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Graphical Abstract

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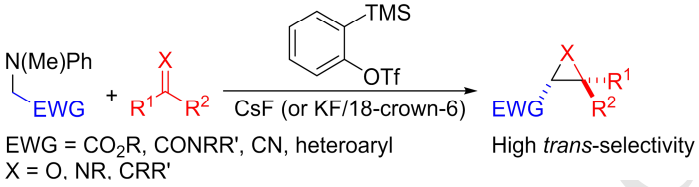

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Facile construction of three-membered rings via benzyne-promoted Darzens-type reaction of tertiary amines

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ABSTRACT

A range of tertiary amines having electron-withdrawing groups were activated in situ by benzyne, generated from 2-(trimethylsilyl)phenyl triflate and a fluoride source, and participated in the Darzens-type reaction with carbonyl compounds, imines, and vinyl ketones to afford structurally diverse epoxides, aziridines, and cyclopropanes, respectively, in moderate to excellent yields with high *trans*-selectivity. The reaction involves in situ formation of unstrained ammonium ylides from tertiary amines and benzyne, proceeds in the absence of transition metals and strong bases, and tolerates a wide variety of functional groups.

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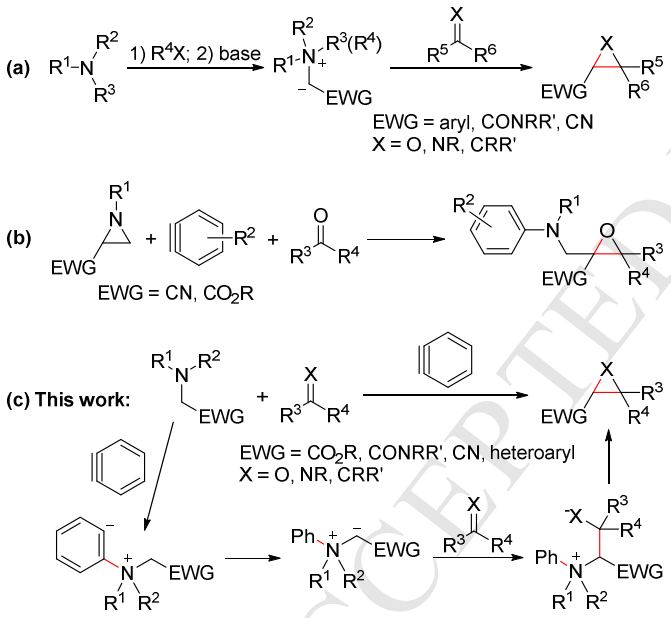
1. Introduction

Three-membered rings are present in many biologically relevant molecules and serve as versatile intermediates in chemical synthesis.[1] Among the general approaches for the construction of three-membered rings, the well-known Darzens reaction proves powerful for the synthesis of epoxides by treating aldehydes or ketones with α-halo carbonyl compounds in the presence of bases.[2] To expand the scope of the Darzens reaction, many efforts have been devoted to find readily accessible surrogates of α-halo carbonyl compounds. In addition to sulfonium ylides,[3] ammonium ylides have been explored to replace α-halo carbonyl compounds in the Darzens-type reaction to access epoxides, despite that the substrate scope is limited to aryl-, carbamoyl-, and cyano-stabilized ammonium ylides, which are prepared by *N*-alkylation of tertiary amines followed by treatment with bases (Scheme 1, a).[4] The Darzens-type reaction of ammonium ylides has been extended to imines and electron-deficient alkenes, yielding the corresponding aziridines and cyclopropanes, respectively.[4a-c,e,i,n-p,r,s] Related strained aziridinium ylides, generated in situ from aziridines and arynes, have also been reported to add to aldehydes to afford *N*-aryl α-amino epoxides (Scheme 1, b).[5] Herein we report a modified Darzens-type reaction by in situ formation of unstrained ammonium ylides from tertiary amines and benzyne in the absence of strong bases and metals for the construction of three-membered rings such as epoxides, aziridines, and cyclopropanes (Scheme 1, c).



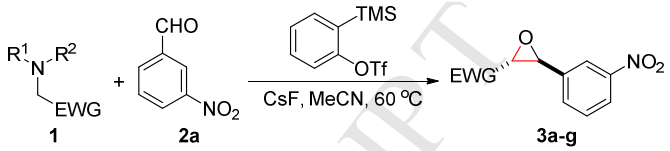
Scheme 1. The Darzens-type reactions of ammonium ylides and aziridinium ylides.

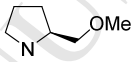
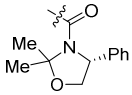
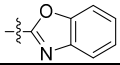
2. Results and discussion

Inspired by the previously reported nucleophilic addition of tertiary amines to arynes generated from 2-(trimethylsilyl)aryl triflates under mild conditions,[6,7] we envisioned that the zwitterions generated from tertiary amines, having an electron-withdrawing group, and benzyne would undergo proton transfer to generate quaternary ammonium ylides,[6j,p,q,s,t] which would participate in nucleophic addition to aldehydes, imines, and electron-deficient alkenes to afford epoxides, aziridines, and cyclopropanes, respectively (Scheme 1, c).[4] Using 2-(trimethylsilyl)phenyl triflate as a benzyne precursor, we surveyed a few fluoride sources, such as CsF, KF, and tetrabutylammonium fluoride (TBAF), in the model Darzens-type reaction of tertiary amine **1a** with aldehyde **2a** in acetonitrile under air at 60 °C and found that the use of CsF afforded epoxide **3a** in the best yield (72%) with 98:2 *trans/cis*-selectivity (Table 1, entry 1).[8-11] We also examined more solvents such as toluene (trace), tetrahydrofuran (trace), 1,2-dimethoxyethane (32% yield), and dimethyl sulfoxide (trace), but unfortunately, failed to enhance the yield.

Table 1

Benzyne-promoted Darzens-type reaction of tertiary amines with aldehyde **2a**.[a]



Entry	**1**	NR^1R^2	EWG	**3**	Yield (%)[b]	dr (*trans* /*cis*)[c]
1	**1a**	N(Me)Ph	CO_2Et	**3a**	72	98:2
2	**1b**	NMe_2	CO_2Et	**3a**	56	>98:2
3	**1c**		CO_2Et	**3a**	52	>98:2
4	**1d**		CO_2Et	**3a**	53	>98:2
5[d]	**1e**		CO_2Et	**3a**	28	98:2
6[e]	**1f**	NHMe	CO_2Et	**3a**	67	>98:2
7	**1g**	N(Me)Ph	CO_2Bn	**3b**	83	98:2
8	**1h**	N(Me)Ph	$CO_2{}^tBu$	**3c**	61	>98:2
9	**1i**	N(Me)Ph	CONHMe	**3d**	44	90:10
10[f]	**1j**	N(Me)Ph		**3e**	76	87:13
11	**1k**	N(Me)Ph	CN	**3f**	90	50:50
12	**1l**	N(Me)Ph		**3g**	31	>98:2

[a] Reaction conditions: **1** (0.24 mmol), **2a** (0.20 mmol), 2-(trimethylsilyl)phenyl triflate (0.30 mmol), CsF (0.60 mmol), acetonitrile (1.2 mL), 60 °C, 24 h.

[b] Isolated yield.

[c] Determined by ^{1}H NMR spectroscopic analysis.

[d] 25% ee for **3a**.

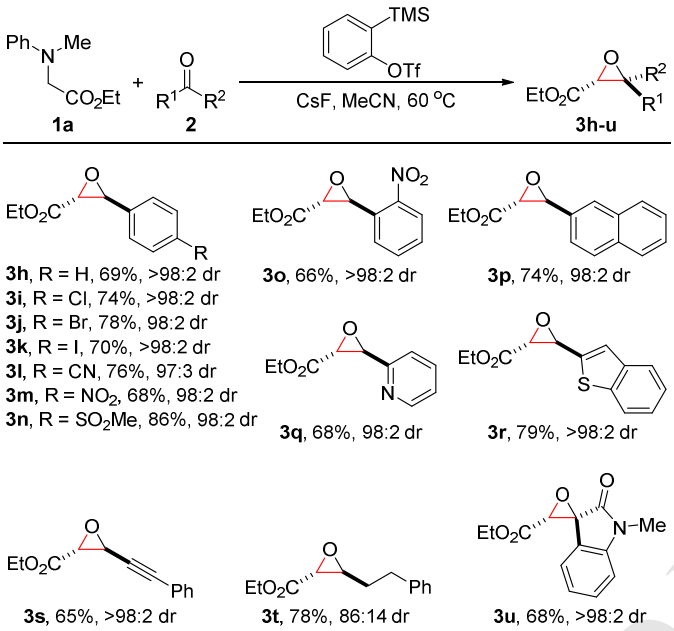
[e] 2-(trimethylsilyl)phenyl triflate (0.60 mmol) and CsF (0.80 mmol) were used.

[f] 98% de for **3e** (*trans*).

The benzyne-promoted Darzens-type reaction of tertiary amines was significantly affected by the *N*-substituents. When the *N*-methyl group and the *N*-phenyl group of tertiary amine **1a** were replaced with *N*,*N*-dialkyl groups, epoxide **3a** was obtained in much lower yields but still with high *trans*-selectivity (Table 1, entries 2-5). The introduction of an *L*-proline-derived *N*-substituent permitted the synthesis of optically active epoxide **3a** albeit in a low yield with poor chirality transfer (Table 1, entry 5). To our delight, in situ generation of amine **1a** from secondary amine **1f** also led to the formation of epoxide **3a** in a good yield (Table 1, entry 6). In addition to ester groups, we examined more electron-withdrawing groups such as carbamoyl, cyano, and 2-benzoxazolyl, delivering a range of functionalized epoxides in varied yields and *trans/cis*-selectivity (Table 1, entries 9-12). It is noteworthy that the reaction of substrate **1j**, having a chiral

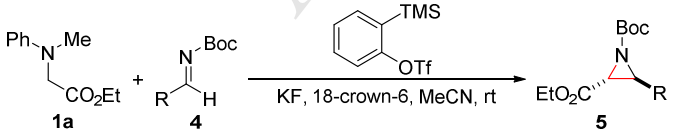
carbamoyl group,[40] afforded epoxide **3e**, the major *trans*-isomer, with 98% de (Table 1, entry 10).

A range of aromatic and heteroaromatic aldehydes were examined in the benzyne-promoted Darzens-type reaction of amine **1a**, and in general, the corresponding functionalized epoxides were obtained in moderate to good yields with high *trans*-selectivity (Scheme 2, **3h-r**). A variety of functional groups were introduced into the epoxide products by employing the corresponding aromatic aldehydes having such groups. The reaction was successfully extended to a propargylic aldehyde, an aliphatic aldehyde, and an activated ketone such as isatin (Scheme 2, **3s-u**). In these cases, the corresponding epoxides were also obtained in good yields with high *trans*-selectivity.

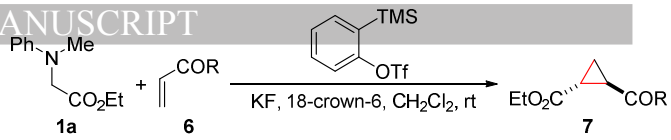


Scheme 2. Benzyne-promoted Darzens-type reaction of amine **1a** with carbonyl compounds. [a] Reaction conditions: **1a** (0.24 mmol), **2** (0.20 mmol), 2-(trimethylsilyl)phenyl triflate (0.30 mmol), CsF (0.60 mmol), acetonitrile (1.2 mL), 60 °C, 24 h. [b] Isolated yields and dr (*trans/cis*) were given.

Changing the reaction conditions was able to extend the benzyne-promoted Darzens-type reaction to the construction of more types of three-membered rings (Scheme 3). In the presence of 2-(trimethylsilyl)phenyl triflate, KF, and 18-crown-6, amine **1a** reacted with *N*-Boc aromatic imines in acetonitrile at room temperature, delivering aziridines **5a-e** in moderate to good yields with high *trans*-selectivity. Simply replacing acetonitrile with dichloromethane as the solvent, the reaction worked well with a range of vinyl ketones to afford cyclopropanes **7a-e** in good to excellent yields with high *trans*-selectivity.



5a, R = Ph, 78%, >98:2 dr
5b, R = 4-MeC$_6$H$_4$, 80%, >98:2 dr
5c, R = 4-ClC$_6$H$_4$, 60%, >98:2 dr
5d, R = 4-O$_2$NC$_6$H$_4$, 66%, >98:2 dr
5e, R = 2-naphthyl, 40%, >98:2 dr



7a, R = Ph, 98%, >98:2 dr
7b, R = 4-MeOC$_6$H$_4$, 85%, >98:2 dr
7c, R = 4-ClC$_6$H$_4$, 85%, >98:2 dr
7d, R = 2-naphthyl, 95%, >98:2 dr
7e, R = 2-furyl, 60%, >98:2 dr

Scheme 3. Benzyne-promoted Darzens-type reaction of amine **1a** with imines or vinyl ketones.

3. Conclusion

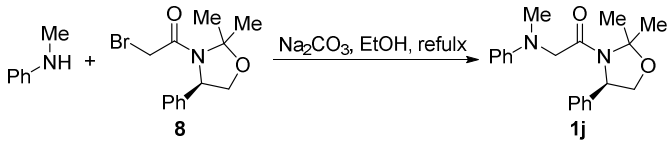
In summary, a modified Darzens-type reaction has been developed to access three-membered rings through in situ formation of unstrained ammonium ylides from tertiary amines and benzyne. With 2-(trimethylsilyl)phenyl triflate as a benzyne precursor, a range of tertiary amines having electron-withdrawing groups were activated in situ to react with carbonyl compounds, imines, and vinyl ketones to afford structurally diverse epoxides, aziridines, and cyclopropanes, respectively, in moderate to excellent yields with high *trans*-selectivity. It is noteworthy that the reaction proceeds in the absence of transition metals and strong bases and tolerates a wide variety of functional groups.

4. Experimental

4.1. General information

Amines **1a-i** and **1k**,[12] imines **4**,[13] vinyl ketones **5**,[14] and compound **8**[40] were prepared according to literature procedures. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker AC-400 FT spectrometer (400 MHz and 100 MHz, respectively) using tetramethylsilane as an internal reference, and chemical shifts (δ) and coupling constants (J) were expressed in ppm and Hz, respectively. High resolution mass spectra (HRMS) were recorded on a LC-TOF spectrometer (Micromass). ESI-mass data were acquired using a Thermo LTQ Orbitrap XL instrument equipped with an ESI source and controlled by Xcalibur software. High pressure liquid chromatography (HPLC) analyses were performed on a Hewlett-Packard 1200 Series instrument equipped with anisostatic pump, using a Daicel Chiralpak column (OD, 250 × 4.6 mm) with isopropanol/hexane as mobile phase, and the UV detection was monitored at 254 nm.

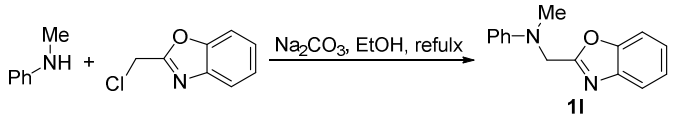
*4.2. Preparation of amine **1j***



To a solution of *N*-methylaniline (1.07 g, 1.08 mL, 10.0 mmol) in ethanol (20 mL) was added sodium carbonate (1.59 g, 15.0 mmol) and compound **8** (2.57 g, 8.6 mmol). The suspension was stirred under reflux for 14 h and cooled to room temperature. The mixture was quenched with water (50 mL) and extracted with ethyl acetate (4 x 20 mL). The combined organic fractions were washed with water (4 x 25 mL) and brine (20 mL), dried over anhydrous sodium sulfate, and concentrated under reduced pressure. The residue was purified by silica gel chromatography, eluting with ethyl acetate/petroleum ether (1:10 v/v), to give (*R*)-1-(2,2-dimethyl-4-phenyloxazolidin-3-yl)-2-(methyl(phenyl)amino)ethan-1-one (**1j**) as a yellow solid (2.56 g, 95% yield). m.p. 84-85 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45-7.39 (m, 2H), 7.38-7.32 (m, 3H), 7.15-7.09 (m, 2H), 6.67 (t, J =

7.2 Hz, 1H), 6.41 (d, *J* = 8.0 Hz, 2H), 4.97 (dd, *J* = 6.4, 2.4 Hz, 1H), 4.41 (dd, *J* = 8.8, 6.4 Hz, 1H), 3.94 (dd, *J* = 8.8, 2.4 Hz, 1H), 3.87 (d, *J* = 16.8 Hz, 1H), 3.56 (d, *J* = 16.8 Hz, 1H), 2.93 (s, 3H), 1.87 (s, 3H), 1.64 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.6, 149.2, 141.0, 129.3, 129.2, 128.4, 126.2, 117.1, 112.2, 97.0, 60.8, 56.2, 39.8, 25.6, 23.5; HRMS (ESI) calcd for $C_{20}H_{24}N_2O_2Na^+$ $(M + Na)^+$ 347.1730, found 347.1730.

*4.3. Preparation of amine **1l***



1l

To a solution of *N*-methylaniline (214 mg, 0.21 mL, 2.0 mmol) in ethanol (10 mL) was added sodium carbonate (317 mg, 3.0 mmol) and 2-chlorobenzoxazole (335 mg, 2.0 mmol). The suspension was stirred under reflux for 14 h, cooled to room temperature, quenched with water (20 mL), and extracted with ethyl acetate (4 x 10 mL). The combined organic fractions were washed with water (4 x 10 mL) and brine (20 mL), dried over anhydrous sodium sulfate, and concentrated under reduced pressure. The residue was purified by silica gel chromatography, eluting with ethyl acetate/petroleum ether (1:10 v/v), to give *N*-(benzo[*d*]oxazol-2-ylmethyl)-*N*-methylaniline (**1l**) as a pale yellow oil (424 mg, 89% yield).[15] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71-7.66 (m, 1H), 7.49-7.44 (m, 1H), 7.32-7.27 (m, 2H), 7.25 (t, *J* = 8.0, 2H), 6.89 (d, *J* = 8.4 Hz, 2H), 6.77 (t, *J* = 7.2 Hz, 1H), 4.74 (s, 2H), 3.18 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.0, 151.0, 148.8, 141.1, 129.4, 125.1, 124.5, 120.2, 117.9, 113.1, 110.8, 50.6, 39.4.

*4.4. General procedure for synthesis of epoxide **3***

A mixture of amine **1** (46.4 mg, 0.24 mmol), 2-(trimethylsilyl)phenyl triflate (89.5 mg, 0.30 mmol), CsF (91.1 mg, 0.60 mmol), and acetonitrile (0.80 mL) in a sealed tube was heated at 60 ^{o}C (oil bath) for 10 min, and a solution of aldehyde **2** (0.20 mmol) in acetonitrile (0.40 mL) was added. The mixture was stirred at 60 ^{o}C for 24 h, cooled to room temperature, and purified by silica gel chromatography, eluting with ethyl acetate/petroleum ether (1:10 v/v), to give epoxide **3**.

*4.4.1. Ethyl trans-3-(3-nitrophenyl)oxirane-2-carboxylate (**3a**)*

Obtained as a 98:2 mixture of *trans*- and *cis*-isomers. White solid (34.2 mg, 72% yield), m.p. 51-52 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24-8.16 (m, 2H), 7.65 (d, *J* = 7.6 Hz, 1H), 7.58 (t, *J* = 8.0 Hz, 1H), 4.36-4.24 (m, 2H), 4.22 (d, *J* = 1.6 Hz, 1H), 3.52 (d, *J* = 1.6 Hz, 1H), 1.35 (t, *J* = 7.2 Hz, 3H); Partial ^{1}H NMR for the *cis*-isomer: δ 3.89 (d, *J* = 4.4 Hz, 1H), 1.07 (t, *J* = 7.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.5, 148.6, 137.5, 131.8, 130.0, 124.0, 121.0, 62.3, 57.0, 56.8, 14.2; HRMS (ESI) calcd for $C_{11}H_{11}NO_5Na^+$ $(M + Na)^+$ 260.0529, found 260.0529.

Table 1, entry 5: The ee was determined to be 25% by HPLC analysis (Chiralpak OD column, λ = 254 nm, hexane/isopropanol = 95/5, flow rate = 1.0 mL/min): tR(major) = 24.8 min, tR(minor) = 32.0 min. $[\alpha]_D^{20}$ = -1.4 (*c* = 0.30, $CHCl_3$).

*4.4.2. Benzyl trans-3-(3-nitrophenyl)oxirane-2-carboxylate (**3b**)*

Obtained as a 98:2 mixture of *trans*- and *cis*-isomers. Yellow oil (49.7 mg, 83% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22-8.14 (m, 2H), 7.62 (d, *J* = 8.0 Hz, 1H), 7.55 (t, *J* = 8.0 Hz, 1H), 7.41-7.34 (m, 5H), 5.30 (d, *J* = 12.4 Hz, 1H), 5.24 (d, *J* = 12.4 Hz, 1H), 4.23 (d, *J* = 1.6 Hz, 1H), 3.56 (d, *J* = 1.6 Hz, 1H); Partial ^{1}H NMR for the *cis*-isomer: δ 4.33 (d, *J* = 4.4 Hz, 1H), 3.92 (d, *J* = 4.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.3, 148.6, 137.4, 134.8, 131.8, 130.0, 128.9, 128.8, 128.7, 124.0, 121.0, 67.9, 56.9, 56.8; HRMS (ESI) calcd for $C_{16}H_{14}NO_5^+$ $(M + H)^+$ 300.0867, found 300.0858.

*4.4.3. tert-Butyl trans-3-(3-nitrophenyl)oxirane-2-carboxylate (**3c**)*

Yellow oil (32.4 mg, 61% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23-8.16 (m, 2H), 7.65 (d, *J* = 7.6 Hz, 1H), 7.57 (t, *J* = 7.6 Hz, 1H), 4.15 (d, *J* = 1.6 Hz, 1H), 3.43 (d, *J* = 1.6 Hz, 1H), 1.53 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.5, 148.6, 137.8, 131.9, 129.9, 123.9, 121.1, 83.4, 57.6, 56.5, 28.1; HRMS (ESI) calcd for $C_{13}H_{15}NO_5Na^+$ $(M + Na)^+$ 288.0842, found 288.0842.

*4.4.4. N-Methyl trans-3-(3-nitrophenyl)oxirane-2-carboxamide (**3d**)*

Obtained as a 90:10 mixture of *trans*- and *cis*-isomers. Yellow solid (19.5 mg, 44% yield), m.p. 143-144 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23-8.19 (m, 1H), 8.15 (s, 1H), 7.64-7.53 (m, 2H), 6.27 (s, br, 1H), 4.01 (d, *J* = 1.6 Hz, 1H), 3.54 (d, *J* = 1.6 Hz, 1H), 2.89 (d, *J* = 5.2 Hz, 3H); Partial ^{1}H NMR for the *cis*-isomer: δ 6.07 (s, br, 1H), 4.37 (d, *J* = 4.8 Hz, 1H), 3.88 (d, *J* = 4.8 Hz, 1H), 2.59 (d, *J* = 5.2 Hz, 3H); HRMS (ESI) calcd for $C_{10}H_{10}N_2O_4Na^+$ $(M + Na)^+$ 245.0533, found 245.0533.

*4.4.5. ((R)-2,2-Dimethyl-4-phenyloxazolidin-3-yl)((2R,3S)-3-(3-nitrophenyl)oxiran-2-yl)methanone (**3e**)*[4o]

Obtained as an 87:13 mixture of *trans*- and *cis*-isomers. White solid (56.0 mg, 76% yield), m.p. 119-120 ^{o}C; $[\alpha]_D^{20}$ = -40.0 (*c* = 0.50, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (ddd, *J* = 8.0, 2.4, 0.8 Hz, 1H), 7.60-7.57 (m, 1H), 7.38-7.32 (m, 1H), 7.17-7.07 (m, 5H), 7.03-6.97 (m, 1H), 5.09 (dd, *J* = 6.8, 4.8 Hz, 1H), 4.42 (dd, *J* = 9.2, 6.8 Hz, 1H), 3.87 (dd, *J* = 9.2, 4.8 Hz, 1H), 3.71 (d, *J* = 2.0 Hz, 1H), 3.22 (d, *J* = 2.0 Hz, 1H), 1.89 (s, 3H), 1.72 (s, 3H); Partial ^{1}H NMR for the *cis*-isomer: δ 5.20 (dd, *J* = 6.8, 4.8 Hz, 1H), 3.68 (d, *J* = 4.8 Hz, 1H), 2.85 (d, *J* = 6.0 Hz, 1H), 1.58 (s, 3H), 1.47 (s, 3H).

*4.4.6. trans-3-(3-Nitrophenyl)-oxirane-2-carbonitrile (**3f**)*[16]

Compound **3f** was separated from the corresponding *cis*-isomer **3f-cis** on silica gel chromatography.

3f: White solid (17.1 mg, 45% yield), m.p. 115-116 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29-8.24 (m, 1H), 8.18-8.15 (m, 1H), 7.68-7.59 (m, 2H), 4.44 (d, *J* = 1.6 Hz, 1H), 3.49 (d, *J* = 1.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.8, 135.2, 131.8, 130.4, 124.8, 120.9, 115.3, 57.4, 44.9.

3f-cis: White solid (17.1 mg, 45% yield), m.p. 111-112 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33-8.28 (m, 2H), 7.76 (d, *J* = 8.0 Hz, 1H), 7.66 (t, *J* = 8.0 Hz, 1H), 4.39 (d, *J* = 3.6 Hz, 1H), 3.89 (d, *J* = 3.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.5, 133.9, 132.0, 130.2, 124.8, 122.0, 114.4, 56.7, 45.2.

*4.4.7. trans-2-(3-(3-Nitrophenyl)oxiran-2-yl)benzo[d]oxazole (**3g**)*

White solid (17.4 mg, 31% yield), m.p. 145-146 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29-8.23 (m, 2H), 7.79-7.72 (m, 2H), 7.65-7.55 (m, 2H), 7.45-7.36 (m, 2H), 4.68 (d, *J* = 2.0 Hz, 1H), 4.21 (d, *J* = 2.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.3, 150.9, 148.8, 141.0, 137.5, 131.8, 130.1, 126.2, 125.2, 124.1, 121.0, 120.6, 111.1, 58.8, 55.3; HRMS (ESI) calcd for $C_{15}H_{10}N_2O_4Na^+$ $(M + Na)^+$ 305.0531, found 305.0533.

*4.4.8. Ethyl trans-3-phenyloxirane-2-carboxylate (**3h**)*[17]

Colorless oil (26.5 mg, 31% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40-7.33 (m, 3H), 7.34-7.27 (m, 2H), 4.35-4.21 (m,

2H), 4.09 (d, *J* = 2.0 Hz, 1H), 3.51 (d, *J* = 2.0 Hz, 1H), 1.33 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.3, 135.1, 129.1, 128.8, 125.9, 61.9, 58.0, 56.9, 14.2.

*4.4.9. Ethyl trans-3-(4-chlorophenyl)oxirane-2-carboxylate (**3i**)*[17]

Colorless oil (33.6 mg, 74% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (d, *J* = 8.8 Hz, 2H), 7.23 (d, *J* = 8.8 Hz, 2H), 4.36-4.21 (m, 2H), 4.07 (d, *J* = 1.6 Hz, 1H), 3.46 (d, *J* = 1.6 Hz, 1H), 1.33 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.1, 135.0, 133.7, 129.1, 127.3, 62.1, 57.4, 56.9, 14.3.

*4.4.10. Ethyl trans-3-(4-bromophenyl)oxirane-2-carboxylate (**3j**)*

Obtained as a 98:2 mixture of *trans*- and *cis*-isomers. Yellow oil (42.3 mg, 78% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (d, *J* = 8.4 Hz, 2H), 7.17 (d, *J* = 8.4 Hz, 2H), 4.36-4.21 (m, 2H), 4.05 (d, *J* = 1.6 Hz, 1H), 3.45 (d, *J* = 1.6 Hz, 1H), 1.33 (t, *J* = 7.2 Hz, 3H); Partial ^{1}H NMR for the *cis*-isomer: δ 3.81 (d, *J* = 4.4 Hz, 1H), 1.07 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.0, 134.2, 132.0, 127.6, 123.1, 62.0, 57.4, 56.9, 14.2; HRMS (ESI) calcd for $C_{11}H_{11}BrO_3Na^+$ $(M + Na)^+$ 292.9784, found 292.9787.

*4.4.11. Ethyl trans-3-(4-iodophenyl)oxirane-2-carboxylate (**3k**)*

Yellow oil (44.5 mg, 70% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, *J* = 8.4 Hz, 2H), 7.04 (d, *J* = 8.4 Hz, 2H), 4.36-4.21 (m, 2H), 4.04 (d, *J* = 1.6 Hz, 1H), 3.45 (d, *J* = 1.6 Hz, 1H), 1.33 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.0, 137.9, 134.9, 127.7, 94.8, 62.1, 57.6, 56.9, 14.3; HRMS (ESI) calcd for $C_{11}H_{11}IO_3Na$ $(M + Na)^+$ 340.9645, found 340.9648.

*4.4.12. Ethyl trans-3-(4-cyanophenyl)oxirane-2-carboxylate (**3l**)*[18]

Obtained as a 97:3 mixture of *trans*- and *cis*-isomers. Yellow oil (33.0 mg, 76% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 8.4 Hz, 2H), 7.42 (d, *J* = 8.4 Hz, 2H), 4.37-4.23 (m, 2H), 4.15 (d, *J* = 1.6 Hz, 1H), 3.47 (d, *J* = 1.6 Hz, 1H), 1.34 (t, *J* = 7.2 Hz, 3H); Partial ^{1}H NMR for the *cis*-isomer: δ 3.88 (d, *J* = 4.4 Hz, 1H), 1.05 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.5, 140.5, 132.6, 126.6, 118.5, 113.0, 62.3, 57.1, 57.0, 14.3; HRMS (ESI) calcd for $C_{12}H_{11}NO_3Na^+$ $(M + Na)^+$ 240.0631, found 240.0632.

*4.4.13. Ethyl trans-3-(4-nitrophenyl)oxirane-2-carboxylate (**3m**)*

Obtained as a 98:2 mixture of *trans*- and *cis*-isomers. White solid (32.3 mg, 68% yield), m.p. 65-66 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (d, *J* = 8.8 Hz, 2H), 7.48 (d, *J* = 8.8 Hz, 2H), 4.38-4.24 (m, 2H), 4.21 (d, *J* = 1.6 Hz, 1H), 3.49 (d, *J* = 1.6 Hz, 1H), 1.35 (t, *J* = 7.2 Hz, 3H); Partial ^{1}H NMR for the *cis*-isomer: δ 3.90 (d, *J* = 4.4 Hz, 1H), 1.05 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.4, 148.5, 142.4, 126.8, 124.1, 62.3, 57.1, 56.8, 14.3; HRMS (ESI) calcd for $C_{11}H_{11}NO_5Na^+$ $(M + Na)^+$ 260.0529, found 260.0530.

*4.4.14. Ethyl trans-3-(4-(methylsulfonyl)phenyl)oxirane-2-carboxylate (**3n**)*

Obtained as a 98:2 mixture of *trans*- and *cis*-isomers. Yellow solid (46.5 mg, 86% yield), m.p. 141-142 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 8.0 Hz, 2H), 7.52 (d, *J* = 8.0 Hz, 2H), 4.34-4.25 (m, 2H), 4.20 (s, 1H), 3.49 (s, 1H), 3.06 (s, 3H), 1.35 (t, *J* = 7.2 Hz, 3H); Partial ^{1}H NMR for the *cis*-isomer: δ 3.90 (d, *J* = 4.8 Hz, 1H), 1.06 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.5, 141.4, 141.1, 127.9, 126.9, 62.2, 57.0, 56.9, 44.6, 14.2; HRMS (ESI) calcd for $C_{12}H_{14}O_5SNa^+$ $(M + Na)^+$ 293.0454, found 293.0455.

*4.4.15. Ethyl trans-3-(2-nitrophenyl)oxirane-2-carboxylate (**3o**)*

White solid (31.3 mg, 66% yield), m.p. 64-65 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (dd, *J* = 8.4, 1.2 Hz, 1H), 7.71 (dt, *J* = 7.2, 0.8 Hz, 1H), 7.64-7.60 (m, 1H), 7.58-7.51 (m, 1H), 4.69 (d, *J* = 1.6 Hz, 1H), 4.35 (q, *J* = 7.2 Hz, 2H), 3.39 (d, *J* = 1.6 Hz, 1H), 1.36 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.7, 147.5, 134.7, 132.3, 129.5, 127.4, 125.0, 62.2, 56.3, 56.0, 14.3; HRMS (ESI) calcd for $C_{11}H_{11}NO_5Na^+$ $(M + Na)^+$ 260.0529, found 260.0529.

*4.4.16. Ethyl trans-3-(naphthalen-2-yl)oxirane-2-carboxyate (**3p**)*[17]

Obtained as a 98:2 mixture of *trans*- and *cis*-isomers. Yellow oil (35.9 mg, 74% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83-7.9 (m, 4H), 7.52-7.45 (m, 2H), 7.31 (dd, *J* = 8.4, 1.6 Hz, 1H), 4.37-4.22 (m, 2H), 4.26 (d, *J* = 1.6 Hz, 1H), 3.61 (d, *J* = 1.6 Hz, 1H), 1.33 (t, *J* = 7.2 Hz, 3H); Partial ^{1}H NMR for the *cis*-isomer: δ 3.89 (d, *J* = 4.4 Hz, 1H), 0.95 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.3, 133.7, 133.1, 132.5, 128.7, 128.0, 127.9, 126.7, 126.6, 126.1, 122.6, 61.9, 58.3, 56.9, 14.2.

*4.4.17. Ethyl trans-3-(pyridin-2-yl)oxirane-2-carboxylate (**3q**)*[19]

Obtained as a 98:2 mixture of *trans*- and *cis*-isomers. Yellow oil (26.2 mg, 68% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60 (d, *J* = 4.4 Hz, 1H), 7.72 (dt, *J* = 7.6, 1.6 Hz, 1H), 7.32-7.28 (m, 2H), 4.36-4.22 (m, 2H), 4.25 (d, *J* = 1.6 Hz, 1H), 3.72 (d, *J* = 1.6 Hz, 1H), 1.33 (t, *J* = 7.2 Hz, 3H); Partial ^{1}H NMR for the *cis*-isomer: δ 3.90 (d, *J* = 4.4 Hz, 1H), 1.09 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.0, 154.5, 149.9, 137.1, 123.9, 120.7, 62.0, 58.1, 55.8, 14.2.

*4.4.18. Ethyl trans-3-(benzo[b]thiophen-2-yl)oxirane-2-carboxylate (**3r**)*

Yellow oil (39.2 mg, 79% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81-7.77 (m, 1H), 7.75-7.71 (m, 1H), 7.41 (s, 1H), 7.34-7.30 (m, 2H), 4.41 (d, *J* = 1.2 Hz, 1H), 4.37-4.22 (m, 2H), 3.73 (d, *J* = 1.2 Hz, 1H), 1.34 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.8, 139.5, 139.4, 139.3, 125.2, 124.8, 124.3, 123.8, 122.6, 62.2, 57.3, 55.4, 14.3; HRMS (ESI) calcd for $C_{13}H_{12}SO_3Na^+$ $(M + Na)^+$ 271.0399, found 271.0399.

*4.4.19. Ethyl trans-3-(phenylethynyl)oxirane-2-carboxylate (**3s**)*

Yellow oil (28.1 mg, 65% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47-7.43 (m, 2H), 7.37-7.28 (m, 3H), 4.34-4.21 (m, 2H), 3.82 (d, *J* = 1.6 Hz, 1H), 3.70 (d, *J* = 1.6 Hz, 1H), 1.33 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.6, 132.1, 129.4, 128.5, 121.4, 84.7, 83.4, 62.2, 54.8, 45.6, 14.2; HRMS (ESI) calcd for $C_{13}H_{12}O_3Na^+$ $(M + Na)^+$ 239.0679, found 239.0679.

*4.4.20. Ethyl trans-3-phenethyloxirane-2-carboxylate (**3t**)*[17]

Obtained as an 86:14 mixture of *trans*- and *cis*-isomers. Colorless oil (34.4 mg, 78% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32-7.26 (m, 2H), 7.23-7.17 (m, 3H), 4.28-4.12 (m, 2H), 3.20 (s, 2H), 2.89-2.70 (m, 2H), 2.08-1.81 (m, 2H), 1.29 (t, *J* = 7.2 Hz, 3H); Partial ^{1}H NMR for the *cis*-isomer: δ 3.50 (d, *J* = 4.4 Hz, 1H).

*4.4.21. Ethyl trans-1-methyl-2-oxospiro[indoline-3,2'-oxirane]-3'-carboxylate (**3u**)*[20]

Yellow solid (33.6 mg, 68% yield), m.p. 107-108 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (dd, *J* = 7.6, 0.8 Hz, 1H), 7.41 (td, *J* = 8.0, 1.2 Hz, 1H), 7.07 (td, *J* = 8.0, 0.8 Hz, 1H), 6.92 (d, *J* = 8.0 Hz, 1H), 4.36-4.22 (m, 2H), 4.21 (s, 1H), 3.28 (s, 3H), 1.29 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.0, 165.8, 145.7, 131.2, 124.8, 123.2, 119.3, 109.0, 62.3, 60.2, 59.8, 26.9, 14.2.

*4.5. General procedure for synthesis of aziridine **5***

To a reaction tube equipped with a magnetic stir bar was charged with benzaldimine **4** (0.20 mmol), KF (34.9 mg, 0.60 mmol), and 18-crown-6 (159 mg, 0.60 mmol). The tube was sealed with a septum, evacuated and backfilled with nitrogen three times. Amine **1** (46.4 mg, 0.24 mmol), 2-(trimethylsilyl)phenyl triflate (89.5 mg, 0.30 mmol), and acetonitrile (1.2 mL) were added via syringe under nitrogen atmosphere. The mixture was stirred at room temperature for 24 h, and purified by silica gel chromatography, eluting with ethyl acetate/petroleum ether (1:10 v/v), to give aziridine **5**.

*4.5.1. 1-(tert-Butyl) 2-ethyl trans-3-phenylaziridine-1,2-dicarboxylate (**5a**)*[21]

Yellow oil (45.4 mg, 78% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-7.29 (m, 5H), 4.34-4.19 (m, 2H), 3.81 (d, J = 2.4 Hz, 1H), 3.09 (d, J = 2.4 Hz, 1H), 1.46 (s, 9H), 1.33 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.6, 158.5, 135.5, 128.7, 128.5, 126.6, 82.3, 62.0, 45.1, 44.2, 28.1, 14.4.

*4.5.2. 1-(tert-Butyl) 2-ethyl trans-3-(p-tolyl)aziridine-1,2-dicarboxylate (**5b**)*

Yellow oil (48.8 mg, 80% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (d, J = 8.0 Hz, 2H), 7.12 (d, J = 8.0 Hz, 2H), 4.05-3.93 (m, 2H), 3.79 (d, J = 6.8 Hz, 1H), 3.39 (d, J = 6.8 Hz, 1H), 2.32 (s, 3H), 1.48 (s, 9H), 0.99 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4, 160.8, 138.0, 130.2, 128.9, 127.6, 82.5, 61.3, 44.6, 42.8, 28.0, 21.3, 14.0; HRMS (ESI) calcd for $C_{17}H_{23}NO_4Na^+$ $(M + Na)^+$ 328.1519, found 328.1519.

*4.5.3. 1-(tert-Butyl) 2-ethyl trans-3-(4-chlorophenyl)aziridine-1,2-dicarboxylate (**5c**)*

Yellow oil (39.1 mg, 60% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (d, J = 8.4 Hz, 2H), 7.25 (d, J = 8.4 Hz, 2H), 4.36-4.17 (m, 2H), 3.78 (d, J = 2.4 Hz, 1H), 3.03 (d, J = 2.4 Hz, 1H), 1.47 (s, 9H), 1.33 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.4, 158.3, 134.3, 134.2, 128.9, 128.0, 82.5, 62.2, 44.4, 44.3, 28.1, 14.3; HRMS (ESI) calcd for $C_{16}H_{20}ClNO_4Na^+$ $(M + Na)^+$ 348.0973, found 348.0975.

*4.5.4. 1-(tert-Butyl) 2-ethyl trans-3-(4-nitrophenyl)aziridine-1,2-dicarboxylate (**5d**)*

Yellow oil (44.4 mg, 66% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (d, J = 8.4 Hz, 2H), 7.50 (d, J = 8.4 Hz, 2H), 4.37-4.19 (m, 2H), 3.90 (d, J = 2.0 Hz, 1H), 3.06 (d, J = 2.0 Hz, 1H), 1.49 (s, 9H), 1.34 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.9, 157.9, 148.0, 143.0, 127.5, 124.0, 82.9, 62.4, 44.8, 43.8, 28.0, 14.3; HRMS (ESI) calcd for $C_{16}H_{20}N_2O_6Na^+$ $(M + Na)^+$ 359.1213, found 359.1214.

*4.5.5. 1-(tert-Butyl) 2-ethyl trans-3-(naphthalen-2-yl)aziridine-1,2-dicarboxylate (**5e**)*

Yellow oil (27.3 mg, 40% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83-7.79 (m, 4H), 7.49-7.45 (m, 2H), 7.39-7.35 (m, 1H), 4.36-4.21 (m, 2H), 3.98 (d, J = 2.0 Hz, 1H), 3.17 (d, J = 2.0 Hz, 1H), 1.48 (s, 9H), 1.34 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.6, 158.5, 133.4, 133.2, 133.0, 128.5, 128.0, 127.9, 126.6, 126.4, 126.2, 123.8, 82.4, 62.1, 45.3, 44.4, 28.1, 14.4; HRMS (ESI) calcd for $C_{20}H_{23}NO_4Na^+$ $(M + Na)^+$ 364.1519, found 364.1515.

*4.6. General procedure for synthesis of cyclopropane **7***

To a mixture of amine **1** (46.4 mg, 0.24 mmol), KF (34.9 mg, 0.60 mmol), and 18-crown-6 (159 mg, 0.60 mmol) in dichloromethane (1.2 mL) was added 2-(trimethylsilyl)aryl triflate (89.5 mg, 0.30 mmol) and vinyl ketone **6** (0.20 mmol). The mixture was stirred at room temperature for 4 h, and concentrated under reduced pressure. The residue was purified by silica gel chromatography, eluting with ethyl acetate/petroleum ether (1:10 v/v), to give cyclopropane **7**.

*4.6.1. Ethyl trans-2-benzoylcyclopropane-1-carboxylate (**7a**)*[22]

Colorless oil (42.8 mg, 98% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04-7.99 (m, 2H), 7.62-7.55 (m, 1H), 7.50-7.45 (m, 2H), 4.18 (q, J = 7.2 Hz, 2H), 3.19 (ddd, J = 8.4, 5.6, 3.6 Hz, 1H), 2.38 (ddd, J = 8.4, 5.6, 3.6 Hz, 1H), 1.66-1.56 (m, 2H), 1.29 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.1, 172.4, 137.1, 133.4, 128.7, 128.4, 61.2, 26.0, 24.7, 17.9, 14.3; HRMS (ESI) calcd for $C_{13}H_{14}O_3Na^+$ $(M + Na)^+$ 241.0835, found 241.0834.

*4.6.2. Ethyl trans-2-(4-methoxybenzoyl)cyclopropane-1-carboxylate (**7b**)*

Colorless oil (42.2 mg, 85% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, J = 9.2 Hz, 2H), 6.96 (d, J = 9.2 Hz, 2H), 4.18 (q, J = 7.2 Hz, 2H), 3.88 (s, 3H), 3.14 (ddd, J = 8.8, 6.0, 4.0 Hz, 1H), 2.35 (ddd, J = 8.8, 6.0, 4.0 Hz, 1H), 1.63-1.52 (m, 2H), 1.29 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.5, 172.7, 163.9, 130.7, 130.2, 113.9, 61.2, 55.7, 25.8, 24.5, 17.8, 14.3; HRMS (ESI) calcd for $C_{14}H_{16}O_4Na^+$ $(M + Na)^+$ 271.0941, found 271.0941.

*4.6.3. Ethyl trans-2-(4-chlorobenzoyl)cyclopropane1-1-carboxylate (**7c**)*

Colorless oil (43.0 mg, 85% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, J = 8.4 Hz, 2H), 7.47 (d, J = 8.4 Hz, 2H), 4.19 (q, J = 7.2 Hz, 2H), 3.13 (ddd, J = 9.2, 5.6, 3.6 Hz, 1H), 2.39 (ddd, J = 9.2, 5.6, 3.6 Hz, 1H), 1.65-1.56 (m, 2H), 1.29 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.0, 172.3, 140.0, 135.4, 129.8, 129.1, 61.4, 26.0, 24.9, 18.2, 14.3; HRMS (ESI) calcd for $C_{13}H_{13}O_3ClNa^+$ $(M + Na)^+$ 275.0447, found 275.0445.

*4.6.4. Ethyl trans-2-(2-naphthoyl)cyclopropane-1-carboxylate (**7d**)*[22]

Colorless oil (51.0 mg, 95% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58 (s, 1H), 8.05 (dd, J = 8.4, 1.6 Hz, 1H), 7.99 (d, J = 8.0 Hz, 1H), 7.93-7.86 (m, 2H), 7.64-7.53 (m, 2H), 4.21 (q, J = 7.2 Hz, 2H), 3.36 (ddd, J = 8.4, 5.6, 3.6 Hz, 1H), 2.45 (ddd, J = 8.4, 5.6, 3.6 Hz, 1H), 1.70-1.62 (m, 2H), 1.31 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.0, 172.6, 135.8, 134.5, 132.6, 130.4, 129. 8, 128.8, 128.7, 127.9, 127.0, 124.0, 61.3, 26.2, 24.8, 18.2, 14.3.

*4.6.5. Ethyl trans-2-(furan-2-carbonyl)cyclopropane-1-carboxylate (**7e**)*

Colorless oil (25.0 mg, 60% yield) as a colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (dd, J = 1.6, 0.8 Hz, 1H), 7.29 (dd, J = 3.6, 0.8 Hz, 1H), 6.58 (dd, J = 3.6, 1.6 Hz, 1H), 4.18 (q, J = 7.2 Hz, 2H), 3.08 (ddd, J = 8.4, 6.4, 3.6 Hz, 1H), 2.36 (ddd, J = 8.4, 6.4, 3.6 Hz, 1H), 1.63-1.53 (m, 2H), 1.29 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 185.7, 172.3, 152.8, 147.1, 118.0, 112.6, 61.3, 26.2, 24.5, 17.5, 14.3; HRMS (ESI) calcd for $C_{11}H_{12}O_4Na^+$ $(M + Na)^+$ 231.0628, found 231.0627.

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Supplementary Material

Copies of ^{1}H NMR and ^{13}C NMR spectra and HPLC traces.

References and notes

[1]. For reviews, see: (a) H. N. C. Wong, M.-Y. Hon, C.-W. Tse, Y.-C. Yip, Chem. Rev. 89 (1989) 165−198;
(b) D. Tanner, Angew. Chem. Int. Ed. 33 (1994) 599−619;
(c) C. Lauret, Tetrahedron: Asymmetry 12 (2001) 2359–2383;
(d) J. B. Sweeney, Chem. Soc. Rev. 31 (2002) 247–258;
(e) C. Schneider, Synthesis (2006) 3919–3944;
(f) G. S. Singh, M. D'hooghe, N. De Kimpe, Chem. Rev. 107 (2007) 2080−2135;
(g) Y. Zhu, Q. Wang, R. G. Cornwall, Y. Shi, Chem. Rev. 114 (2014) 8199−8256;
(h) S. Meninno, A. Lattanzi, Catal. Today. 285 (2017) 39–48.

[2]. For a review, see: T. Rosen, in Comprehensive Organic Synthesis, Vol. 2 (Eds.: B. M. Trost, I. Fleming), Pergamon, New York, 1991, pp. 409–441.

[3]. For reviews, see: (a) V. K. Aggarwal, J. Richardson, Chem Commun. (2003) 2644–2651;
(b) V. K. Aggarwal, C. L. Winn, Acc. Chem. Res. 37 (2004) 611−620;
(c) E. M. McGarrigle, E. L. Myers, O. Illa, M. A. Shaw, S. L. Riches, V. K. Aggarwal, Chem. Rev. 107 (2007) 5841−5883;
(d) L.-Q. Lu, T.-R. Li, Q. Wang, W.-J. Xiao, Chem. Soc. Rev. 46 (2017) 4135−4145.

[4]. (a) S. S. Bhattacharjee, H. Ila, H. Junjappa, Synthesis (1982) 301–303;
(b) A. Jończyk, A. Konarska, Synlett (1999) 1085–1087;
(c) C. D. Papageorgiou, S. V. Ley, M. J. Gaunt, Angew. Chem. Int. Ed. 42 (2003) 828−831;
(d) V. K. Aggarwal, J. N. Harvey, R. Robiette, Angew. Chem. Int. Ed. 44 (2005) 5468−5471;
(e) A. Kowalkowska, D. Suchołbiak, A. Jończyk, Eur. J. Org. Chem. (2005) 925–933;
(f) T. Kimachi, H. Kinoshita, K. Kusaka, Y. Takeuchi, M. Aoe, M. Ju-ichi, Synlett (2005) 842−844;
(g) R. Robiette, M. Conza, V. K. Aggarwal, Org. Biomol. Chem. 4 (2006) 621–623;
(h) A. Alex, B. Larmanjat, J. Marrot, F. Couty, O. David, Chem. Commun. (2007) 2500–2502;
(i) L. D. S. Yadav, R. Kapoor, Garima, Synlett (2009) 3123–3126;
(j) H. Kinoshita, A. Ihoriya, M. Ju-ichi, T. Kimachi, Synlett (2010) 2330–2334;
(k) X. Xiao, D. Lin, S. Tong, H. Mo, Synlett (2011) 2823–2826;
(l) M. Waser, R. Herchl, N. Müller, Chem. Commun. 47 (2011) 2170–2172;
(m) R. Herchl, M. Stiftinger, M. Waser, Org. Biomol. Chem. 9 (2011) 7023–7027;
(n) S. Aichhorn, G. N. Gururaja, M. Reisinger, M. Waser, RSC Adv. 3 (2013) 4552–4557;
(o) M. Pichler, J. Novacek, R. Robiette, V. Poscher, M. Himmelsbach, U. Monkowius, N. Müller, M. Waser, Org. Biomol. Chem. 13 (2015) 2092–2099;
(p) J. Novacek, L. Roiser, K. Zielke, R. Robiette, M. Waser, Chem. Eur. J. 22 (2016) 11422–11428;
(q) L. Roiser, R. Robiette, M. Waser, Synlett 27 (2016) 1963–1968;
(r) S. P. Midya, E. Gopi, N. Satam, I. N. N. Namboothiri, Org. Biomol. Chem. 15 (2017) 3616–3627;
(s) L. Roiser, K. Zielke, M. Waser, Asian J. Org. Chem. 7 (2018) 852 – 864.

[5]. T. Roy, M. Thangaraj, R. G. Gonnade, A.T. Biju, Chem. Commun. 52 (2016) 9044−9047.

[6]. (a) A. A. Cant, G. H. V. Bertrand, J. L. Henderson, L. Roberts, M. F. Greaney, Angew. Chem. Int. Ed. 48 (2009) 5199–5202;
(b) T. Aoki, S. Koya, R. Yamasaki, S. Saito, Org. Lett. 14 (2012) 4506−4509;
(c) S. S. Bhojgude, T. Kaicharla, A. T. Biju, Org. Lett. 15 (2013) 5452−5455;
(d) D. Stephens, Y. Zhang, M. Cormier, G. Chavez, H. Arman, O. V. Larionov, Chem. Commun. 49 (2013) 6558−6560;
(e) C.-Y. Tang, G. Wang, X.-Y. Yang, X.-Y. Wu, F. Sha, Tetrahedron Lett. 55 (2014) 6447–6450;
(f) A. V. Varlamov, N. I. Guranova, T. N. Borisova, F. A. A. Toze, M. V. Ovcharov, S. Kristancho, L. G. Voskressensky, Tetrahedron 71 (2015) 1175−1181;
(g) T. Roy, D. R. Baviskar, A.T. Biju, J. Org. Chem. 80 (2015) 11131−11137;
(h) S. S. Bhojgude, D. R. Baviskar, R. G. Gonnade, A. T. Biju, Org. Lett. 17 (2015) 6270−6273;
(i) M. Hirsch, S. Dhara, C. E. Diesendruck, Org. Lett. 18 (2016) 980−983;
(j) J. Zhang, Z.-X. Chen, T. Du, B. Li, Y. Gu, S.-K. Tian, Org. Lett. 18 (2016) 4872−4875;
(k) S. S. Bhojgude, T. Roy, R. G. Gonnade, A. T. Biju, Org. Lett. 18 (2016) 5424−5427;
(l) T. Roy, M. Thangaraj, T. Kaicharla, R. V. Kamath, R. G. Gonnade, A. T. Biju, Org. Lett. 18 (2016) 5428−5431;
(m) K. Okuma, H. Kinoshita, N. Nagahora, K. Shioji, Eur. J. Org. Chem. (2016), 2264–2267;
(n) T. Roy, S. S. Bhojgude, T. Kaicharla, M. Thangaraj, B. Garai A. T. Biju, Org. Chem. Front. 3 (2016) 71–76;
(o) S. G. Moss, I. A. Pocock, J. B. Sweeney, Chem. Eur. J. 23 (2017) 101−104;
(p) Y. Gui, S.-K. Tian, Org. Lett. 19 (2017) 1554−1557;
(q) J.-Y. Guo, C.-H. Zhong, Z.-Y. He, S.-K. Tian, Asian J. Org. Chem. 7 (2018) 119–122;
(r) N. S. V. M. R. Mangina, R. Guduru, G. V. Karunakar, Org. Biomol. Chem. 16 (2018) 2134–2142;
(s) X. Pan, Z. Liu, Org. Chem. Front. 5 (2018) 1798–1810;
(t) M.-G. Zhou, R.-H. Dai, S.-K Tian, Chem. Commun. 54 (2018) 6036−6039;
(u) G. Min, J. Seo, H. M. Ko, J. Org. Chem. 83 (2018) 8417−8425.

[7]. For recent reviews on aryne chemistry, see: (a) S. S. Bhojgude, A. T. Biju, Angew. Chem. Int. Ed. 51 (2012) 1520−1522;
(b) P. M. Tadross, B. M. Stoltz, Chem. Rev. 112 (2012) 3550−3577;
(c) A. V. Dubrovskiy, N. A. Markina, R. C. Larock, Org. Biomol. Chem. 11 (2013) 191–218;
(d) S. S. Bhojgude, A. Bhunia, A. T. Biju, Acc. Chem. Res. 49 (2016) 1658−1670;
(e) J.-A. García-López, M. F. Greaney, Chem. Soc. Rev. 45 (2016) 6766−6798;
(f) J. Shi, Y. Li, Y. Li, Chem. Soc. Rev. 46 (2017) 1707−1719.

[8]. *N*-Methyl-*N*-phenylaniline was isolated as a side product in 78% yield.

[9]. The use of KF afforded epoxide **3a** in a trace amount, and the use of TBAF gave 60% yield.

[10]. The reaction gave 32% yield at room temperature, 63% yield at 50 °C, 71% yield at 70 °C, and 67% yield at 80 °C.

[11]. The yield was enhanced to 76% by increasing the amount of amine **1a** to 1.5 equivalents and that of 2-(trimethylsilyl)phenyl triflate to 2.0 equivalents.

[12]. (a) G. Grethe, H. L. Lee, M. Uskoković, A. Bross, J. Org. Chem. 33 (1968) 494−503;
(b) H. Böhme, E. Raude, Chem. Ber. 115 (1982) 2050−2056;
(c) M. D. Wang, H. Alper, J. Am. Chem. Soc. 114 (1992) 7018−7024;
(d) S. Bhattacharyya, Synth. Commun. 25 (1995) 2061−2069;
(e) I. Aviv, Z. Gross, Chem. Eur. J. 14 (2008) 3995–4005;
(f) J. Zhang, J. Jiang, Y. Li, Y. Zhao, X. Wan, Org. Lett. 15 (2013) 3222−3225;
(g) H. Shen, L. Hu, Q. Liu, M. I. Hussain, J. Pan, M. Huang, Y. Xiong, Chem. Commun. 52 (2016) 2776−2779.

[13]. (a) L. Huang, W. D. Wulff, J. Am. Chem. Soc. 133 (2011) 8892−8895;
(b) J. J. Smith, D. Best, H. W. Lam, Chem. Commun. 52 (2016) 3770−3772.

[14]. (a) D. Belmessieri, D. B. Cordes, A. M. Z. Slawin, A. D. Smith, Org. Lett. 15 (2013) 3472−3475;
(b) Y.-M. Li, S.-J. Lou, Q.-H. Zhou, L.-W. Zhu, L.-F. Zhu, L. Li, Eur. J. Org. Chem. (2015) 3044–3047;
(c) G. Pandey, J. Vaitla, Org. Lett. 17 (2015) 4890−4893.

[15]. C. K. Prier, D. W. C. MacMillan, Chem. Sci.5 (2014) 4173–4178.

[16]. C. Annese, L. D'Accolti, A. Dinoi, C. Fusco, R.Gandolfi, R. Curci, J. Am. Chem. Soc. 130 (2008) 1197−1204.

[17]. H. Kakei, R.Tsuji, T. Ohshima, M. Shibasaki, J. Am. Chem. Soc. 127 (2005) 8962−8963.

[18]. J. Oleksyszyn, B. Boduszek, C.-M. Kam, J. C. Powers, J. Med. Chem. 37 (1994) 226−231.

[19]. B. A. Lefker, W. A. Hada, P. J. Mcgarry, Tetrahedron Lett. 35 (1994) 5205–5208.

[20]. M. Chouhan, A. Pal, R. Sharma, V. A. Nair, Tetrahedron Lett. 54 (2013) 7119–7123.

[21]. G. A. Molander, P. J. Stengel, Tetrahedron. 53 (1997) 8887−8912.

[22]. T. Piou, T. Rovis, J. Am. Chem. Soc. 136 (2014) 11292−11295.