

Synthesis of Methyl 1-Formylcyclopropanecarboxylate utilizing Ti-Claisen Condensation

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Procedure

A. Methyl 4-chloro-2-formylbutanoate (1). An oven-dried 500-mL, threenecked (24/40), round-bottomed flask equipped with a Teflon-coated magnetic stirring bar (egg-shaped, 32 mm length x 15 mm diameter), an internal thermometer, a 50-mL pressure-equalizing addition funnel fitted with a nitrogen inlet (central neck), and a second 60-mL pressure-equalizing addition funnel is charged with methyl 4-chlorobutanoate (12 mL, 13.7 g, 100 mmol, 1 equiv) (Notes 1 and 2), HCO₂Me (18 mL, 18 g, 300 mmol, 3 equiv) (Note 3), and CH₂Cl₂ (100 mL) (Notes 4 and 5) (Figure 1). The stirred solution is immersed in an ice bath, cooling the internal temperature to 0 °C, and TiCl₄ (24 mL, 41.7 g, 220 mmol, 2.2 equiv) is added dropwise through a 60-mL dropping funnel (Figure 1, right side) (Notes 6 and 7) over a period of 20 min, while maintaining the internal temperature at 5–10 °C (Note 8).

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Figure 1. Reaction Set-up for Step A

Triethylamine (36 mL, 26.3 g, 260 mmol, 2.6 equiv) (Note 9) is then added dropwise to the vigorously stirred yellow reaction mixture over a period of 30 min using the 50-mL addition funnel in the center neck of the flask, while maintaining the internal temperature at 15 °C or lower (Note 10) (Figure 2). After complete addition, the dark orange reaction is stirred (500 rpm) at 0 °C for 1 h (Note 11), then quenched dropwise with water (100 mL) over a period of 10 min to maintain the internal temperature at 10 °C or lower (Note 12). The biphasic mixture is then transferred to a 500mL round-bottomed flask and the initial reaction flask is rinsed with EtOAc (2 x 10 mL). The solution is concentrated using a rotary evaporator (22 °C, 46 mmHg). The mixture is then transferred to a 500-mL separatory funnel with EtOAc (50 mL), and the aqueous phase is separated and re-extracted with EtOAc (50 mL). The combined organic phase is washed with water

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(100 mL) and brine (50 mL), dried over Na₂SO₄ (20 g), filtered through a 150mL medium porosity sintered glass funnel and concentrated using a rotary evaporator (45 °C, 25 mmHg) to furnish α -formyl ester 1 as a yellow liquid (16.39 g), which is used for the next step without any purification (Notes 13 and 14).



Figure 2. Color Transitions Observed in Step A after TiCl₄ addition after Et₃N addition after quench with H₂O

B. Methyl 1-formylcyclopropanecarboxylate [2] (*Note 15*). An oven-dried 250-mL, three-necked (24/40), round-bottomed flask equipped with a Teflon-coated magnetic stirring bar (egg-shaped, 26 mm length x 13 mm diameter), an internal thermometer, a glass stopper (central neck), and a Dryrite drying tube (Note 16) (Figure 3) is charged with crude α-formyl ester **1** (16.39 g) in AcOEt (100 mL). The light orange solution is stirred and immersed in an ice bath, cooling the internal temperature to 0 °C, and then potassium carbonate (K₂CO₃) (13.9 g, 100 mmol, 1 equiv) (Note 17) is added portionwise (split into five equal parts) over 10 min after temporarily removing the glass stopper (Note 18). Immediately after the addition is complete, triethylamine (1.4 mL, 1.00 g, 10.0 mmol, 0.1 equiv) is added in one portion.

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Figure 3. Reaction Set-up for Step B

After stirring (600 rpm) the suspension at 0 °C for 1 h, the reaction is quenched with water (100 mL) and transferred to a 500-mL separatory funnel. The initial reaction flask is rinsed with EtOAc (2 x 5 mL) and H₂O (2 x 5 mL), which are added to the separatory funnel. The organic phase is separated and the aqueous phase is re-extracted with EtOAc (20 mL). The combined organic phase is washed with water (20 mL) and brine (20 mL), dried over Na₂SO₄ (20 g), filtered through a 150-mL medium porosity sintered glass funnel, then concentrated under reduced pressure using a rotary evaporator (45 °C, 25 mmHg) to furnish an amber-colored liquid. The obtained crude product (ca. 12 g) is moved into a 25-mL round-bottomed flask with a Teflon-coated magnetic stir bar (Note 19) (Figure 4). Distillation while immersed in a temperature-controlled oil bath under reduced pressure (84–86 °C, 19–25 mmHg) provides the desired product **2** (8.68 g, 69% overall yield) as a colorless liquid (Notes 20, 21, and 22).

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Figure 4. Distillation Set-up and Pure Final Product

Notes

- 1. The methyl 4-chlorobutanoate, methyl formate, and dichloromethane must be added by temporary removal of one of the addition funnels followed by purging of the system with nitrogen.
- 2. The checkers used methyl 4-chlorobutyrate (98+%) from Acros Organics. The submitters used methyl 4-chlorobutanoate (GC purity >98%) purchased from Tokyo Chemical Industry Co., Ltd. and used as received.
- 3. The checkers used methyl formate (97%, pure) from Acros Organics. The submitters used methyl formate (HCO_2Me) (GC purity >95%) purchased from Tokyo Chemical Industry Co., Ltd. and used as received.

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- 4. The checkers used non-stabilized dichloromethane (20-L drum, ACS Reagent) from J. T. Baker, which was then passed through two packed columns of neutral alumina in a solvent purification system manufactured by SG Water U.S.A., LLC. The submitters used dichloromethane (CH₂Cl₂) (purity 99.5%) was purchased from Wako Pure Chemical Industries, Ltd. and used as received without any purification.
- 5. The submitters studied the use of CH_2Cl_2 and toluene as reaction solvents and noted the reaction to be homogeneous with the former, whereas the use toluene results in formation of yellow precipitate and a viscous reaction mixture. The checkers employed only CH_2Cl_2 .
- 6. The checkers used titanium (IV) chloride (sure-sealed 200 g bottle, ReagentPlus, 99.9% trace metal basis) obtained from Sigma-Aldrich. The submitters used titanium tetrachloride (TiCl₄) (99.0%, 500 g bottle) purchased from Wako Pure Chemical Industries, Ltd. and used as received.
- 7. The checkers charged the 60 mL addition funnel with TiCl₄ (from a sure-sealed bottle) using a syringe. The submitters report delivering the TiCl₄ using a 10 mL pipet, wherein the operation should be rapidly and carefully conducted to take care of white smoke evolution.
- 8. The submitters note this step to be slightly exothermic when using addition rates of 24 mL of $TiCl_4$ over 5–10 min. However, the checkers observed a steady temperature at 5-10 °C when adding 24 mL $TiCl_4$ dropwise over 20 min. A feature not noted by the submitters is the formation of yellow crystals around the tip of the addition funnel. These crystals tend to fall off with time and slowly dissolve in the dichloromethane.
- 9. The checkers purchased triethylamine (≥99.5%) from Sigma-Aldrich and distilled it from CaH₂ immediately prior to use. The submitters used triethylamine (Et₃N) (purity 99%) purchased from Wako Pure Chemical Industries, Ltd. and used it as received.
- 10. The submitters note the reaction to be considerably exothermic. The checkers found that by adding the Et₃N dropwise over 30 min (approx. 1-1.2 mL per minute) it was possible to maintain an internal temperature at 10 °C or lower without affecting the formation of the expected dark orange reaction mixture.
- 11. The checkers note that the reaction progress can be monitored by ${}^{1}\mathrm{H}\,\mathrm{NMR}.$

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- 12. The submitters caution that this quench is exothermic. The checkers found that adding the water dropwise over 10 min was sufficient to maintain an internal temperature at 10 °C or lower, while the submitters' addition over 5 min was sufficient to maintain temperatures below 20 °C.
- 13. The checkers performed two half-scale and two full-scale reaction. The crude yields were 97% (7.94 g), 99% (8.14 g), 98% (16.13 g), and 99% (16.39 g) respectively. Analysis of the crude reaction mixture by ¹H NMR and ¹³C NMR revealed that the mixture consists of three tautomers **1a**, (*Z*)-**1b**, (*E*)-**1b** and a very small amount of by-product tentatively assigned as (*E*)-**1x**, in an approximate ratio of 36:44:16:4.
- 14. Although not necessary for step B the submitters and checkers established in parallel studies that this reaction mixture could be purified via flash chromatography through SiO₂. In the checker's hands 5 g of the crude product was purified using 25 g of silica (Silicycle Silica, Flash P60, 40-63 µm, 230-400 mesh) loaded into a 30 mm diameter column. The column was slurry packed, the sample loaded with hexane and then eluted with a gradient of EtOAc/hexanes (5% increasing by approximately 2% every 10-12 fractions). Fractions were collected (6.7 mL) at a flow rate of 0.8 mL/sec. Overall, 72 fractions were collected and product was observed at fractions 10-32. These fractions were concentrated in vacuo to furnish 2.51 g of a colorless oil, which was determined by ¹H NMR to be (Z)-1b and trace 1a. The submitters note the composition of the chromatographed material (5 g) to be a mixture of 1 (4.45 g, 85%) with cyclopropane 2 (ca. 6% based on ¹H NMR). The checkers did not observe cyclopropane 2 at this stage. Compound 1 has been found to slightly decompose on silica and distillation results in decomposition. Compound 1 gradually solidified at ambient temperature, and over a week undergoes slow tautomerization to enols (Z)-1b and (E)-1b. The checkers note the purified sample of (Z)-1b was observed to undergo slow crystallization, which upon collection and trituration (hexanes) of the resulting white solid revealed them to be (*E*)-**1b** by ¹H NMR.



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Physical and spectroscopic properties of (*Z*)-**1b**: colorless oil; ¹H NMR (400 MHz, CDCl₃) δ : 2.52 (td, *J* = 7.0, 0.7 Hz, 2H), 3.55 (t, *J* = 6.9 Hz, 2H), 3.80 (s, 3H), 7.11 (d, *J* = 12.8 Hz, 1H), 11.49 (d, *J* = 12.7 Hz, 1H); ¹³C NMR (101 MHz, CDCl₃) δ : 31.2, 44.05, 51.8, 101.1, 163.3, 172.1; IR (neat) 2957, 1721, 1672, 1612, 1446, 1397, 1350, 1328, 1281, 1222, 1189, 1166, 1124, 989, 956, 811, 740, 653, 574, 452 cm⁻¹; HRMS (+ESI) *m/z* [M + H]⁺ calcd for C₆H₉ClO₃ 165.0313, found 165.0313; Anal. Calcd for C₆H₉ClO₃: C, 43.79; H, 5.51; Cl, 21.54. Found; C, 43.56; H, 5.48; Cl, 21.28.

Those of (*E*)-**1b**: colorless crystals; mp 72–80 °C; ¹H NMR (400 MHz, CDCl₃) δ : 2.77 (t, *J* = 7.0 Hz, 2H), 3.63 (t, *J* = 6.9 Hz, 2H), 3.73 (s, 3H), 6.17 (br s, 1H), 7.77 (d, *J* = 9.0 Hz, 1H); ¹³C NMR (101 MHz, CDCl₃) δ : 27.4, 43.6, 51.7, 107.3, 155.3, 168.8; IR (neat) 3208, 1667, 1634, 1444, 1397, 1331, 1308, 1283, 1203, 1169, 1105, 746, 731 cm⁻¹.

- 15. Step B should be carried out within a week due to the sensitivity of the starting material.
- 16. The half-scale reaction utilized an oven-dried 100-mL, three-necked, round-bottomed flask equipped with a Teflon-coated magnetic stirring bar (egg-shaped, 20 mm length x 10 mm diameter), an internal thermometer, a glass stopper (central neck) and a CaCl₂ drying tube.
- 17. The checkers used potassium carbonate (anhydrous, 99%) from Alfa Aesar.
- 18. The submitters note this to be a slightly exothermic reaction. The checkers did not observe a rise in temperature when adding the potassium carbonate in five equal portions over 10 min. However, the quench with water after reaction completion is observed to be exothermic, but the temperature can be maintained at 5–10 °C if the water is added over 5 min. Reaction progress monitoring in step B is possible by TLC using KMnO₄ staining [10% AcOEt in hexanes; R_f = 0.23 (1) and 0.33 (2)] or by ¹H NMR comparison of aliquots.
- 19. Full-scale utilized a 25-mL round-bottomed flask equipped with a magnetic stirring bar (egg-shaped, 18 mm length x 10 mm diameter) with a short path distillation apparatus (110 mm height x 110 mm width). Half scale employed a 10-mL round-bottomed flask and a magnetic stirring bar (rod shaped, 10 mm length x 3 mm diameter). The receiving flask is cooled to 0 °C by immersion in an ice-water bath.
- 20. The submitters note: 1st fraction: 42–62 °C / 20 mmHg (bath temp. 82–87 °C), 0.24 g. 2nd fraction: 62–64 °C / 17 mmHg (bath temp. 87–111 °C), 8.82 g (overall yield, 69% in 2 steps). 3rd fraction: 64–52 (fade out) °C / 17 mmHg (bath temp. 111–123 °C), 0.17 g. The

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submitters also noted the bp to be 59–63 °C / 16 mmHg and the purity based on quantitative ¹H NMR analysis was 97-99%. The checkers performed a fractional distillation collecting distillate boiling at 84–86 °C / 25 mmHg (bath temp. 104–124 °C). The checkers note: 1st fraction (135 mg, boiling temp. 84–86 °C / 25 mmHg, bath temp. 100–104 °C). 2nd fraction (8.68 g, boiling temp. 84–86 °C / 25 mmHg, bath temp. 104–124 °C). The collection of the 2nd fraction was not stopped until the internal temperature dropped.

- 21. The checkers performed two half-scale and two full-scale reactions. The yields after distillation were 73% (4.70 g), 68% (4.33 g), 77% (9.82 g), and 69% (8.68 g) respectively.
- 22. Physical and spectroscopic properties of **2**: colorless liquid; ¹H NMR (400 MHz, CDCl₃) δ : 1.58–1.62 (m, 2H), 1.64–1.68 (m, 2H), 3.80 (s, 3H), 10.37 (s, 1H); ¹³C NMR (101 MHz, CDCl₃) δ : 22.5, 33.4, 52.3, 171.4, 198.6; IR (neat) 2958, 2868, 1700, 1440, 1319, 1285, 1196, 1147, 1085, 1047, 1002, 959, 888, 810, 781, 742, 698, 474 cm⁻¹; HRMS (+ESI) *m*/*z* [M + H]⁺ calcd for C₆H₉O₃ 129.0546, found 129.0543; quantitative ¹H NMR analysis was performed with ethylene carbonate (purchased from TCI, purity >99.0%) as the internal standard and obtained in 97.6% purity.

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Discussion

Methyl or ethyl 1-formylcyclopropanecarboxylate (2) or (2') is a unique bifunctional compound with both aldehyde and ester functionalities at the same C-1 position in a simple cyclopropane molecule. Cyclopropane 2 or 2', therefore, serves as a useful synthetic building block, especially for medicinal and process chemistry, and natural product synthesis. As illustrated in Figure 5, characteristic cyclopropane segments are installed in various pharmaceuticals utilizing 2 or 2'. The key feature is the chemoselective condensation of the aldehyde group in preference to the ester group.

(i) A traditional barbituric acid analog I containing a 5spirocyclopropane moiety for a dihydroorotate dehydrogenase inhibitor,² (ii) arylpyrazole compound II containing cyclopropanecarboxamide for a parasiticidal agent,³ arylsulfonylpiperazine (iii) Ш containingcyclopropanecarboxamide for 11β-hydroxysteroid а dehydrogenase inhibitor,4 (iv) 5,7,8,9-tetrahydropyrimido[4,5b][1,4]diazepin-6-ones compound IV containing 3-spirocyclopropane moiety for a protein kinase inhibitor,⁵ (v) oxo-substituted aza-heterocylic compound V containing cyclopropane-carboxylic acid for the treatment and/or prevention of cardiovascular conditions,⁶ (vi) oxazolo[5,4b]pyridine-5-yl compound VI containing cyclopropanecarboxylate

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Figure 5. Pharmaceuticals incorporating cyclopropanecarboxylic acid or ester segments utilizing methyl or ethyl 1-formylcyclopropanecarboxylate (2) or (2')

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for the treatment of cancer,⁷ (vii) 2,6-disubstituted benzobisoxazole compound VII containing cyclopropanecarboxylic acid for lysophosphatidic acid receptor antagonists,⁸ (viii) [1,2,4]triazolopyridine compound VIII containing cyclopropanecarboxylate for phosphodiestererase inhibitors,⁹ and (ix) 3-pyridyl-substituted benzamide compound IX containing 1-(difluoromethyl)cyclopropane for purinergic 2X₇ (P2X₇) receptor inhibitors.¹⁰

As described above, **2** or **2'** has a significant role in the structural scaffolds of a variety of pharmaceuticals possessing cyclopropanecarboxylic acid derivatives. Noteworthy is that application of this manipulation has increased as a screening technique to discover new pharmaceuticals, likely because cyclopropanes are requisite isosteres for the corresponding dimethyl compounds.

On the other hand, cyclopropane **2** contributed as the starting compound to a formal synthesis of aspidospermine, a distinctive aspidosperma alkaloid,^{11,12} in that a notable acid-catalyzed thermal rearrangement of cyclopropyl imine intermediate to 2-pyrroline is the key starting step (Scheme 1).¹³



Scheme 1. Formal synthesis of aspidospermine alkaloid starting from ethyl 1-formylcyclopropanecarboxylate (2')

On the whole, the reported synthetic methods for **2** or **2**' are categorized into four approaches.

(i) As illustrated in Scheme 2, Ayers' half reduction protocol of methyl and ethyl cyclopropanedicarboxylates (**3** and **3'**) is the most representative.¹⁴ Commercially available **3** and **3'** (ca. twice as expensive as methyl 4-

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chlorobutanoate) were converted by the treatment with more than 2.0 equiv of Li(*t*BuO)₃AlH, not to the desired aldehyde **2** and **2'** directly, but to alcohols **4** and **4'** in 88% and 79% yield, respectively.^{4,6,9} Dess-Martin (DM) oxidation of **4** or **4'** using ca. 2 equiv of DM periodinane successfully afforded **2** (24%) or **2'** (76%). The DIBAL reduction method with **3** was also applied, but required harsh conditions such as –78 °C and 7 h.⁵

Although this approach is likely the most accessible, $Li(tBuO)_3AlH$ is quite expensive (ca. \$ 150 / 100 mL, 1.0 M) among commercially available hydride reagents and is not hydride atom-economical.

(ii) As an alternative method to (i),⁷ **3** was converted by a halfhydrolysis reaction to monocarboxylic acid **5**, which was transformed to **2** through mixed anhydride formation and successive NaBH₄ reduction to give common intermediate **4**. TEMPO oxidation of **4** with trichloroisocyanuric acid afforded the desired product **2**, although an accurate yield was not described. This approach, however, is not straightforward and requires tedious procedures.

(iii) As depicted in Scheme 3, this approach utilizes the notable protocol of A. I. Meyer's group.^{15,16} Ethyl cyanoacetate was converted to ethyl 1-cyanocyclopropanecarboxylate **6** (commercially available in 5-g scale, but extremely expensive), which is transformed to masked aldehyde **8** through 1,3-dioxadine formation and successive NaBH₄ reduction. Finally, acid hydrolysis of **8** gave the desired compound **2'**. This method also requires four steps with high (80 °C) and low (40 °C) temperature reactions, the use of large amounts of conc. H₂SO₄, and steam distillation purification.

(iv) Scheme 4 depicts a method starting from γ -butyrolactone developed by Kuraray's group,¹⁷ which is the most relevant for our strategy. γ -Butyrolactone was α -formylated using HCO₂Me/NaH and protected with an ethoxycarbonyl group to give **9**. Conventional ring opening with chlorination using SOCl₂ and ZnCl₂ in EtOH gave precursor **10**. Finally, cyclopropanation concomitant with deprotection was performed to afford **2'**. This approach required a protective and deprotective sequence and afforded a moderate total yield (26%).

Due to the utility of **2** or **2'**, 5-100 g scale production methods have been disclosed in recent medicinal chemistry patents. The reported synthetic methods for **2** or **2'**, however, require column chromatographic purification despite the high volatility, or crude product is used in the next condensation step without purification. Our concise and straightforward method involves purification by simple distillation (the boiling point was

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documented for the first time) without the use of column chromatography, and is performed within short reaction and purification periods.



Scheme 2. Half-reduction method of cyclopropane precursor 3 or 3' derived from dimethyl malonate



Scheme 3. A. I. Meyers' transformation method starting from ethyl cyanoacetate

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Scheme 4. Kuraray group's method starting from γ-butyrolactone

Among the various carbon homologation methods, α -formylation of simple esters with HCO₂Me is a well-recognized useful reaction. A literature survey (SciFinder[®]) revealed reports of ca. 100 examples utilizing base reagent (e.g. NaOR, NaH, LDA, and LiHMDS)-mediated methods and 5 examples using TiCl₄/amine-mediated methods. In general, a major conventional reaction using bases (e.g. NaOR, NaH) requires long reaction periods and results in moderate yield in almost all cases. LDA- and LiHMDS-promoted methods are superb with regard to yield but require rigorous procedures (reaction time schedule and accurate reagent equivalents) and low temperature (–78 °C).

α-Formylation of simple esters utilizing TiCl₄/amine-mediated (Ti-Claisen) condensation^{18,19} for the synthesis of α-formylated esters **11** is depicted in Table 1 (13 examples). Titanium (Ti) (*or* Zr)-self-Claisen condensations between two of the same esters,²⁰⁻²² Ti-crossed-Claisen condensations between esters or acids with acid chlorides,^{23,24} and Ti-Dieckmann (intramolecular Claisen) condensations²⁵⁻²⁷ have several advantages, including: (i) powerful C-C bond forming reactivity; (ii) highly available reagents with robust reactions; (iii) accessible temperature (0 °C to ambient); (iv) compatibility with base-labile functional groups such as γ-halogeno, γ-ketone carbonyl, etc., despite the high reactivity. On the other hand, a mild variant Ti-Claisen condensation method using ketene silyl accetals with acid chlorides also satisfies the four listed features [(i)-(iv)].²⁸

The present α -formylation reaction of methyl 4-chlorobutanoate (1) is a distinctive example of the compatibility with a base-sensitive γ -chloro group. Synthesis of **2** is not possible using the base-mediated α -formylation method due to undesirable and predominant cyclopropane formation leading to methyl cyclopropanecarboxylate.

In conclusion, the present straightforward and robust synthetic strategy for the unique, but useful, building block **2** utilizing Ti-Claisen condensation provides a new promising avenue, especially for pharmaceutical syntheses.

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Appendix Chemical Abstracts Nomenclature (Registry Number)

Methyl 4-chlorobutanoate (3153-37-5) Methyl formate (HCO₂Me) (107-31-3) Titanium tetrachloride (TiCl₄) (7550-45-0) Triethylamine (Et₃N) (121-44-8) Potassium carbonate (K₂CO₃) (584-08-7)



Yuichiro Ashida was born in Fukuchiyama, Kyoto, Japan, in 1989. He received his B. S. degree (2012), and M. S. degree (2014) from Kwansei Gakuin University under the direction Presently, he is of Professor Yoo Tanabe. studies on the engaged in his doctoral development of (E)-, (Z)-stereocomplementary parallel synthesis of multi-substituted $\alpha_{,\beta}$ unsaturated esters utilizing (E)-, (Z)stereodefined enol tosylates and phosphonates, which is directed for process chemistry.

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Satomi Kajimoto was born in Hyogo, Japan, in 1991. She received her B. S. degree (2014) from Kwansei Gakuin University under the supervision of Prof. Yoo Tanabe. Her graduate research focuses on the practical preparation of α -formyl esters from simple esters and methyl formate utilizing Ti-Claisen condensation and its utilization towards useful synthetic building blocks.



Hidefumi Nakatsuji received his B. S. degree (2005) and his Ph. D. degree (2010) from Kwansei Gakuin University under the direction of Professor Yoo Tanabe. Immediately, Dr. Nakatsuji moved to Nagoya University (Professor Kazuaki Ishihara's group) and studied as JSPS Postdoctoral Fellowship and CREST project researcher until 2014. Next, he was promoted to Associate Professor of Yoo Tanabe's group. His research interests are the development of chiral phosphine and phosphine oxide organocatalysts for a MCR type cyclization and of condensation reactions for cost-effective reactions directed for process chemistry.



Yoo Tanabe received his bachelor's degree at Tokyo in the laboratory of Professor Kenji Mori. He received his Ph.D. at Tokyo Inst. Technology under the direction of Professor Teruaki Mukaiyama on the development of practical acylation reactions. After leaving Sumitomo Chemical Co. Ltd, Dr. Tanabe moved to Kwansei Gakuin University in 1991 as Associate Professor and promoted to full Professor in 1997. His research focuses on the exploitation of useful synthetic reactions directed for process chemistry: concise synthesis of useful fine chemicals and of total synthesis of biologically active natural products.

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Bryon K. Anderson obtained his B.S. in Chemistry at Montana State University, Bozeman in 2010. He subsequently obtained his Ph.D. at Montana State University in Organic Chemistry under the direction of Professor Tom Livinghouse in 2015 on the synthesis of the enantiopure tetracyclic cores of asparagamine A and stemofoline alkaloids. He is currently a postdoctoral research associate in the laboratory of Professor John L. Wood at Baylor University.



Yu-Wen Huang was born in Hsinchu, Taiwan (R.O.C.) in 1982. He received his bachelor's degree from National Cheng Kung University in 2005. He then joined M.S. program at National Tsing Hua University, whereas he obtained his master degree under the supervision of Professor Shang-Cheng Hung in carbohydrate synthesis. In 2016, he received his Ph.D. degree at University of Rochester advised by Professor Alison J. Frontier on 1,6-conjugate addition initiated Nazarov reaction and a sequential 1,5-hydride transfer chemistry. He is currently a post-doctoral fellow in CPRIT lab (Baylor University) with Professor Ke Kong and John L. Wood.

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