), 7.73 (dd, J_1 = 5.2 Hz, J_2 = 3.1 Hz, 4H), 4.22−4.14 (m, 4H), 3.85 (s, 2.91H), 3.80 (s, 3.07H), 3.77 (s, 1H), 3.58 (d, J = 0.9 Hz, 1H), 2.15−2.06 (m, 1H), 2.06−1.99 (m, 2H), 1.87 (dd, J_1 = 12.1 Hz, J_2 = 4.4 Hz, 1H), 1.84−1.74 (m, 4H), 1.69−1.60 (m, 2H), 1.23−1.10 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.1, 174.0, 163.6, 134.5, 128.9, 123.5, 82.7, 82.1, 78.1, 53.3, 53.1, 32.4, 32.2, 28.1, 20.0, 19.8; IR (KBr) ν_{max}: 2950, 1730, 1458, 1385, 1251, 1123, 981, 703 cm^{-1}; HRMS (ESI) m/z: calcd for $C_{30}H_{32}N_2NaO_{12}$, 635.1847 [M + Na]$^+$; found, 635.1848.

*DL-Diphenyl 2,3-Dimethyltartrate (DL-**2s**).* White solid, 20 mg, 40% yield; mp 107−109 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45−7.38 (m, 4H), 7.31−7.26 (m, 2H), 7.20−7.12 (m, 4H), 3.98 (s, 2H), 1.83 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.6, 150.4, 129.7, 126.5, 121.3, 79.5, 20.9; IR (KBr) ν_{max}: 2930, 1753, 1592, 1487, 1382, 1185, 1082, 809, 743 cm^{-1}; HRMS (ESI) m/z: calcd for $C_{18}H_{18}NaO_6$, 353.0996 [M + Na]$^+$; found, 353.0993.

*meso-Diphenyl 2,3-Dimethyltartrate (meso-**2s**).* Colorless oil, 21 mg, 42% yield; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40−7.34 (m, 4H), 7.25 (tt, J_1 = 6.7 Hz, J_2 = 1.1 Hz, 2H), 7.14−7.05 (m, 4H), 3.75 (s, 2H), 1.80 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.2, 150.3, 129.7, 126.5, 121.2, 79.0, 20.8; IR (KBr) ν_{max}: 2932, 1752, 1632, 1595, 1487, 1238, 119, 1127, 1077, 745 cm^{-1}; HRMS (ESI) m/z: calcd for $C_{18}H_{18}NaO_6$, 353.0996 [M + Na]$^+$; found, 353.0995.

*DL-Dibenzyl 2,3-Dimethyltartrate (DL-**2t**).* Colorless oil, 21.5 mg, 40% yield; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43−7.29 (m, 10H), 5.21 (d, J = 12.2 Hz, 2H), 5.17 (d, J = 12.2 Hz, 2H), 1.53 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.6, 134.9, 128.7, 128.6, 128.3, 79.0, 68.0, 20.6; IR (KBr) ν_{max}: 2359, 1730, 1635, 1452, 1394, 1248, 1119, 740 cm^{-1}; HRMS (ESI) m/z: calcd for $C_{20}H_{22}NaO_6$, 381.1309 [M + Na]$^+$; found, 381.1310.

*meso-Dibenzyl 2,3-Dimethyltartrate (meso-**2t**).* White solid, 21.5 mg, 40% yield; mp 61−63 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38−7.30 (m, 6H), 7.30−7.22 (m, 4H), 5.10 (d, J = 12.1 Hz, 2H), 4.92 (d, J = 12.1 Hz, 2H), 3.64 (s, 2H), 1.49 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.1, 134.8, 128.6, 128.5, 78.7, 68.1, 20.4; IR (KBr) ν_{max}: 2358, 171, 1635, 1450, 1389, 1254, 1148, 954, 742 cm^{-1}; HRMS (ESI) m/z: calcd for $C_{20}H_{22}NaO_6$, 381.1309 [M + Na]$^+$; found, 381.1308.

*DL-Dicyclohexyl 2,3-Dimethyltartrate (DL-**2u**).* White solid, 20.5 mg, 40% yield; mp 38−41 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.94−4.81 (m, 2H), 3.82 (s, 2H), 1.93−1.82 (m, 4H), 1.76−1.68 (m, 4H), 1.59−1.54 (m, 2H), 1.52 (s, 6H), 1.52−1.50 (m, 2H), 1.50−1.46 (m, 2H), 1.46−1.32 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.2, 78.6, 75.0, 31.3, 31.3, 25.3, 23.5, 20.7; IR (KBr) ν_{max}: 2935, 2859, 1727, 1633, 1450, 1250, 1162, 1089, 1020, 802 cm^{-1}; HRMS (ESI) m/z: calcd for $C_{18}H_{30}NaO_6$, 365.1935 [M + Na]$^+$; found, 365.1936.

*meso-Dicyclohexyl 2,3-Dimethyltartrate (meso-**2u**).* White solid, 22.5 mg, 44% yield; mp 56−58 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.90−4.76 (m, 2H), 3.62 (s, 2H), 1.90−1.82 (m, 4H), 1.75−1.68 (m, 4H), 1.59−1.50 (m, 3H), 1.49 (s, 6H), 1.47−1.42 (m, 3H), 1.42−1.36 (m, 4H), 1.35−1.28 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.9, 78.4, 75.1, 31.4, 31.2, 25.2, 23.6, 23.5, 20.7; IR (KBr) ν_{max}: 2933, 2858, 1726, 1635, 1450, 1391, 1258, 1155, 1111, 1019, 804 cm^{-1}; HRMS (ESI)

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m/*z*: calcd for $C_{18}H_{30}NaO_6$, 365.1935 [M + Na]$^+$; found, 365.1938.

*DL-Di-tert-butyl 2,3-Dimethyltartrate (DL-**2v**).* White solid, 16 mg, 38% yield; mp 76−78 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.79 (s, 2H), 1.51 (s, 18H), 1.48 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.0, 83.2, 78.6, 27.9, 21.1; IR (KBr) ν_{max}: 2970, 2360, 1721, 1633, 1397, 1264, 1155, 1113, 802 cm^{-1}; HRMS (ESI) *m*/*z*: calcd for $C_{14}H_{26}NaO_6$, 313.1622 [M + Na]$^+$; found, 313.1624.

*meso-Di-tert-butyl 2,3-Dimethyltartrate (meso-**2v**).* White solid, 17 mg, 40% yield; mp 101−102 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.63 (s, 2H), 1.49 (s, 18H), 1.44 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.6, 83.2, 78.5, 28.0, 21.1; IR (KBr) ν_{max}: 2968, 2358, 1725, 1635, 1395, 1265, 1150, 1110, 1025, 803 cm^{-1}; HRMS (ESI) *m*/*z*: calcd for $C_{14}H_{26}NaO_6$, 313.1622 [M + Na]$^+$; found, 313.1621.

*DL-Di-((R)-1-phenylethyl) 2,3-Dimethyltartrate (DL-**2w**).* Colorless oil, 26 mg, 41% yield; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41−7.31 (m, 5H), 7.30−7.25 (m, 3H), 7.18−7.09 (m, 2H), 5.93 (q, *J* = 6.5 Hz, 1H), 5.65 (q, *J* = 6.6 Hz, 1H), 3.63 (s, 1H), 3.59 (s, 1H), 1.60 (d, *J* = 6.5 Hz, 3H), 1.57 (s, 3H), 1.42 (s, 3H), 1.41 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.7, 173.5, 140.9, 140.2, 128.6, 128.5, 128.4, 128.1, 126.6, 125.8, 78.6, 78.3, 75.1, 74.78, 21.8, 21.8, 20.7, 20.4; IR (KBr) ν_{max}: 3167, 1732, 1399, 1257, 1062, 698 cm^{-1}; HRMS (ESI) *m*/*z*: calcd for $C_{22}H_{26}NaO_6$, 409.1622 [M + Na]$^+$; found, 409.1622.

*meso-Di-((R)-1-phenylethyl) 2,3-Dimethyltartrate (meso-**2w**).* Colorless oil, 24 mg, 45% yield; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.53−7.27 (m, 6H), 5.93 (p, *J* = 6.5 Hz, 1H), 3.81 (d, *J* = 7.4 Hz, 1H), 1.59 (d, *J* = 6.8 Hz, 3H), 1.57 (s, 2H), 1.50 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.3, 173.8, 140.8, 140.5, 128.6, 128.6, 128.2, 128.2, 126.1, 126.0, 78.8, 78.7, 74.9, 74.7, 22.1, 21.9, 20.8, 20.4; IR (KBr) ν_{max}: 2984, 1732, 1209, 1158, 1060, 698 cm^{-1}; HRMS (ESI) *m*/*z*: calcd for $C_{22}H_{26}NaO_6$, 409.1622 [M + Na]$^+$; found, 409.1624.

*Methyl 2-(Adamantan-1-yl)-2-hydroxyacetate (**2f-ol**).* White solid, 21.5 mg, 32% yield; mp 39−41 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.78 (s, 3H), 3.66 (d, *J* = 8.1 Hz, 1H), 2.60 (d, *J* = 8.1 Hz, 1H), 1.99 (s, 3H), 1.70 (d, *J* = 12.2 Hz, 3H), 1.65−1.58 (m, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.4, 79.1, 52.0, 37.9, 37.0, 36.9, 28.2; IR (KBr) ν_{max}: 2906, 2852, 173, 1633, 1447, 1253, 1211, 1706, 988, 733, 609 cm^{-1}; HRMS (ESI) *m*/*z*: calcd for $C_{13}H_{20}NaO_3$, 247.1305 [M + Na]$^+$; found, 247.1304.

*Diethyl 2-Hydroxymalonate (**2r-ol**).*[26] Colorless oil, 27 mg, 46% yield; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.68 (d, *J* = 8.3 Hz, 1H), 4.37−4.19 (m, 4H), 3.54 (d, *J* = 8.3 Hz, 1H), 1.29 (t, *J* = 7.1 Hz, 6H); MS (ESI) *m*/*z*: 177 [M + 1]$^+$, 199 [M + 23]$^+$.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acsomega.7b00749.

Radical-trapping experiments; gram-scale preparations of **2b**, **2e**, and **2t** and optical resolutions; electrochemical measurement of **1a**; and copies of ^{1}H and ^{13}C NMR spectra for all compounds (PDF)

X-ray single-crystal data of *meso*-**2e** (CIF)

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Notes

The authors declare no competing financial interest.

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