HETEROCYCLES, Vol. 100, No. 1, 2020, pp. 12 - 23. © 2020 The Japan Institute of Heterocyclic Chemistry
Received, 30th June, 2019, Accepted, 2nd September, 2019, Published online, 24th September, 2019
DOI: 10.3987/COM-19-14124

ALTERNATIVE CHIRAL PREPARATIONS OF A SWAMINATHAN KETONE *VIA* ASYMMETRIC ALDOL REACTIONS MEDIATED BY CHIRAL AMINES BEARING A PYRROLIDINE

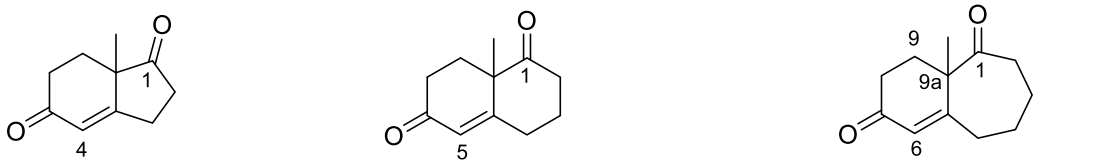
Yuichi Akahane, Arisa Miura, and Kohei Inomata*

Department of Pharmacy, Tohoku Medical and Pharmaceutical University, 4-4-1 Komatsushima, Aoba-ku, Sendai 981-8558, Japan, E-mail: inomata@tohoku-mpu.ac.jp

This paper is dedicated to the anniversary of achieving Volume 100 of HETEROCYCLES.

Abstract – We established a novel chiral route to provide a Swaminathan ketone (**3**) bearing a 7-membered ring *via* intramolecular aldol reaction of trione (**7**) mediated by chiral pyrrodinylmethylamine derivatives. Despite the moderate enantioselectivity of **3**, we succeeded in increasing optical purities by using a lipase-mediated asymmetric esterification of an alcohol (**16**) at a later synthetic stage. The absolute configuration was determined by Mosher's ester method, and relations between absolute configurations and optical rotations of **3** were clarified.

Hajos-Parrish (**1**) and Wieland-Miescher (**2**) ketones, which include carbobicyclic enediones, are highly useful synthons in the total synthesis of many natural products and pharmaceutically important compounds (Figure 1).[1-5]

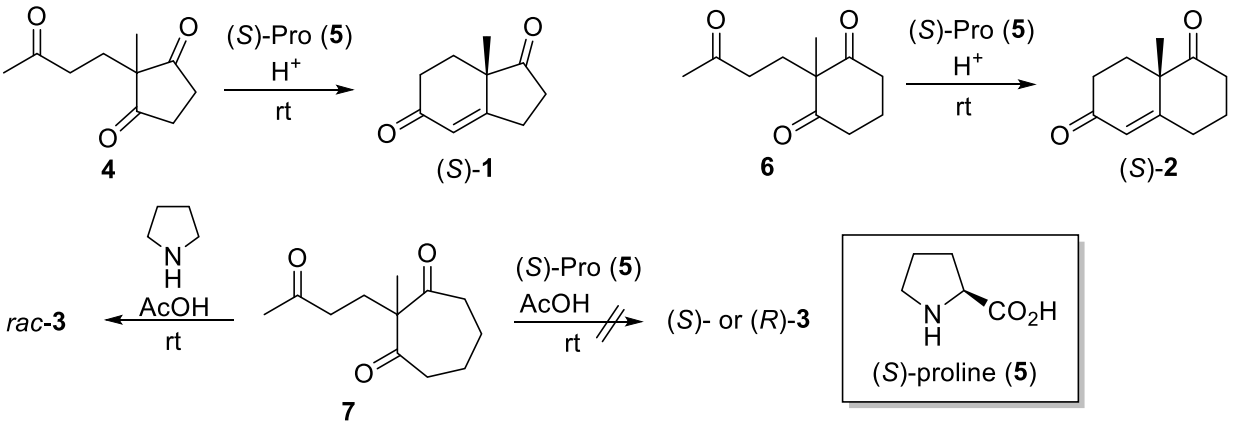


1: (Hajos-Parrish ketone) **2**: (Wieland-Miescher ketone) **3**: (Swaminathan ketone)

Figure 1

These useful enediones can be easily prepared by proline-mediated asymmetric intramolecular aldol reactions.[6] This asymmetric aldol reaction was first reported by Hajos *et al.* and is widely recognized to involve an enamine-based mechanism.[7-9] However, few reports regarding the preparation of **3** bearing a

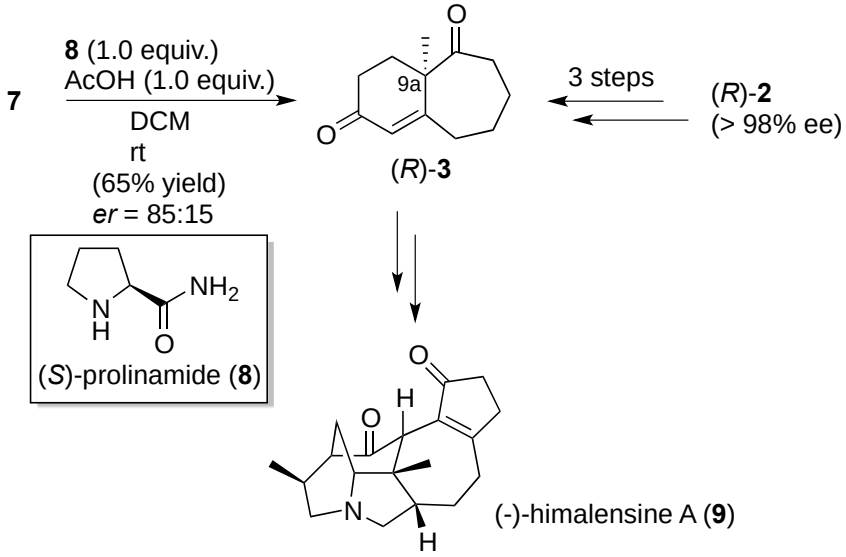
7-membered ring have been published.[10-12] Since many pharmaceutically important natural products containing 7-membered carbocycles have been published,[13] enedione (**3**) is an attractive potential chiral synthon to be used to achive total synthesis of these important products. The pioneering studies for obtaining **3** were reported by Swaminathan *et al.*,[10] synthesizing **3** as a racemic material *via* a pyrrolidine-mediated aldol reaction of trione (**7**) in the presence of acetic acid (AcOH). The authors also reported that similar reactions mediated by (*S*)-proline (**5**) did not yield the expected optically active **3** (Scheme 1).[10b]



Scheme 1

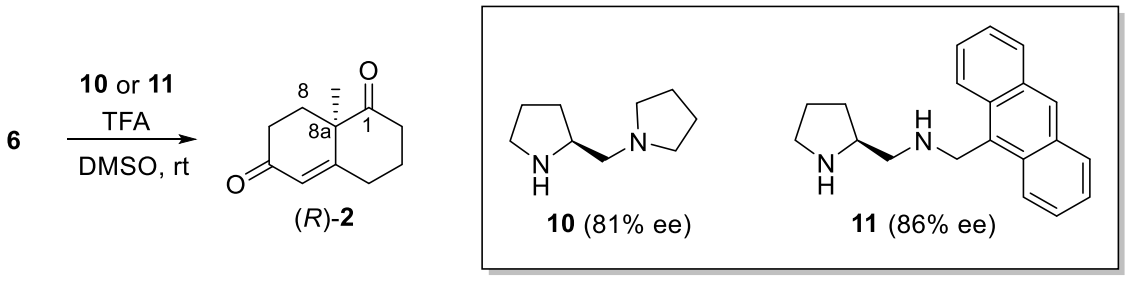
Uwai *et al*. first reported the lipase-mediated aldol reactions of **7** to afford (*S*)-(+)-**3** with a low enantioselectivity (8% ee) and retention times for both enantiomers of **3** on an HPLC instrument equipped with a chiral stationary phase column (Chiralcel OB). However, the authors did not provide any evidence for the determination of an absolute configuration of **3**.[12a] Although Pericàs *et al*. reported catalytic asymmetric aldol reactions of **7** mediated by a polymer-supported chiral amine, affording (*R*)-**3** with 53% ee, they did not discuss the details of its absolute configuration and optical rotation.[12b] Recently, Xu *et al*. reported the practical chiral preparation of (*R*)-**3** (70% ee) using aldol reactions of **7** mediated by (*S*)-prolinamide (**8**), elegantly achieving the total synthesis of (−)-himalensine A (**9**) starting from (*R*)-**3**.[12c] The authors determined an absolute configuration from single crystal X-ray analysis of (*R*)-**3** which was alternatively derived from commercially available (*R*)-**2** (> 98% ee). In their total synthesis, a chiral center at C-9a in (*R*)-**3** was directly reflected to natural (−)-himalensine A (**9**). This study indicated that the absolute configuration of (*R*)-**3** can be unambiguously identified (Scheme 2). However, both optical rotations and retention times of (*R*)- and (*S*)-**3** on the HPLC instrument equipped with a chiral stationary phase column have not been reported. Therefore, a method to determine the absolute configuration of **3** remains to be developed. Additionally, according to Xu's method, (*R*)-prolinamide (*ent*-**8**), which is derived from unnatural (*R*)-proline (*ent*-**5**), is necessary to form (*S*)-**3**. From these

reasons, novel and alternative chiral routes for **3** to clarify the relations among absolute configurations, optical rotations, and behaviors using HPLC of (*R*)- and (*S*)-**3** are required.



Scheme 2

We previously reported the asymmetric intramolecular aldol reaction of **6** mediated by chiral diamines (**10**) or (**11**) in the presence of trifluoroacetic acid (TFA).[1] These reactions afforded (*R*)-**2** in high yield and enantioselectivity (Scheme 3). According to this method, we attempted to use these chiral amines in the aldol reactions of **7**. Herein, we report the details of these reactions, chiral properties of (*R*)- and (*S*)-**3** including optical rotations and HPLC behaviors, and methods to increase optical purities through lipase-mediated asymmetric esterifications for **3** derived compounds.

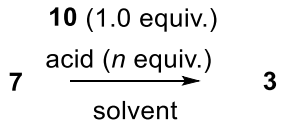


Scheme 3

First, we studied the aldol reactions of **7** mediated by a stoichiometric amount of **10**[14,15] in the presence of a Brønsted acid, and the results are summarized in Table 1. According to Xu's method,[12c] the reactions were performed in dichloromethane (DCM) at room temperature in the presence of AcOH or TFA. The reactions proceeded very slowly to afford **3** in low yields and low enantioselectivities (entries 1-4). Under

these conditions, the reactions did not proceed to completion. The reactions were then performed according to our previously developed method. A similar reaction in dimethyl sulfoxide (DMSO) at room temperature slightly improved the yield of **3** accompanied with a high enantioselectivity (entry 5). However, the reaction did not proceed to completion even after 93 h. The same reaction as entry 5 at 50 °C completed after a short time and greatly improved the yield of (*S*)-**3** with an acceptable enantioselectivity (entry 6). Details of the procedure used to determine the absolute configuration of **3** are described later (*vide infra*). The reaction conditions described in entry 6 were used for further studies.

Table 1. The aldol reaction of **7** mediated by **10**

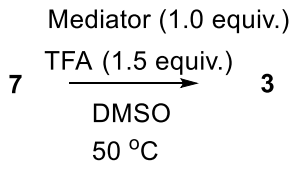


Entry[a]	Solvent	Acid (equiv.)	Temperature	Time (h)	Yield[b,c] (%)	Ee[d] (%)	Absolute configuration of **3**
1	DCM	TFA (1.0)	rt	44	trace	ND[e]	ND[e]
2	DCM	AcOH (1.0)	rt	44	15	14	*R*
3	DCM	TFA (0.5)	rt	90	9 (19)	2.9	*R*
4	DCM	AcOH (0.5)	rt	90	18 (31)	6.5	*S*
5	DMSO	TFA (1.5)	rt	93	47 (63)	64	*S*
6	DMSO	TFA (1.5)	50 °C	26	92	55	*S*

[a] 100 mg of **7** was used for all reactions.
[b] Isolated yield.
[c] Yields based on a recovery of starting **7** were shown in parentheses.
[d] Determined by HPLC equipped with a chiral stationary phase column.
[e] Not determined.

The reactions were studied in the presence of other chiral amines bearing a pyrrolidine and the obtained results are summarized in Table 2. The reaction mediated by (*S*)-proline (**5**) proceeded to afford (*R*)-**3** in a moderate yield and low enatioselectivity (entry 1). The reaction mediated by **8** was also performed to compare the Xu's method. However, lower yield and enantioselectivity were observed than the results reported in Ref. 12c (entry 2). The mediator (**11**),[1b] which exhibited high enantioselectivity in the aldol reaction of **6**, was unsuccessful in this reaction (entry 3), because of the lower yield and enantioselectivity compared to the reaction mediated by **10**. Although enantioselectivities under each conditions were not satisfactory, we planned to use enzymatic reactions focusing on two oxygen functionalities at C-1 and C-7 in (*S*)-**3** to increase the obtained optical purities.

Table 2. The aldol reaction of **7** mediated by chiral pyrrolidines



Entry[a]	Mediator	Time (h)	Yield[b,c] (%)	Ee[d] (%)	Absolute configuration of **3**
1	**5**	17.5	54	16	*R*
2	**8**	398[e]	36 (54)	56	*R*
3	**11**	48	27	33	*S*

[a] 100 mg of **7** was used for all reactions.

[b] Isolated yield.

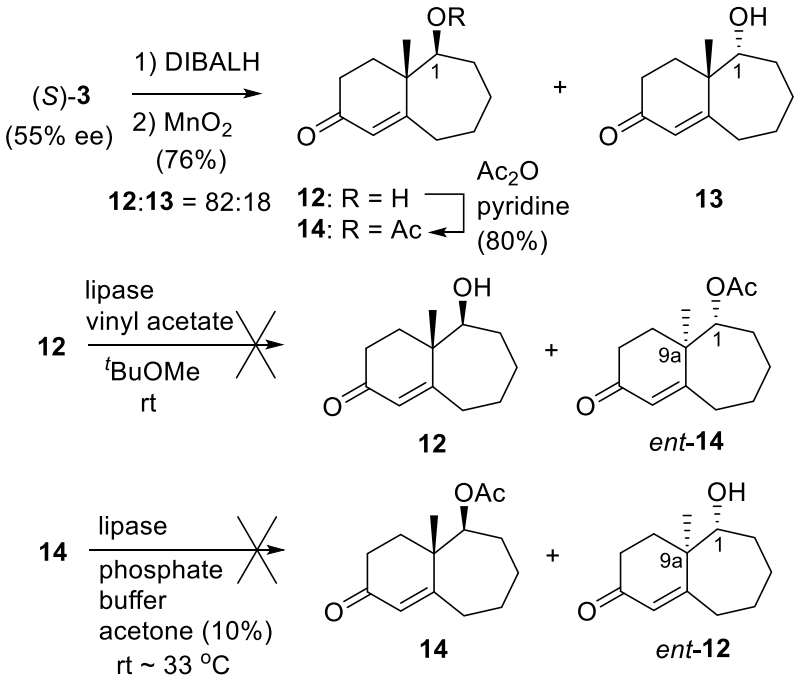
[c] Yields based on a recovery of starting **7** were shown in parentheses.

[d] Determined by HPLC equipped with a chiral stationary phase column.

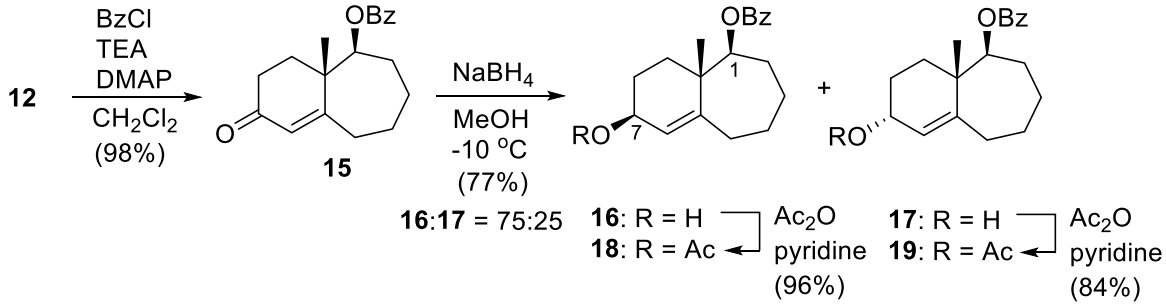
[e] The reaction was performed at rt.

The reduction of both carbonyl groups in (*S*)-**3** with diisobutylaluminum hydride (DIBALH) and following allylic oxidation in the presence of MnO_2 afforded known alcohols (**12**) and (**13**)[11c] with 82:18 diastereoselectivity. The major alcohol (**12**) was converted to acetate (**14**) using a common method. Unfortunately, both lipase-mediated asymmetric esterification[16] of **12** and asymmetric hydrolysis of **14** hardly proceeded to yield the expected alcohol (**12**) or acetate (**14**) with higher ee than the starting materials. In all cases, the starting **12** or **14** was completely recovered. These results indicated that **12** and **14** exist in the *cis*-orientation between the hydroxy group at C-1 and methyl group at C-9a and were unsuitable substrates for the lipases (Scheme 4).

We next focused on the oxygen functionality at C-7. The optical purities were determined using HPLC, so a benzoyl group was introduced to the major alcohol (**12**) as a UV chromophore. Sodium borohydride reduction of **15** in methanol afforded a diastereomeric mixture of **16** and **17** in a 75:25 ratio, which were readily separated by silica gel column chromatography. Acetylations of the obtained alcohols (**16**) and (**17**) using a typical method yielded the corresponding acetates (**18**) and (**19**), respectively (Scheme 5). NOE correlations of **19**, shown in Figure 2, indicated that the angular methyl at C-9a and the acetoxy group at C-7 existed in a *trans*-orientation. Therefore, the other diastereomeric acetate (**18**) must exist in the *cis*- configuration.



Scheme 4



Scheme 5

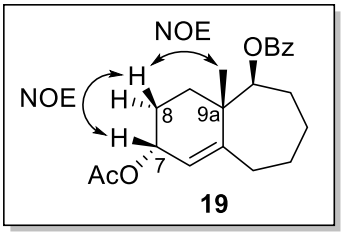
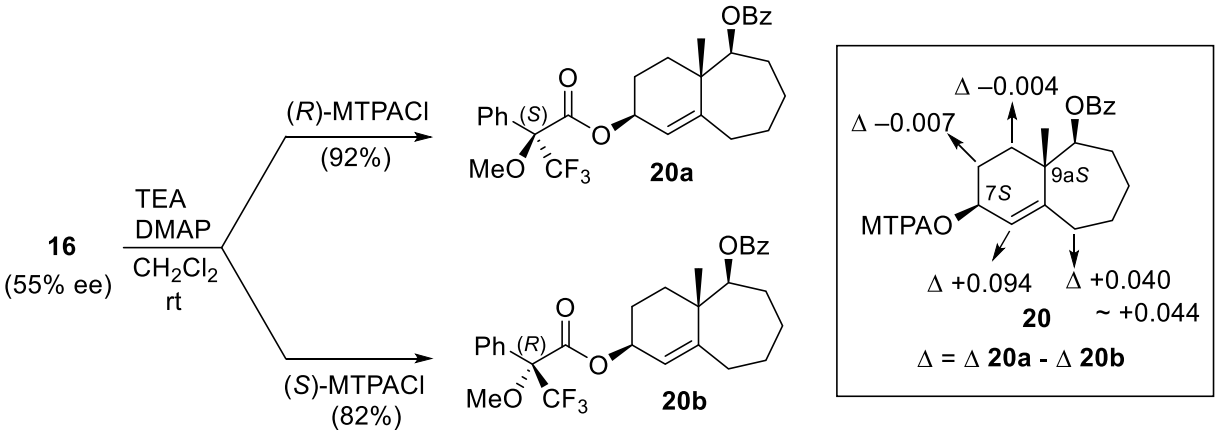


Figure 2

The absolute configuration of **16** was determined using Mosher's ester method.[17] Mosher's esters (**20a**) and (**20b**) were synthesized from **16** using (*R*)- or (*S*)-α-methoxy-α-(trifluoromethyl)phenylacetyl (MTPA) chloride. The difference values (δ = δ**20a** - δ**20b**) of the chemical shifts in the ^{1}H-NMR spectra are shown in Scheme 6. We observed high field shifts of the protons on C-8 and C-9 and low field shifts

of the protons on C-5 and C-6. These results strongly indicated that the absolute configuration at C-7 was *S*. Because the relative configuration between the hydroxy group at C-7 and angular methyl at C-9a was *cis* (*vide supra*), the absolute configuration at C-9a must be *S*. This indicated that the aldol reaction of entry 6 in Table 1 afforded (*S*)-**3**.



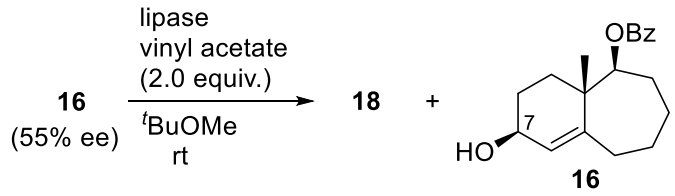
Scheme 6

The lipase-mediated asymmetric esterification of **16** was subsequently examined to increase the obtained optical purities. All reactions were performed in *tert*-butyl methyl ether (^{t}BuOMe) in the presence of 2.0 equiv. of vinyl acetate, and the obtained results are summarized in Table 3. All reactions afforded the acetate (**18**) with higher ee than the starting **16**. Especially, lipase AS was effective for increasing the optical purity and affording **18** with high ee (entry 4). In all reactions, the major enantiomer of the unreacted **16** remained in the same 7*S* configuration as the starting **16**, but with a lower ee. This indicated that enantioselectivity of lipase at C-7 was not high. However, these results revealed that the obtained (*S*)-**3** can be used a chiral synthon despite of its moderate ee, because it was possible to increase optical purity at a later synthetic stage.

Finally, we clarified the relationship between the absolute configurations, optical rotations, and HPLC retention times of both enantiomers of **3** and the obtained results are summarized in Table 4. It was observed that (*S*)-**3**, prepared from entry 6 in Table 1, exhibited similar optical rotations (*dextrorotatory*), and similar HPLC retention times on a OB-H column (entry 2) as entry 1, which was reported in Ref. 12a. However, the retention times of (*R*)- and (*S*)-**3** on the HPLC equipped with AS-H were different from those reported in Ref. 12b (entry 4 vs 5). Thus, we observed short retention time for (*R*)-**3** and long retention time for (*S*)-**3**, opposite to that of entry 5. Because the optical rotation data for (*R*)-**3** was not reported in Ref. 12b or 12c, we prepared (*R*)-**3** according to Xu's method. The obtained (*R*)-**3**, which exhibited slightly lower ee than that previously reported, exhibited similar retention times for (*R*)- and (*S*)-**3** as entry 4 (entry 6). Additionally, (*R*)-**3** was *levorotatory* and the absolute values of $[\alpha]_D$ between

(*R*)- and (*S*)-**3** were similar. Therefore, the behaviors of (*R*)- and (*S*)-**3** on HPLC with AS-H (entries 4 and 6), were reliable and it was clear that (*S*)-(+)-**3** was obtained from the asymmetric aldol reactions.

Table 3. Lipase-mediated asymmetric eaterifications of **16**



Entry[a]	Lipase[b]	Time (h)	18		16	
			Yield[g]	Ee[h i]	Yield[g]	Ee[h i]
1	AK[c]	61.5	19	75 (7*S*)	76	50 (7*S*)
2	PS-D[d]	7	53	73 (7*S*)	42	52 (7*S*)
3	AYS[e]	22.5	33	82 (7*S*)	54	39 (7*S*)
4	AS[f]	68	23	88 (7*S*)	76	45 (7*S*)

[a] 50 mg of **16** was used for all reactions.
[b] All lipases were commercially available from Amano Pharmaceutical Co., LTD.
[c] *Pseudomonas fluorescens*.
[d] *Pseudomonas cepacia* (immobilized on ceramic).
[e] *Candida rugosa*.
[f] *Aspergillus niger*.
[g] Isolated yield.
[h] Determined using an HPLC equipped with a chiral stationary phase column.
[i] Absolute configuration at C-7 of the major enantiomer was shown in parentheses.

Table 4. The relations of (*R*)- and (*S*)-**3** among absolute configurations, optical rotations, and HPLC retention times

Entry	Compound (ee)	$[\alpha]_D$[a] (in $CHCl_3$)	Column[b]	Eluent (v/v)	*Rt* (*R*, min)	*Rt* (*S*, min)
1[c]	(*S*)-**3** (8)	+7.9	OB	hexane: 2-propanol = 96:4[d]	27.7	23.7
2			OB-H	hexane: 2-propanol = 96:4[f]	40.7	27.8
3	(*S*)-**3**[e] (55)	+49.7	OJ-H	hexane: 2-propanol = 9:1[f]	15.2	17.3
4			AS-H	hexane: ethanol = 9:1[f]	37.0	42.5
5[g]	(*R*)-**3** (53)	NR[h]	AS-H	hexane: ethanol = 9:1[f]	37.0	34.4
6	(*R*)-**3**[i] (51)	−47.2	AS-H	hexane: ethanol = 9:1[f]	36.7	44.2

[a] The observed $[\alpha]_D$ accompanied with the corresponding enantiomeric excess.
[b] All of chiral stationary phase columns were commercially available as CHIRALCEL® or

CHIRALPAK® from Daicel Co., LTD.

[c] Data from Ref. 12a.

[d] Flow rate of 0.5 mL/min.

[e] Obtained *via* aldol reaction of entry 6 in Table 1.

[f] Flow rate of 1.0 mL/min.

[g] Data from Ref. 12b.

[h] Not reported.

[i] Obtained using the same method as in Ref. 12c.

In conclusion, we established a novel chiral route to provide a Swaminathan ketone (**3**) bearing a 7-membered ring *via* intramolecular aldol reaction of trione (**7**) mediated by chiral amines bearing a pyrrolidine. Although the enantioselectivity of **3** was moderate, we successfully increased the optical purities by using a lipase-mediated asymmetric esterification of alcohol (**16**) at a later synthetic stage. The absolute configuration was determined by Mosher's ester method, and the relationship between absolute configuration and optical rotation of **3** was determined. Further studies regarding the detailed reaction mechanism and development of a more efficient mediator for the reactions is currently in progress.

REFERENCES

1. For a collection of relevant references consult: (a) Y. Akahane, N. Inage, K. Inomata, and Y. Endo, *Heterocycles*, 2007, **74**, 637; (b) Y. Akahane, K. Inomata, and Y. Endo, *Heterocycles*, 2011, **82**, 1727.
2. For a review of **2**: B. Bradshaw and J. Bonjoch, *Synlett*, 2012, **23**, 337.
3. Selected recent preparations of **1** and/or **2**: (a) X.-M. Zhang, M. Wang, Y.-Q. Tu, C.-A. Fang, Y.-J. Jiang, S.-Y. Zhang, and F.-M. Zhang, *Synlett*, 2008, 2831; (b) O. H. Rubio, A. L. Fuentes de Arriba, L. M. Monleon, F. Sanz, L. Simon, V. Alcazar, and J. R. Moran, *Tetrahedron*, 2015, **71**, 1297; (c) P. Vizcaino-Milla, J. M. Sansano, C. Najera, B. Fiser, and E. Gomez-Bengoa, *Eur. J. Org. Chem.*, 2015, 2614; (d) J. Yu and B. Yu, *Chin. Chem. Lett.*, 2015, **26**, 1331; (e) Y. Hayashi, T. Mukaiyama, M. Benohoud, N. R. Gupta, T. Ono, and S. Toda, *Chem. Eur. J.*, 2016, **22**, 5868.
4. Selected recent applications of **1**: (a) M. M. Logan, T. Toma, R. Thomas-Tran, and J. D. Bois, *Science*, 2016, **354**, 865; (b) D. Niroula, L. P. Hallada, S. Rogelj, and R. Tello-Aburto, *Tetrahedron*, 2017, **73**, 359; (c) G. Liu, J.-C. Han, and C.-C. Li, *Tetrahedron*, 2017, **73**, 3629; (d) M. Annamalai, S. Hristeva, M. Bielska, R. Ortega, and K. Kumar, *Molecules*, 2017, **22**, 827; (e) K. Motoyama, T. Nagata, J. Kobayashi, A. Nakamura, N. Miyoshi, M. Kazui, K. Sakurai, and T. Sakakura, *Bioorg. Med. Chem. Lett.*, 2018, **28**, 2222.
5. Selected recent applications of **2**: (a) C. Bürki, J. Bonjoch, B. Bradshaw, G. Villa, and P. Renaud,

Chem. Eur. J., 2015, **21**, 395; (b) N. Richter, R. C. Simon, H. Lechner, W. Kroutil, J. M. Ward, and H. C. Hailes, *Org. Biomol. Chem.*, 2015, **13**, 8843; (c) R. Riclea and J. S. Dickschat, *Angew. Chem. Int. Ed.*, 2015, **54**, 12167; (d) P. Bichovski, T. M. Haas, M. Keller, and J. Streuff, *Org. Biomol. Chem.*, 2016, **14**, 5673; (e) A. Letort, D.-L. Long, and J. Prunet, *J. Org. Chem.*, 2016, **81**, 12318; (f) D. H. Dethe, B. D. Dherange, S. Ali, and M. M. Parsutkar, *Org. Biomol. Chem.*, 2017, **15**, 65; (g) J. Krieger, T. Smeilus, O. Schackow, and A. Giannis, *Chem. Eur. J.*, 2017, **23**, 5000; (h) C. L. Chapelain, *Org. Biomol. Chem.*, 2017, **15**, 6242; (i) M. A. Haque and C. K. Jana, *Chem. Eur. J.*, 2017, **23**, 13300; (j) Y. Wang, A. Jäger, M. Gruner, T. Lübken, and P. Metz, *Angew. Chem. Int. Ed.*, 2017, **56**, 15861; (k) S. Yin, K. Sugimoto, H. Nemoto, and Y. Matsuya, *Heterocycles*, 2017, **95**, 187; (l) K. Sakata, Y. Wang, D. Urabe, and M. Inoue, *Org. Lett.*, 2018, **20**, 130; (m) R. R. Karimov, D. S. Tan, and D. Y. Gin, *Tetrahedron*, 2018, **74**, 3370; (n) T. Muraoka, M. Enomoto, T. Teranishi, and Y. Ogura, *Tetrahedron Lett.*, 2018, **59**, 4107.

6. Selected reviews of organocatalytic aldol reactions: (a) B. M. Trost and C. S. Brindle, *Chem. Soc. Rev.*, 2010, **39**, 1600; (b) A Moyano and R. Rios, *Chem. Rev.*, 2011, **111**, 4703; (c) S. K. Panday, *Tetrahedron: Asymmetry*, 2011, **22**, 1817.
7. (a) Z. G. Hajos and D. R. Parrish, German Patent DE 2102623, 1971; (b) U. Eder, G. Sauer, and R. Wiechert, German Patent DE 2014757, 1971; (c) U. Eder, G. Sauer, and R. Wiechert, *Angew. Chem.*, 1971, **83**, 492; (d) Z. G. Hajos and D. R. Parrish, *J. Org. Chem.*, 1973, **38**, 3239; (e) Z. G. Hajos and D. R. Parrish, *J. Org. Chem.*, 1974, **39**, 1615.
8. (a) K. L. Brown, L. Damm, J. D. Dunitz, A. Eschenmoser, R. Hobi, and C. Kratky, *Helv. Chim. Acta*, 1978, **61**, 3108; (b) C. Agami and H. Sevestre, *J. Chem. Soc., Chem. Commun.*, 1984, 1385; (c) C. Agami, C. Puchot, and H. Sevestre, *Tetrahedron Lett.*, 1986, **27**, 1501; (d) C. Agami and C. Puchot, *J. Mol. Catal.*, 1986, **38**, 341; (e) C. Agami, N. Platzer, and K. Sevestre, *Bull. Soc. Chim. Fr.*, 1987, 358; (f) C. Agami and N. Platzer, *Bull. Soc. Chim. Fr.*, 1998, 499; (g) N. Gathaergood, *Aust. J. Chem.*, 2002, **55**, 615.
9. (a) S. Bahmanyar and K. N. Houk, *J. Am. Chem. Soc.*, 2001, **123**, 11273; (b) S. Bahmanyar and K. N. Houk, *J. Am. Chem. Soc.*, 2001, **123**, 12911; (c) L. Hoang, S. Bahmanyar, K. N. Houk, and B. List, *J. Am. Chem. Soc.*, 2003, **125**, 16; (d) S. Bahmanyar, K. N. Houk, H. J. Martin, and B. List, *J. Am. Chem. Soc.*, 2003, **125**, 2475; (e) B. List, L. Hoang, and H. J. Martin, *Proc. Nat. Acad. Sci. U. S. A.*, 2004, **101**, 5839; (f) B. List, *Acc. Chem. Res.*, 2004, **37**, 548; (g) C. Allemann, R. Gordillo, F. R. Clemente, P. H.-Y. Cheong, and K. N. Houk, *Acc. Chem. Res.*, 2004, **37**, 558; (h) P. H.-Y. Cheong and K. N. Houk, *Synthesis*, 2005, 1533.
10. (a) R. Selvarajan, J. P. John, K. V. Narayanan, and S. Swaminathan, *Tetrahedron*, 1966, **22**, 949; (b) D. Rajagopal, R. Narayanan, and S. Swaminathan, *Proc. Ind. Acad. Sci.*, 2001, **113**, 197; (c) R.

Malathi, D. Rajagopal, Z. G. Hajos, and S. Swaminathan, *J. Chem. Sci*., 2004, **116**, 159.

11. (a) J. S. Dutcher, J. G. Macmillan, and C. H. Heathcock, *J. Org. Chem*., 1976, **41**, 2663; (b) H. Hagiwara and H. Uda, *J. Org. Chem*., 1988, **53**, 2308; (c) X. Wang, S. C. Butler, J. C. Gallucci, and L. A. Paquette, *J. Org. Chem*., 2009, **74**, 6825.
12. (a) K. Sano, Y. Kohari, H. Nakano, C. Seki, M. Takeshita, M. Tokiwa, Y. Hirose, and K. Uwai, *Synth. Commun*., 2016, **46**, 46; (b) S. Cañellas, C. Ayats, A. H. Henseler, and M. Pericàs, *ACS Catal*., 2017, **7**, 1383; (c) Y. Chen, J. Hu, L.-D. Guo, W. Zhong, C. Ning, and J. Xu., *Angew. Chem. Int. Ed*., 2019, **58**, 7390.
13. (a) S. F. Brady, M. P. Singh, J. E. Janso, and J. Clardy, *J. Am. Chem. Soc*., 2000, **122**, 2116; (b) S. F. Brady, S. M. Bondi, and J. Clardy, *J. Am. Chem. Soc*., 2001, **123**, 9900; (c) F. Marion, D. E. Williams, B. O. Patrick, I. Hollander, R. Mallon, S. C. Kim, D. M. Roll, L. Feldberg, R. V. Soest, and R. J. Andersen, *Org. Lett*., 2006, **8**, 321; (d) J. Kobayashi and T. Kubota, *Nat. Prod. Rep*., 2009, **26**, 936; (e) S.-P. Yang and J.-M. Yue, *Acta Pharm. Sinica*, 2012, **33**, 1147; (f) A. K. Chattopadhyay and S. Hanessian, *Chem. Rev*., 2017, **117**, 4104.
14. M. Asami, *Bull. Chem. Soc. Jpn*., 1990, **63**, 721.
15. Selected recent applications of **10**: (a) C. Bournaud, E. Marchal, A. Quintard, S. S.-Mossé, and A. Alexakis, *Terahedron: Asymmetry*, 2010, **21**, 1666; (b) N. Mase, M. Fukasawa, N. Kitagawa, F. Shibagaki, N. Moshio, and K. Tanabe, *Synlett*, 2010, 2340; (c) A. Massi, A. Cavazzini, L. D. Zoppo, O. Pandoli, V. Costa, L. Pasti, and P. P. Giovannini, *Tetrahedron Lett*., 2011, **52**, 619; (d) D. A. Borkin, S. M. Landge, and B, Török, *Chirality*, 2011, **23**, 612; (e) R. Chowdhury and S. K. Ghosh, *Synthesis*, 2011, 1936; (f) F. Feluga, C. Forzato, P. Nitti, G. Pitacco, F. Prati, E. Valentin, and E. Zangrando, *Chirality*, 2012, **24**, 1005; (g) T. I. Houjeiry, S. L. Poe, and D. T. McQuade, *Org. Lett*., 2012, **14**, 4394; (h) J. L. Galman, D. Steadman, L. D. Haigh, and H. C. Hailes, *Org. Biomol. Chem*., 2012, **10**, 2621; (i) M. Vasiloiu, D. Rainer, P. Gaerner, C. Reichel, C. Schröder, and K. Bica, *Catal. Today*, 2013, **200**, 80; (j) A. M. F. Phillips and M. T. Barros, *Eur. J. Org. Chem*., 2014, 152; (k) S. L. Clarke, C. M. McSweeney, and G. P. McGlacken, *Tetrahedron: Asymmetry*, 2014, **25**, 356; (l) P. K. Shyam and H.-Y. Jang, *Eur. J. Org. Chem*., 2014, 1817; (m) F. Thuaudm, F. Ruhrbacher, A. Zwicky, and J. W. Bode, *Helv. Chim. Acta*, 2016, **99**, 868; (n) E. J. Rastelli, N. T. Truong, and D. M. Coltart, *Org. Lett*., 2016, **18**, 5588; (o) R. Nouch, M. Cini, M. Magre, M. Abid, M. Diéguez, O. Pàlmies, S. Woodward, and W. Lewis, *Chem. Eur. J*., 2017, **23**, 17195.
16. Selected reviews of lipase-mediated asymmetric esterification: (a) Z.-F. Xie, *Tetrahedron: Asymmetry*, 1991, **2**, 733; (b) G. M. Ziarani, P. Gholamzadeh, P. Asadiatouei, and N. Lashgari, *J. Mol. Catal. B: Enzym*., 2015, **122**, 93.
17. (a) J. A. Dale and H. S. Mosher, *J. Am. Chem. Soc*., 1973, **95**, 512; (b) G. R. Sullivan, J. A. Dale,

and H. S. Mosher, *J. Org. Chem*., 1973, **38**, 2143; (c) T. R. Hoye and M. K. Renner, *J. Org. Chem*., 1996, **61**, 2056; (d) I. Ohtani, T. Kusumi, Y. Kashman, and H. Kakisawa, *J. Am. Chem. Soc*., 1991, **113**, 4092; (e) D. Parker, *Chem. Rev*., 1991, **91**, 1441; (f) J. M. Seco, E. Quinoa, and R. Riguera, *Chem. Rev*., 2004, **104**, 17; (g) T. R. Hoye, C. S. Jeffrey, and F. Shao, *Nat. Protocol*., 2007, **2**, 2451.