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New Class of Pyridine Catalyst Having a Conformation Switch System: Asymmetric Acylation of Various *sec*-Alcohols

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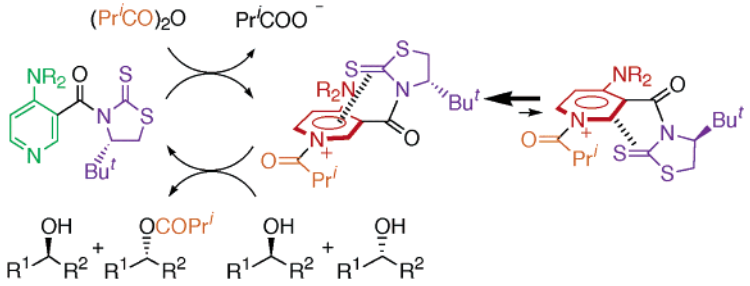

We have developed a new class of pyridine catalyst for asymmetric acylation of *sec*-alcohols having a conformation switch system in which interconversion between self-complexation and uncomplexation is induced by acylation and deacylation steps, respectively. Kinetic resolution of various *sec*-alcohols is performed by the asymmetric acylation with isobutyric anhydride using 0.05 to 0.5 mol % catalyst **1a** with *s* values of up to 30. In addition, *dl*-diols are also resolved in a similar manner in good selectivity. Moreover, asymmetric desymmetrization of *meso*-1,*X*-diols ($X = 2-6$) are achieved in the presence of 0.5−5 mol % catalyst **1a**. A working model for the reaction mechanism is proposed on the basis of the ^{1}H NMR measurements, X-ray structural analyses, and AM1 and DFT calculations, where the conformation switch system governed by an intramolecular cation−π interaction between a pyridinium ring and a thiocarbonyl group would play a key role to attain both good selectivity and high catalytic activity.

Introduction

4-(Dimethylamino)pyridine (DMAP) derivatives are one of the most important organocatalysts for acyl-transfer reaction of various alcohols.[1] The chiral version of the DMAP derivatives has been extensively developed over the past decade[2] because of the significant importance of asymmetric acylation of alcohols for production of chiral alcohols. In the design of such chiral DMAP catalysts, the key feature is selective blocking of the pyridinium face by an aromatic moiety to discriminate enantiomeric alcohols. A variety of aromatic moieties such as pentaphenylcyclopentadienyl,[3] naphthyl,[4] binaphthyl,[5] biaryl,[6] and substituted aryl[7] groups have been employed; however, a nonaromatic system has not yet been reported.

We have recently found a new type of cation−π interaction[8] between a pyridinium ring and a thiocarbonyl group.[9] This interaction enables nucleophiles to attack the less-hindered side

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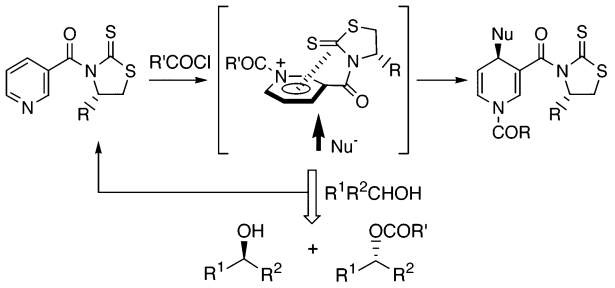
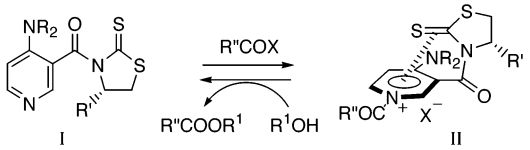
SCHEME 1. Face-Selective Addition of a Nucleophile to a Pyridinium Salt and Expected Kinetic Resolution of a *sec*-Alcohol



SCHEME 2. New Class of DMAP Catalyst with a Conformation Switch System



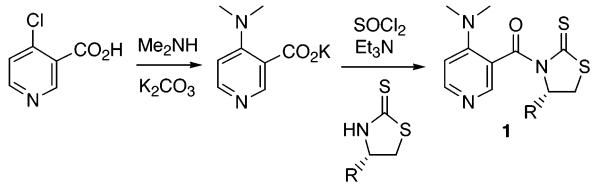
to give chiral 1,4-dihydropyridines as shown in Scheme 1.[10] We expected that if a *sec*-alcohol is employed as a nucleophile, it would attack the *N*-acyl group from the nonshielded side to achieve enantiomer-selective acylation with recovery of a chiral alcohol and the starting pyridine compound.

This prospect prompted us to develop a new DMAP catalyst as shown in Scheme 2. The key feature is that the catalyst has a conformation switch system based on the interconversion between uncomplexed form **I** and self-complexed form **II** induced by *N*-acylation and deacylation steps as outlined in Scheme 2.[11] The self-complexation by $Py^{+}\cdots S{=}C$ interaction provides a chiral environment around the active site, which is required for discrimination of the racemic *sec*-alcohols, although the chiral center is apart from the active site. The recovered uncomplexed catalyst undergoes smooth *N*-acylation with an acid anhydride to form self-complex **II** repeatedly. This conformation change in the catalyst would solve the selectivity−reactivity dilemma[4] similar to the induced-fit-type catalyst[4,7a] developed by Kawabata. In this paper, we report a new class of pyridine catalysts having a conformation switch system which serve as asymmetric acylating catalysts for *sec*-alcohols.

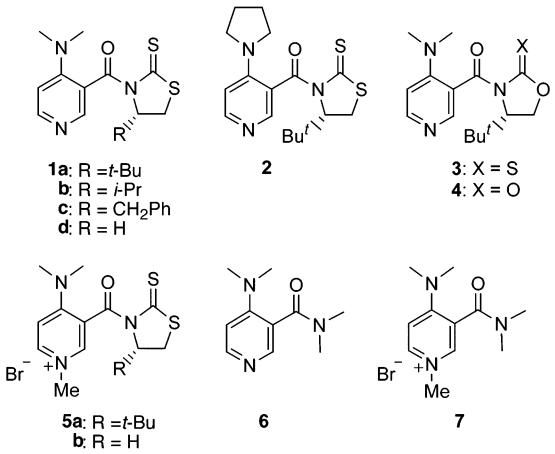
Results and Discussion

Synthesis of Catalysts. We prepared DMAP analogues **1** possessing chiral thiazolidine-2-thione.[12] These catalysts can be readily prepared from commercially available 4-chloronicotinic acid as outlined in Scheme 3. Introduction of a dimethylamino group at the 4-position[13] gave potassium 4-(dimethylamino)-3-carboxylate. After conversion into the corresponding acid chloride with $SOCl_2$, coupling with chiral thiazolidine-2-thione derivatives afforded catalysts **1**. Catalysts **2**−**4** were also

SCHEME 3. Synthesis of New DMAP Catalysts



prepared in a similar manner using oxazolidine-2-thione or oxazolidine-2-one as a chiral auxiliary. Compounds **5**−**7** are reference compounds for structural studies of the catalysts.



Kinetic Resolution of Compound 8. Acylation of 1-(2-naphthyl)ethanol (**8**) with isobutyric anhydride smoothly proceeded in the presence of 5 mol % catalysts **1**−**4** in toluene at 0 °C (Table 1, entries 1−6). The selectivity[14] largely depends on the substituent of the chiral auxiliary; **1a** having a bulky *tert*-butyl group provides the highest selectivity among **1a**−**1c**. **2** and **3** also served as effective acylating catalysts, whereas **4** was less effective, suggesting the importance of the C═S group to attain high enantioselectivity. The absolute configuration of the recovered alcohol was assigned to be *S* by comparison of the specific rotation with that of the literature.[15]

A survey of acylating reagents revealed that isobutyric anhydride gave the most satisfactory results among the anhydrides that we have investigated. The solvents significantly affect the *s* values[14] (entries 7−11); use of acyclic ethers Et_2O, *i*-Pr_2O, and *t*-BuOMe remarkably improved the selectivity (entries 9−11), whereas polar solvents were less effective (entries 7 and 8). The reaction temperature is also an important factor for the stereoselectivity (entries 11−13); lowering the temperature increases the *s* value. There have been known a variety of acylation catalysts that show excellent levels of *s* values such as chiral phosphines,[17] diamines,[18] dihydroimidazopyridines,[19] and peptide-based catalysts.[20,21] Since it has been well docu-

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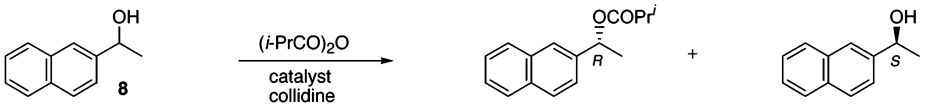
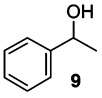
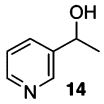
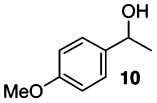
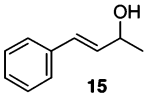
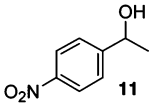
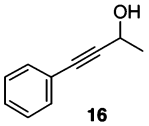
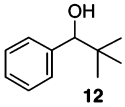
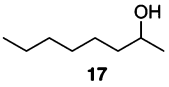
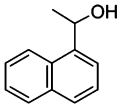
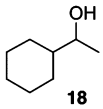
TABLE 1. Kinetic Resolution of 1-Naphthylethyl Alcohol Catalyzed by 1−4[a]



entry	cat. (concn, mol %)	solv	temp (°C)	time (h)	conv[b] (%)	ee (%)	s[c]
1	**1a** (5)	toluene	0	3	59	87	11
2	**1a** (5)	toluene	0	3	55	74	9.1
3	**1c** (5)	toluene	0	3	58	73	7.0
4	**2** (5)	toluene	0	3	61	88	9.8
5	**3** (5)	toluene	0	3	57	82	11
6	**4** (5)	toluene	0	3	53	37	2.7
7	**1a** (5)	CH_3CN	0	3	61	68	5.0
8	**1a** (5)	THF	0	3	60	80	7.6
9	**1a** (5)	Et_2O	0	3	61	96	15
10	**1a** (5)	*i*-Pr_2O	0	3	50	78	19
11	**1a** (5)	*t*-BuOMe	0	3	57	95	24
12	**1a** (5)	*t*-BuOMe	25	3	64	99	18
13	**1a** (5)	*t*-BuOMe	−30	5	56	97	30
14	**1a** (0.5)	*t*-BuOMe	25	12	57	92	17
15	**1a** (0.05)	*t*-BuOMe	25	72	55	87	17

[a] A 0.7 equiv sample of $(i\text{-PrCO})_2O$ and an 0.8 equiv sample of collidine were used. [b] Conversion (%) = (ee of recovered **8**)/(ee of recovered **8** + ee of ester); see ref 16. [c] Selectivity factor $s = k$(fast-reacting enantiomer)/k(slow-reacting enantiomer); see ref 14.

TABLE 2. Kinetic Resolution of Various Alcohols Catalyzed by 1a[a]

substrate	% ee[b] (config)[c]	s[d] (% conv)[e]	substrate	% ee[b] (config)[c]	s[d] (% conv)[e]
 **9**	89 (*S*)	7.6 (65)	 **14**	92 (*S*)	8.1[g] (66)
 **10**	97 (*S*)	10 (68)	 **15**	94 (*S*)	9.8[g] (65)
 **11**	98 (*S*)	8.9 (72)	 **16**	78 (*S*)	6.6[g] (61)
 **12**	88[f] (*S*)	9.6 (62)	 **17**	25 (*S*)	2.2 (48)
 **13**	97 (*S*)	13 (65)	 **18**	31 (-)[h]	2.3 (52)

[a] All reactions were conducted in the presence of 0.5 mol % **1a**, 0.8 equiv of $(i\text{-PrCO})_2O$, and 0.9 equiv of Et_3N at rt for 12 h unless otherwise noted. [b] Determined by HPLC using chiral stationary phases. [c] The absolute configuration was determined by comparison of $[\alpha]_D$ values with those reported: compd **9**, ref 23; compd **10**, ref 24; compd **11**, ref 25; compd **12**, ref 26; compd **13**, ref 26; compd **14**, ref 27; compd **15**, ref 28; compd **16**, ref 29; compd **17**, ref 30. [d] Selectivity factor $s = k$(fast-reacting enantiomer)/k(slow-reacting enantiomer); see ref 14. [e] Conversion (%) = (ee of recovered alcohol)/(ee of recovered alcohol + ee of ester); see ref 16. [f] The reaction time is 72 h. [g] Temperature −30 °C, time 48 h. [h] The absolute configuration was not determined.

mented that one of the merits of DMAP catalysts is high activity,[1] we examined the influence of the catalyst amount on the reactions (entries 12, 14, and 15). Reducing the catalyst amount from 5 to 0.5 mol % had little effect on the s value, and the reactions were completed within 12 h. Remarkable is that further reducing the catalyst to 0.05 mol % resulted in the same selectivity as in the case of entry 15, though the reaction required 72 h to reach 55% conversion.

Kinetic Resolution of Various *sec*-Alcohols. This catalysis is applicable to various *sec*-alcohols as shown in Table 2. Acylation of **9**−**18** with isobutyric anhydride in the presence of 0.5 mol % **1a** and Et_3N[22] gave esters **9a**−**18a** with recovery of (*S*)-alcohol. The electron-donating and -withdrawing groups

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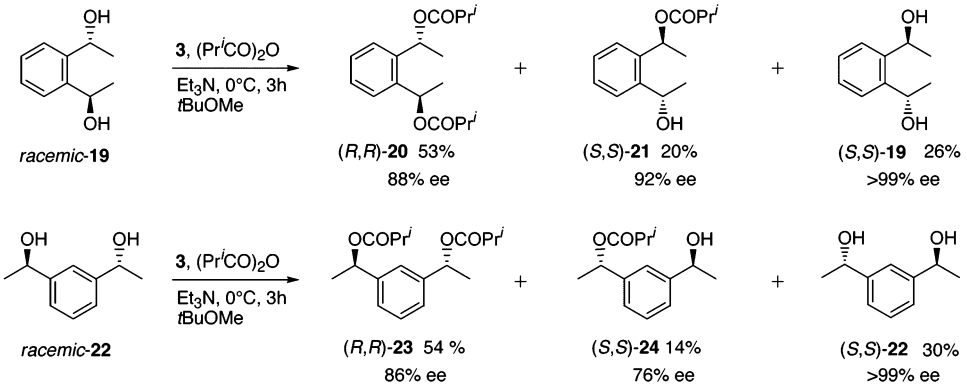
(22) Triethylamine was used instead of collidine because of little difference in the selectivities.

SCHEME 4. Kinetic Resolution of Racemic 19 and 22



at the *para*-position on **10** and **11**, respectively, had little effect on the *s* values. These conditions are also effective for sterically hindered alcohol **12**. Kinetic resolution of 1-(1-naphthyl)ethanol (**13**) gave a result similar to that of its isomer **8**. This method is applicable to heterocyclic *sec*-alcohol **14** and allylic and propargylic alcohols **15** and **16**; lowering the temperature to −30 °C improved the selectivity. Acylation of aliphatic alcohols **17** and **18** resulted in much lower selectivities, suggesting the importance of an aromatic moiety or π-electrons around the hydroxy group to attain efficient resolution. In most cases the *s* values are larger than 7, showing the practical usefulness of this method.[14]

Kinetic Resolution of *dl*-Diols. Kinetic resolution of *dl*-diols is also achieved by using this catalysis. Since C_2-symmetric chiral diols are useful as chiral auxiliaries,[31] chiral ligands,[32] and intermediates of a wide variety of chiral compounds,[33] resolution of *dl*-diols is of significant importance in synthetic organic chemistry. Various 1,2- and 1,3-diols have been resolved by asymmetric acylation using transition-metal catalysts, whereas 1,*X*-diols ($X > 3$) are scarcely employed except for a few examples[3] due to the difficulty of the formation of a chelate ring with a catalyst. Kinetic resolution of acyclic 1,4-diol **19** with 1.5 equiv of isobutyric anhydride in the presence of 5 mol % catalyst gave a mixture of (*R*,*R*)-diester **20** and (*S*,*S*)-monoester **21** with recovery of (*S*,*S*)-diol **19**[34] in excellent optical purity (Scheme 4). Similar results were obtained for 1,5-diol **22**; (*R*,*R*)-diester **23**, (*S*,*S*)-monoester **24**, and (*S*,*S*)-diol **22**[35] were produced in good to excellent selectivities. The assignment of the absolute configuration of **20** and **21**, and **23** and **24**, was performed after hydrolysis into **19** and **22**, respectively, by comparison of the specific rotations with those reported.[33,34]

Desymmetrization of *meso*-Diols. Next, we turned our attention to asymmetric desymmetrization of *meso*-diols[36,37] because chiral hydroxy esters would be theoretically available in quantitative yields. The product monoesters are valuable synthetic intermediates due to having two different functional groups, which are employed for the synthesis of crown ethers,[38] acetals,[31] polymers,[39] and chiral ligands.[32] Table 3 summarizes the results for the desymmetrization of various *meso*-1,*X*-diols using 5 mol % **1a**. Catalytic desymmetrization of 1,2-diol **25** and 1,3-diol **26** with isobutyric anhydride in THF gave the corresponding monoesters in 72% ee and 59% ee, respectively. The lower yield of the monoester of **25** may be due to migration of the acyl group and successive second acylation. Acylation of 1,4-diol **27** afforded a monoester in much higher selectivity. On the other hand, desymmetrization of cyclic 1,4-diol **28** gave much lower selectivity despite having a partial structure similar to that of **27**. Optimized geometries of **27** and **28** predicted by DFT calculations at the B3LYP/6-31G* level[40] were significantly different from each other; the two hydroxy groups of **28** occupy pseudoaxial and equatorial positions in the six-membered ring, whereas both hydroxy groups of **27** are perpendicular to the phenyl ring with formation of a hydrogen bond. This conformational difference may have resulted in very different selectivities. The absolute configuration of **27a** was determined after conversion into ketone **31**; comparison of the specific rotation of **31** {$[\alpha]_D^{26.5}$ +3.6 (*c* 0.95, $CHCl_3$)} with that of authentic (*R*)-**31** {$[\alpha]_D^{26.5}$ +2.8 (*c* 1.42, $CHCl_3$)} derived from (*R*,*R*)-**21** clarified the *R*,*S* configuration of **27a** (Scheme 5).

(23) The absolute configuration was assigned by comparison with the HPLC retention time of a commercially available authentic sample.

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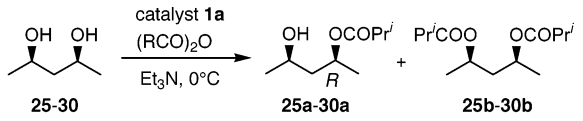
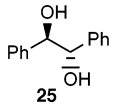
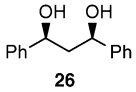
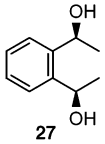
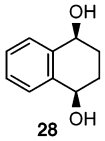
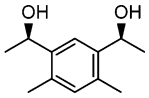
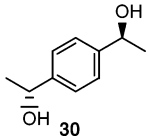
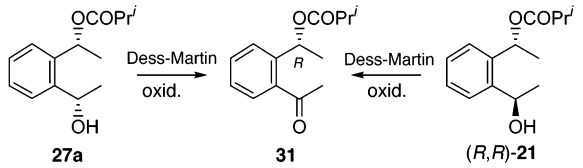
TABLE 3. Desymmetrization of Various *meso*-Diols Catalyzed by 1a[a]



diol	time (h)	monoester[b] (%)	ee(%)[c] config[d]	diester[b] (%)	diol[b] (%)
 **25**	3	31	72[e](*S*)	48	21
 **26**	3	61	59 (-)[f]	24	14
 **27**	2	87	97(*R*)	13	-
 **28**	5	44	18(-)[f]	21	35
 **29**	3	87	88(*R*)[g]	11	2
 **30**	3	69	96(*R*)	24	5

[a] All reactions were conducted in the presence of 5 mol % **1a**, 1.1 equiv of (*i*-PrCO)$_2$O, and 1.1 equiv of Et$_3$N in TBME at rt unless otherwise noted. [b] Isolated yield. [c] Determined by HPLC analysis; see the Supporting Information. [d] The absolute configuration was determined by comparison of $[\alpha]_D$ values with those reported: compd **25a**, ref 40. [e] THF was used as a solvent due to the insolvability of the substrate. [f] The absolute configuration was not determined. [g] The sign of the $[\alpha]_D$ value of monoacetate is the same as that reported; see ref 36b.

SCHEME 5. Determination of the Absolute Configuration of 27a



1,5-Diol **29** and 1,6-diol **30** are also good substrates for the desymmetrization reaction; 88% ee and 96% ee and good yields were obtained, respectively. The absolute configuration of the monoester of **30** was determined after conversion into reported 4-(1-hydroxyethyl)acetophenone **32**; comparison of the $[\alpha]_D^{24}$ value with that of the literature[34] revealed the *R* configuration of **30**.

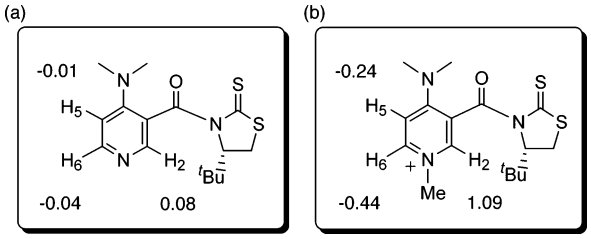


FIGURE 1. $\Delta\delta$ values for (a) **1a** and (b) **5a** in $CDCl_3$.

Structural Studies of Intermediary Pyridinium Salts. ^{1}H NMR studies of **1a**, **5a**, **6**, and **7** provided insight into the geometrical differences between **1a** and the pyridinium salt **5a**. Figure 1 shows $\Delta\delta$(**1a**) and $\Delta\delta$(**5a**) values, which are the chemical shift differences of **1a** and **5a** with reference compounds **6** and **7**, respectively. These values reflect the effect of the thiocarbonyl moiety on the chemical shifts of the pyridine and pyridinium protons. Comparison of $\Delta\delta$(**1a**) and $\Delta\delta$(**5a**) clearly shows significant differences between them. The $\Delta\delta_{H2}$ and $\Delta\delta_{H6}$ values for **5a** are 1.09 and −0.44, respectively, the absolute values of which are much larger than those of **1a** (0.08 and −0.04). These observations are comparable to those of the previously reported related cation−π complex.[9] The significant differences in the $\Delta\delta$ values between **1a** and **5a** clarify that **5a** has a fixed conformation with close proximity of the C═S group toward the pyridinium face, whereas the chiral auxiliary of the C−(C═O) bond of **1a** rotates much faster.

Dynamic NMR experiments for **1a** and **5a** were carried out to investigate the differences in the behavior in solution between them. Figure 2 depicts the ^{1}H NMR spectra of them. The spectrum of **1a** at 253 K clearly shows two rotamers with respect to the C−(C═O) bond, the ratio of which is about 1:1. The equilibrium state between the two rotamers was supported by the fact that the ^{1}H NMR spectrum at 293 K shows coalescence of the two rotamers. On the other hand, only one rotamer appears for the spectrum of **5a** in the range of 193−323 K, strongly suggesting that the equilibrium shifts toward one of the two rotamers. This also indicates a higher rotational barrier in **5a** than **1a**, which is in agreement with the larger $\Delta\delta$ values of **5a**.

NOE experiments of the *N*-isobutyryl salt of **1a** clarified that the *N*-acyl carbonyl is close to H6. Irradiation of H2 resulted in 17.6% NOE for the methine proton of the isobutyryl group, whereas 0.5% NOE was observed between H6 and the methine proton (Figure 3). In addition, irradiation of the methine proton resulted in 8.1% and 0.9% enhancement for H2 and H6, respectively. These NMR studies clarified that the conformation of the pyridinium salt is much more fixed than that of catalyst **1a**, suggesting that the C═S···Py$^+$ interaction governs the conformation of both the pyridinium ring and the *N*-acyl group.

The existence of intramolecular interaction between a thiocarbonyl group and a pyridinium ring was confirmed by X-ray structural analysis. Since crystals of **5a** were unsuitable for X-ray analysis, the X-ray structure of **5b** was compared with that of reference compound **1d**. The intramolecular distances between the sulfur atom of the thiocarbonyl group and C2, C3, and C4 are 3.491, 3.111, and 3.695 Å, respectively, while those of **1d** are 3.422, 3.214, and 4.071 Å, respectively. Superimposition of their X-ray structures shown in Figure 4 clarified that the thiocarbonyl group of **5b** is closer to the pyridinium face than **1d**. This is in agreement with our previous structural studies of

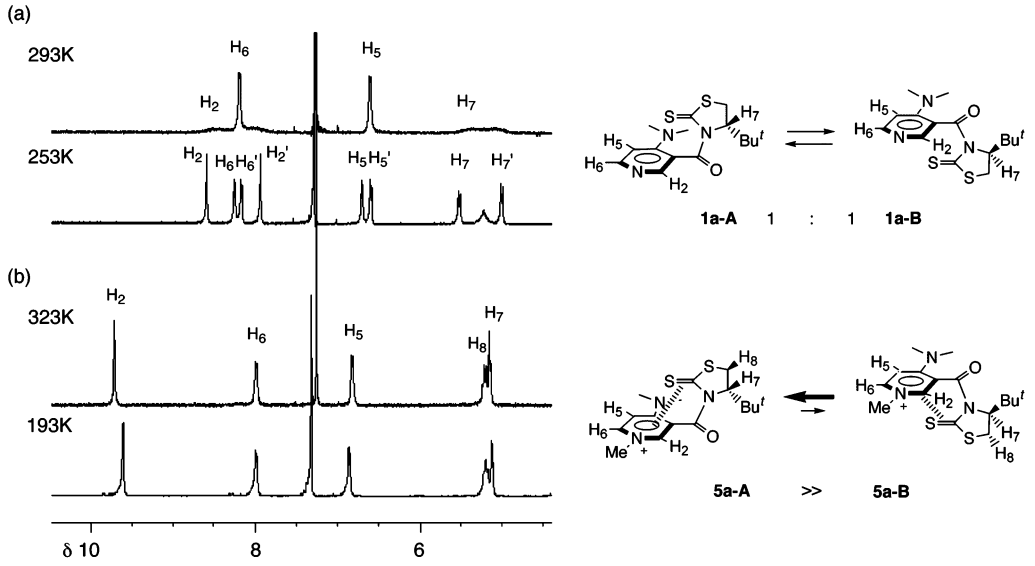


FIGURE 2. ^{1}H NMR spectra for (a) **1a** at 253 and 293 K and (b) **5a** at 193 and 323 K and their schematic equilibrium equations.

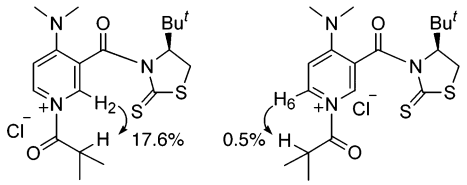


FIGURE 3. NOEs for salts of **1a**.

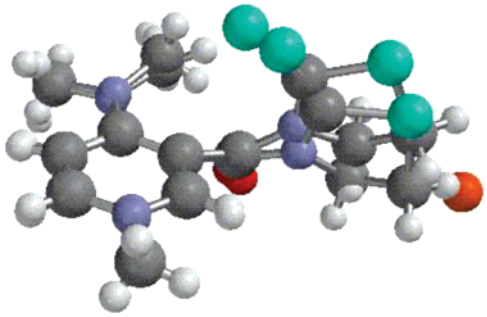


FIGURE 4. Superimposition of the X-ray structures of **1d** and **5b**.

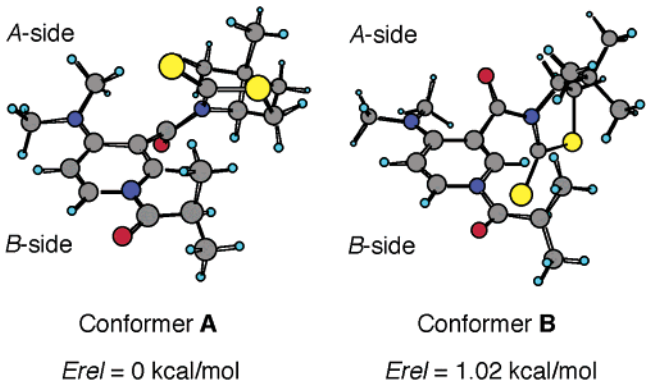
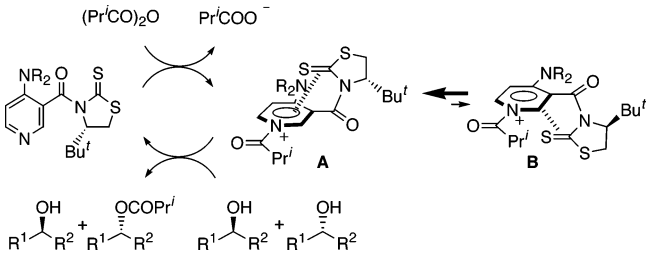


FIGURE 5. Optimized geometries for the isobutyrylpyridinium of **1a** and their relative energies.

SCHEME 6. Plausible Catalytic Cycle for Acymmetric Acylation of *sec*-Alcohols



a similar system,[9] strongly suggesting an intramolecular interaction between C═S and Py$^+$.

Structural optimization of the intermediary *N*-isobutyrylpyridinium of **1a** was carried out by DFT calculations at the B3LYP/6-31G* level. Figure 5 shows two stable conformers, **A** and **B**, and their energy difference is 1.02 kcal/mol. The A side[42] of conformer **A** is blocked by the C═S group. On the other hand, the C═S group of conformer **B** blocks the B side of the pyridinium plane, and the *t*-Bu group blocks the A side of it. In both conformers, orientation of the *N*-acyl groups is in agreement with that predicted by NOE experiments as described above. The energy difference between the two conformers can explain the observation of equilibrium shifts in the ^{1}H NMR studies as indicated in Figure 2. Moreover, the population for the two types of conformers, **A** and **B**, was predicted to be in a ratio of 99.3:0.7 on the basis of the conformer distribution calculated by the AM1 method, supporting the preference of conformer **A**.

Working Model for the Reaction Mechanism. Scheme 6 outlines a plausible catalytic cycle. Acylation of the catalyst with isobutyric anhydride gives conformationally fixed *N*-acylpyridinium salt **A** as a result of an intramolecular cation−π interaction. One of the enantiomers of racemic *sec*-alcohols preferentially attacks the intermediate **A** from the B side[42] to give the corresponding ester with recovery of the catalyst. The catalyst restored conformational freedom allows smooth *N*-acylation of the next cycle.

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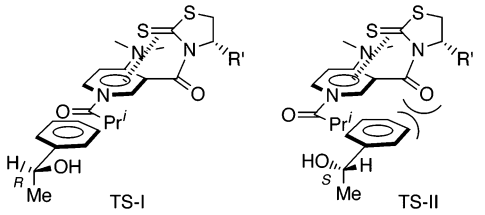

FIGURE 6. Schematic favored (TS-I) and disfavored (TS-II) transition structures for acylation of (*R*)- and (*S*)-alcohols, respectively.

The *R* selectivity in the kinetic resolution can be explained by comparing the two plausible transition-state models TS-I and TS-II for the acylation of (*R*)- and (*S*)-2-phenylethyl alcohols, respectively (Figure 6). Each hydroxy group would approach the B side of the pyridinium in a face-to-face manner due to an intermolecular cation−π interaction between the pyridinium and the phenyl rings.[43] While the (*R*)-alcohol can effectively attack the *N*-acyl group, the (*S*)-hydroxy moiety receives considerable steric repulsion with the chiral auxiliary; therefore, the acylation would preferentially proceed through TS-I to give the (*R*)-ester predominantly. A similar explanation can also be adapted for the acylation of *dl*-diols and *meso*-diols.

The fact that the substituent at the aromatic ring did not affect the *s* values as shown in Table 2 may suggest that the interaction energy is enough to form a hypothetical transition structure even if the alcohol has an electron-withdrawing group. The much lower selectivities in the case of aliphatic alcohols **17** and **18** can be attributable to the absence of the intermolecular cation−π interactions.

Conclusions

We have developed a new class of acylating catalyst having a conformation switch system. The kinetic resolution of various *sec*-alcohols and *dl*-diols and desymmetrization of *meso*-1,*X*-diols ($X = 2-6$) were achieved in good selectivities in the presence of 0.05−5 mol % catalyst **1a**. The structural studies of the catalyst and its intermediate by ^{1}H NMR measurements, X-ray analysis, and AM1 and DFT calculations led to a working model for the reaction mechanism. The key feature in this catalytic acylation reaction is a conformation switch process between self-complexation and uncomplexation induced by *N*-acylation and deacylation steps, respectively, which would play an important role in attaining both good stereoselectivity and high catalyitic activity. Since this catalyst has a compact structure with small molecular weight, and it can be readily prepared from a commercially available pyridine compound with a chiral auxiliary, it is of significant synthetic utility from a practical point of view.

Experimental Section

Preparation of Potassium 4-(Dimethylamino)nicotinate. A mixture of 3-carboxy-4-chloropyridinium hydrochloride (1.1 g, 5.67 mmol) and Me_2NH (40% aqueous solution, 4.0 mL) was stirred at 75 °C for 2 h in a sealed tube. After being cooled to room temperature, the reaction mixture was concentrated. Saturated K_2CO_3 (3.1 g, 22.4 mmol) aqueous solution was added, and the mixture was stirred for 15 min. The reaction mixture was evaporated in vacuo. EtOH was added to the residue, and the reaction mixture was filtered through Celite. The filtrate was concentrated, and EtOH was added. The solution was filtered through Celite again. The residue was evaporated in vacuo at 50 °C to give potassium 4-(dimethylamino)nicotinate (1.3 g, pale brown powder). The mixture was used in the next reaction without further purification.

General Procedure for the Synthesis of 4-(Dimethylamino)-nicotinamides 1−4. A mixture of crude potassium 4-(dimethylamino)nicotinate (408 mg), thionyl chloride (7 mL), and a catalytic amount of dimethylformamide was heated at 78 °C for 12 h. The reaction mixture was concentrated in vacuo to give crude acid chloride. To a solution of the crude acid chloride in dry CH_2Cl_2 (8 mL) were added dropwise (*S*)-4-*tert*-butyl-1,3-thiazolidine-2-thione (468 mg, 2.67 mmol) and Et_3N (1.2 mL, 8.6 mmol) in dry CH_2Cl_2 under a nitrogen atmosphere at 0 °C. The reaction mixture was stirred for 3 h at room temperature. Saturated aqueous $NaHCO_3$ solution was added, and the reaction mixture was extracted twice with CH_2Cl_2. The combined organic layer was washed with brine and dried over anhydrous $MgSO_4$. After removal of the solvent, the residue was purified by silica gel column chromatography (AcOEt:MeOH = 20:1) to afford pure 4-(dimethylamino)nicotinamide (400 mg, 1.24 mmol, 70% for two steps). Recrystallization from AcOEt/hexane gave an analytical specimen of **1a**.

Data for (*S*)-(4-*tert*-butyl-2-thioxothiazolidin-3-yl)[4-(dimethylamino)pyridin-3-yl]methanone (1a): yellow crystals; 70% yield for two steps; mp 159−160 °C; IR (KBr) 3437, 2955, 1674, 1593, 1544, 1313, 1230, 1199, 1130 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, 50 °C) δ 8.22 (br, 1H), 8.18 (d, J = 6.4 Hz, 1H), 6.59 (d, J = 6.4 Hz, 1H), 5.21 (br, 1H), 3.70 (t, J = 8.8 Hz, 1H), 3.38 (d, J = 11.6 Hz, 1H), 2.99 (s, 6H), 1.17 (s, 9H); ^{13}C NMR (100.4 MHz, $CDCl_3$) δ 204.2, 167.7, 153.3, 149.9, 116.2, 108.8, 72.9, 60.3, 42.0, 38.1, 27.0; MS *m*/*z* 323 (M^+, 60), 290 (30), 149 (100), 121 (30), 78 (27); HRMS *m*/*z* calcd for $C_{15}H_{21}ON_3S_2$ 323.1126, found 323.1086; $[\alpha]_D^{24}$ +644 (*c* 1.04, $CHCl_3$).

(*S*)-[4-(Dimethylamino)pyridin-3-yl](4-isopropyl-2-thioxothiazolidin-3-yl)methanone (1b). Purification of **1b** was performed by column chromatography (silica gel, AcOEt:MeOH = 10:1). Recrystallization from CH_2Cl_2/hexane gave an analytical specimen of **1b**: yellow crystals; 34% yield for two steps; mp 163−164 °C; IR (KBr) 2965, 1668, 1589, 1541, 1312, 1201, 808 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, 50 °C) δ 8.19 (s, 1H), 8.18 (d, J = 6.0 Hz, 1H), 6.59 (d, J = 6.0 Hz, 1H), 5.08−5.02 (m, 1H), 3.61 (td, J = 9.6, 3.2 Hz, 1H), 3.23 (dd, J = 11.6, 3.2 Hz, 1H), 2.98 (s, 6H), 2.62−2.54 (m, 1H), 1.15−1.07 (m, 6H); ^{13}C NMR (100.4 MHz, $CDCl_3$) δ 202.8, 167.7, 153.5, 150.2, 116.6, 108.8, 71.8, 42.2, 19.3; MS *m*/*z* 309 (M^+, 75), 276 (53), 149 (100), 121 (40), 78 (32); HRMS *m*/*z* calcd for $C_{14}H_{19}ON_3S_2$ 309.0970; found 309.1003, $[\alpha]_D^{24}$ +354 (*c* 1.01, $CHCl_3$).

(*S*)-(4-Benzyl-2-thioxothiazolidin-3-yl)[4-(dimethylamino)pyridin-3-yl]methanone (1c). Purification of **1c** was performed by column chromatography (silica gel, AcOEt:MeOH = 10:1): yellow oil; 41% yield for two steps; IR (neat) 3019, 2927, 1676, 1590, 1541, 1310, 1233, 1206, 965 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$, 50 °C) δ 8.20 (d, J = 6.4 Hz, 1H), 8.19 (s, 1H), 7.35−7.27 (m, 5H) 6.61 (d, J = 6.4 Hz, 1H), 5.35−5.27 (m, 1H), 3.52 (td, J = 12, 3.7 Hz, 2H), 3.15−3.06 (m, 2H), 3.01 (s, 6H); ^{13}C NMR (100.4 MHz, $CDCl_3$) δ 200.9, 167.5, 153.4, 149.8, 136.0, 129.2, 128.8, 108.7, 68.4, 65.0, 42.2, 39.9, 38.1, 32.9; MS *m*/*z* 357 (M^+, 19), 324 (19), 149 (100), 91 (29), 78 (17); HRMS *m*/*z* calcd for $C_{18}H_{19}ON_3S_2$ 357.0970, found 357.1012; $[\alpha]_D^{24}$ +97.4 (*c* 1.00, $CHCl_3$).

(*S*)-(4-*tert*-Butyl-2-thioxothiazolidin-3-yl)(4-pyrrolidin-1-ylpyridin-3-yl)methanone (2). Purification was performed by column chromatography (silica gel, AcOEt:MeOH = 10:1); yellow crystals; 84% yield for two steps; mp 149.5−151 °C; IR (KBr) 2968, 2864, 1673, 1592, 1534, 1514, 1373, 1313, 1298, 1262, 1246, 1190, 1146, 1021, 980, 821 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, 50 °C) δ 8.50−7.50 (br s, 1H), 6.49 (d, J = 4.8 Hz, 1H), 5.60−4.75 (br s, 1H), 3.71 (br, 1H), 3.38−3.20 (m, 5H), 1.99 (br s, 4H), 1.16 (s, 9H); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (br s, 0.5 H), 8.14 (br s, 1H), 7.92 (br s, 0.5 H), 6.50 (br s, 1H), 5.54 (br s, 0.5 H), 4.99 (br s, 0.5 H), 3.73 (br s, 1 H), 3.50−3.00 (m, 5H), 2.25−1.80 (m, 4H), 1.15 (s, 9H); ^{13}C NMR (100.4 MHz, $CDCl_3$) δ 205.9, 202.5, 167.3,

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152.3, 150.1, 149.7, 149.4, 147.4, 147.1, 115.9, 115.0, 108.7, 108.2, 73.4, 73.2, 72.7, 50.8, 50.0, 38.5, 38.3, 38.2, 32.7, 29.7, 29.6, 27.3, 29.7, 25.9, 25.8, 25.7, 25.5; MS *m*/*z* 349 (M^+, 28), 316 (57), 175 (100), 174 (58), 157 (54), 156 (42), 146 (57); HRMS *m*/*z* calcd for $C_{17}H_{23}ON_3S_2$ 349.1283, found 349.1266; $[\alpha]_D^{24}$ +666 (*c* 1.48, $CHCl_3$).

(*S*)-(4-*tert*-Butyl-2-thioxooxazolidin-3-yl)[4-(dimethylamino)-pyridin-3-yl]methanone (3). Purification of **3** was performed by column chromatography (silica gel, AcOEt): colorless amorphous; 34% yield for two steps; IR (KBr) 2967, 1683, 1591, 1539, 1362, 1334, 1317, 1246, 1206, 1178, 963 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, 50 °C) δ 8.47 (br s, 1H), 8.23 (d, J = 6.4 Hz, 1H), 6.65 (d, J = 6.4 Hz, 1H), 4.91 (br s, 1H), 4.55 (m, 2H), 3.01 (s, 6H), 1.05 (s, 9H); ^{13}C NMR (100.4 MHz, $CDCl_3$) δ 187.2 168.6, 153.8, 151.9, 150.4, 115.3, 108.9, 69.7, 64.5, 42.4, 36.3, 26.7, 25.8; MS *m*/*z* 307 (M^+, 15), 274 (17), 149 (100), 148 (44), 121 (12); HRMS *m*/*z* calcd for $C_{15}H_{21}N_3O_2S$ 307.1355, found 307.1339; $[\alpha]_D^{24}$ +164 (*c* 1.39, $CHCl_3$).

(*S*)-4-*tert*-Butyl-3-[[4-(dimethylamino)pyridin-3-yl]carbonyl]-oxazolidin-2-one (4). Purification of **4** was performed by column chromatography (silica gel, AcOEt:MeOH = 10:1); light yellow oil; 27% yield; IR (KBr) 2958, 1767, 1673, 1589, 1539, 1519, 1333, 1310, 1267, 1219, 1072, 964 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.46 (s, 1H), 8.26 (d, J = 5.6 Hz, 1H), 6.69 (d, J = 5.6 Hz, 1H), 4.70 (s, 1H), 4.37 (m, 2H), 2.94 (s, 6H), 0.96 (s, 9H); ^{13}C NMR (100.4 MHz, $CDCl_3$) δ 168.0, 153.9, 151.3, 150.7, 114.5, 109.0, 64.9, 60.2, 41.9, 36.2, 25.6; mp 143−144 °C; MS *m*/*z* 291 (M^+, 16.1), 149 (91), 148 (100), 121 (18), 119 (11); HRMS *m*/*z* calcd for $C_{15}H_{21}O_3N_3$ 291.1583, found 291.1559; $[\alpha]_D^{24}$ +280 (*c* 1.03, $CHCl_3$).

General Procedure for the Synthesis of Pyridinium Salts 5 and 7. Gaseous MeBr was bubbled into a solution of 4-(alkylamino)nicotinamide (0.31 mmol) in dry CH_3CN (3 mL), and the solution was stirred for 2 h at room temperature. After evaporation of the solvent, a yellow oily product was yielded quantitatively.

Data for (*S*)-3-[(4-*tert*-butyl-2-thioxothiazolidin-3-yl)carbonyl]-4-(dimethylamino)-1-methylpyridinium bromide (5): yellow oil; IR (neat) 2958, 1682, 1653, 1559, 1290, 1219, 1180 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.55 (s, 1H), 8.08 (d, J = 6.8 Hz, 1H), 6.87 (d, J = 6.8 Hz, 1H), 5.19−5.12 (m, 1H), 4.15 (s, 3H), 3.31−3.23 (m, 8H), 1.12 (s, 9H); ^{13}C NMR (100.4 MHz, $CDCl_3$) δ 208.1, 162.7, 154.2, 142.0, 118.1, 109.8, 74.6, 44.9, 38.4, 34.5, 31.6, 27.5, 22.7, 14.1; MS *m*/*z* 323 (M^+ − 95, 18), 290 (17), 221(18), 175 (29), 149 (96), 129 (100), 57 (29); HRMS *m*/*z* calcd for $C_{15}H_{21}ON_3S_2$ 323.1126, found 323.1125; $[\alpha]_D^{24}$ +603 (*c* 1.00, $CHCl_3$).

Data for 4-(dimethylamino)-3-(dimethylcarbamoyl)-1-methylpyridinium bromide (7): brown oil; IR (neat) 2937, 1652, 1563, 1404, 1225, 1165, 1082, 822 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 8.52 (dd, J = 7.4, 1.9 Hz, 1H), 8.46 (s, 1H), 7.11 (d, J = 7.4 Hz, 1H), 4.24 (s, 3H), 3.23 (s, 6H), 3.19 (s, 3H), 3.12 (s, 3H); ^{13}C NMR (100.4 MHz, $CDCl_3$) δ 165.2, 154.1, 142.9, 142.5, 118.0, 110.6, 45.5, 42.2, 40.1, 35.4; MS *m*/*z* 193 (M^+ − 95, 70), 176 (14), 149 (100), 121 (45), 78 (28); HRMS *m*/*z* calcd for $C_{10}H_{15}ON_3$ 193.1215, found 193.1218.

General Procedure for the Kinetic Resolution of Racemic *sec*-Alcohols 8−18. To a solution of racemic alcohol (1.24 mmol) was added 73 μL (0.00621 mmol) of a CH_2Cl_2 solution of catalyst **1a** (55.0 mg of catalyst in 2.0 mL of CH_2Cl_2). The mixture was concentrated, and *t*-BuOMe (6.2 mL) and Et_3N (138 μL, 0.992 mmol) were added to the residue. Isobutyric anhydride (144 μL, 0.868 mmol) was added to the solution at 0 °C and the resulting solution stirred for 12 h at 0 °C. After addition of a saturated $NaHCO_3$ solution, the reaction mixture was extracted twice with Et_2O. The combined organic layer was washed with brine and dried over anhydrous $MgSO_4$. This was filtered, and the filtrate was concentrated to give a crude product, which was purified by column chromatography (hexane:ethyl acetate = 3:1) to afford (*S*)-alcohol and a corresponding ester. The optical purity of the alcohol was determined by HPLC analysis with Daicel Chiralcel OB-H or OD-H (*i*-PrOH:hexane = 1:9). The optical purity of the ester was also determined by HPLC analysis after hydrolysis with 2 N KOH/MeOH.

General Procedure for the Kinetic Resolution of Racemic Diols 19 and 22. To a solution of racemic diol (0.180 mmol) in *t*-BuOMe (1.0 mL) were added 5 mol % catalyst **1a** (2.9 mg, 0.00897 mmol) and Et_3N (0.270 mmol). Isobutyric anhydride (0.270 mmol) was added to the solution at 0 °C and the resulting solution stirred for 3 h. After addition of methanol, the solution was further stirred for 20 min. Concentration of the reaction mixture gave a crude product, which was purified by column chromatography (hexane:ethyl acetate = 3:1) to afford (*R*,*R*)-diester, (*S*,*S*)-monoester, and (*S*,*S*)-diol. The optical purity of the alcohol was determined by HPLC analysis with Daicel Chiralcel OB-H or AD (*i*-PrOH: hexane = 1:9). The optical purity of the esters was also determined by HPLC analysis after hydrolysis into diols with 2 N KOH/MeOH.

Data for 1,2-bis[(1*R*)-(isobutyryloxy)ethyl]benzene (20): IR (neat) 3036, 2977, 1736, 1470, 1388, 1259, 1158, 1058, 761 cm^{-1}; ^1H NMR (400 Hz, $CDCl_3$) δ 1.13 (d, J = 7.0 Hz, 6H), 1.17 (d, J = 7.0 Hz, 6H), 1.60 (d, J = 6.4 Hz, 6H), 2.57 (sept, J = 7.0 Hz, 2H), 6.11 (q, J = 6.4 Hz, 2H), 7.26−7.28 (m, 2H), 7.37−7.39 (m, 2H); MS *m*/*z* 306 (M^+, 0.5), 218 (71), 175 (56), 148 (100), 131 (75), 71 (81); HRMS *m*/*z* calcd for $C_{18}H_{26}O_4$ (M^+) 306.1831, found 306.1859.

Data for 1-[(1*S*)-(isobutyryloxy)ethyl]-2-[(1*S*)-hydroxyethyl]-benzene (21): IR (neat) 3423, 3035, 2976,1735, 1589, 1453, 1375, 1261, 1159, 1060, 761 cm^{-1}; ^1H NMR (400 Hz, $CDCl_3$) δ 1.13 (d, J = 7.0 Hz, 3H), 1.16 (d, J = 7.0 Hz, 3H), 1.56 (d, J = 6.4 Hz, 3H), 1.57 (d, J = 6.4 Hz, 3H), 2.39 (br, 1H), 2.55 (sept, J = 7.0 Hz, 1H), 5.21 (q, J = 6.4 Hz, 1H), 6.11 (q, J = 6.4 Hz, 1H), 7.28−7.30 (m, 2H), 7.41−7.45 (m, 2H); MS *m*/*z* 236 (M^+, 0.4), 218 (2.5) 148 (73), 133 (100), 131 (59); HRMS *m*/*z* calcd for $C_{14}H_{18}O_2$ ($M^+ - H_2O$) 218.1307, found 218.1284.

Data for 1,3-bis[(1*R*)-(isobutyryloxy)ethyl]benzene (23): IR (neat) 2979, 1734, 1612, 1472, 1387, 1258, 1156, 1066, 706 cm^{-1}; ^1H NMR (400 Hz, $CDCl_3$) δ 1.16 (d, J = 7.2 Hz, 6H), 1.18 (d, J = 7.2 Hz, 6H), 1.52 (d, J = 6.4 Hz, 6H), 2.58 (sept, J = 7.2 Hz, 2H), 5.87 (q, J = 6.4 Hz, 2H), 7.23−7.35 (m, 4H); MS *m*/*z* 219 ($M^+ - 87$, 100), 218 (41), 148 (68), 131 (81), 71 (44); HRMS *m*/*z* calcd for $C_{14}H_{19}O_2$ ($M^+ - C_4H_8O_2$) 219.1385, found 219.1382.

Data for 1-[(1*S*)-(isobutyryloxy)ethyl]-3-[(1*S*)-hydroxyethyl]-benzene (24): IR (neat) 3449, 2979, 1735, 1610, 1388, 1261, 1158, 1065, 707 cm^{-1}; ^1H NMR (400 Hz, $CDCl_3$) δ 1.16 (d, J = 6.8 Hz, 3H), 1.18 (d, J = 6.8 Hz, 3H), 1.50 (d, J = 6.4 Hz, 3H), 1.52 (d, J = 6.4 Hz, 3H), 1.80 (s, 1H), 2.57 (sept, J = 6.8 Hz, 1H), 4.91 (q, J = 6.4 Hz, 1H), 5.87 (q, J = 6.4 Hz, 1H), 7.24−7.36 (m, 4H); MS *m*/*z* 236 (M^+, 0.2), 219 (29), 218 (41), 166 (22), 149 (100), 105 (67), 71 (29); HRMS *m*/*z* calcd for $C_{14}H_{19}O_2$ ($M^+ - OH$) 219.1385, found 219.1341.

General Procedure for Desymmetrization of *meso*-Diols. To a solution of a *meso*-diol (0.15 mmol) and **1a** (0.0077 mmol) in 1 mL of *t*-BuOMe were added Et_3N (17 μL, 0.23 mmol) and isobutyric anhydride (38 μL, 0.23 mmol) at 0 °C. The mixture was stirred for 3 h at 0 °C, and after addition of MeOH, the reaction mixture was further stirred for 30 min. After concentration of the solution, the residue was purified by column chromatography (hexane:AcOEt = 3:1) to give monoester, diester, and recovered *meso*-diol. The optical purity was determined by HPLC analysis with Daicel Chiralpak AD (*i*-PrOH:hexane = 1:9).

Data for (1*R*,2*S*)-1,2-bis(isobutyryloxy)-1,2-diphenylethane (25b): IR (KBr) 3068, 2975, 1727, 1606, 1458, 1346, 1256, 1156, 1078, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.37 (m, 10H), 6.07 (s, 2H), 2.48 (sept, J = 6.8 Hz, 2H), 1.06 (d, J = 6.8 Hz, 6H), 1.03 (d, J = 6.8 Hz, 6H); MS *m*/*z* 267 ($M^+ - 87$, 6.3), 196 (11), 177 (68), 105 (11), 71 (100); HRMS *m*/*z* calcd for $C_{18}H_{19}O_2$ ($M^+ - C_4H_7O_2$) 267.1385, found 267.1361.

Data for (1*R*,3*S*)-1,3-diphenyl-1-(isobutyryloxy)-3-propanol (26a): IR (neat) 3447, 2975, 1733, 1604, 1456, 1387, 1258, 1156, 1068, 700 cm^{-1}; ^1H NMR (400 Hz, $CDCl_3$) δ 1.13 (d, J = 7.0

Hz, 3H), 1.17 (d, $J = 7.0$ Hz, 3H), 1.21 (d, $J = 7.0$ Hz, 1H), 2.10−2.17 (m, 1H), 2.43−2.48 (m, 1H), 2.53 (sept, $J = 7.0$ Hz, 1H), 4.63 (dd, $J = 5.0$HZ, 7.0 Hz, 1H), 5.84 (t, $J = 6.8$HZ, 1H), 7.28−7.36 (m, 10H); MS *m*/*z* 298 (M^+, 0.2), 280 (7.0), 237 (7.4), 210 (85), 104 (100); HRMS *m*/*z* calcd for $C_{19}H_{20}O_2$ ($M^+ - H_2O$) 280.1463, found 280.1493.

Data for (1*R*,3*S*)-1,3-bis(isobutyryloxy)-1,3-diphenylpropane (26b): IR (neat) 3035, 2975, 1737, 1587, 1470, 1387, 1252, 1153, 1067, 700 cm^{-1}; ^1H NMR (400 Hz, $CDCl_3$) δ 1.13 (d, $J = 7.3$ Hz, 6H), 1.18 (d, $J = 7.3$ Hz, 6H), 2.17−2.23 (m, 1H), 2.54 (sept, $J = 7.3$ Hz, 2H), 2.57−2.63 (m, 1H), 5.63 (t, $J = 6.8$ Hz, 2H), 7.34−7.34 (m, 10H); MS *m*/*z* 368 (M^+, 0.7), 280 (40), 237 (35), 210 (94), 105 (60) 104 (49), 71 (100); HRMS *m*/*z* calcd for $C_{23}H_{28}O_4$ (M^+) 368.1988, found 368.1941.

Data for 1-[(1*R*)-(isobutyryloxy)ethyl]-2-[(1*S*)-hydroxyethyl]-benzene (27a): IR (neat) colorless oil; 87% yield; 3475, 2977, 1734, 1471, 1374, 1262, 1198, 1061, 762 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.52 (d, $J = 6.8$ Hz, 1H), 7.39 (d, $J = 6.8$ Hz, 1H), 7.30 (m, 2H), 6.13 (q, $J = 6.4$ Hz, 1H), 5.33 (q, $J = 6.4$ Hz, 1H), 2.53 (sept, $J = 6.8$ Hz, 1H), 1.55 (d, $J = 6.8$ Hz, 6H), 1.14 (d, $J = 6.8$ Hz, 3H), 1.10 (d, $J = 6.8$ Hz, 3H); MS *m*/*z* 236 (M^+, 6.5), 148 (37) 133 (100); HRMS *m*/*z* calcd for $C_{14}H_{20}O_3$ 236.1412, found 236.1387.

Data for 1-[(1*R*)-(isobutyryloxy)ethyl]-2-[(1*S*)-(isobutyryloxy)-ethyl]benzene (27b): colorless oil; 13% yield; IR ($CHCl_3$) 2977, 1734, 1472, 1387, 1260, 1157, 1056, 761 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.42 (m, 2H), 7.34 (m, 2H), 6.19 (q, $J = 6.8$ Hz, 2H), 2.56 (sept, $J = 6.8$ Hz, 2H), 1.55 (d, $J = 5.4$ Hz, 6H), 1.19 (d, $J = 6.8$ Hz, 6H), 1.15 (d, $J = 6.8$ Hz, 6H); MS *m*/*z* 306 (M^+, 4.3), 218 (7.3) 43 (100); HRMS *m*/*z* calcd for $C_{14}H_{18}O_2$ ($M^+ - C_4H_8O_2$) 218.1307, found 218.1277.

Data for isobutyric acid (1*R*,4*S*)-4-hydroxy-1,2,3,4-tetrahydronaphthalen-1-yl ester (28a): IR ($CHCl_3$) 3419, 3020, 2976, 1720, 1456, 1388, 1259, 1198, 1041, 756 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.55 (m, 1H), 7.38−7.26 (m, 3H), 5.93 (m, 1H), 4.77 (m, 1H), 2.59 (sept, $J = 6.8$ Hz, 1H), 2.12−2.01 (m, 4H), 1.21 (d, $J = 7.3$ Hz, 3H), 1.19 (d, $J = 6.8$ Hz, 3H); MS *m*/*z* 216 ($M^+ - 18$, 7.3), 147 (14), 146 (100), 129 (56), 71 (22); HRMS *m*/*z* calcd for $C_{14}H_{16}O_2$ ($M^+ - H_2O$) 216.1150, found 216.1090.

Data for isobutyric acid (1*R*,4*S*)-4-(isobutyryloxy)-1,2,3,4-tetrahydronaphthalen-1-yl ester (28b): IR (neat) 3036, 2874, 3036, 2975, 1733, 1471, 1387, 1254, 1154, 993, 775 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.33−7.27 (m, 4H), 5.95 (m, 2H), 2.61 (sept, $J = 6.8$ Hz, 2H), 2.16−2.03 (m, 2H), 1.21 (d, $J = 7.37$ Hz, 12H); MS *m*/*z* 216 ($M^+ - 88$, 21), 146 (100), 129 (90), 71 (33); HRMS *m*/*z* calcd for $C_{14}H_{16}O_2$ ($M^+ - C_4H_8O_2$) 216.1150, found 216.1082.

Data for 1-[(1*R*)-(isobutyryloxy)ethyl]-3-[(1*S*)-hydroxyethyl]-2,4-dimethylbenzene (29a): colorless oil; 87% yield; IR (neat) 3447, 2975, 1734, 1506, 1456, 1387, 1259, 1159, 1079, 870 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.34 (s, 1H), 7.26 (s, 1H), 6.02 (q, $J = 6.8$ Hz, 1H), 5.10 (q, $J = 6.4$ Hz, 1H), 2.58 (sept, $J = 6.8$ Hz, 1H), 2.32 (s, 3H), 2.29 (s, 3H), 1.50 (d, $J = 6.4$ Hz, 3H), 1.47 (d, $J = 6.4$ Hz, 3H) 1.20 (d, $J = 6.8$ Hz, 3H), 1.17 (d, $J = 6.8$ Hz, 3H); MS *m*/*z* 264 (M^+, 1.5), 176 (87), 161 (100), 133 (33); HRMS *m*/*z* calcd for $C_{16}H_{24}O_3$ 264.1725, found 264.1707; $[\alpha]_D^{24}$ +49.9 (*c* 1.0, MeOH).

Data for 1-[(1*R*)-(isobutyryloxy)ethyl]-3-[(1*S*)-(isobutyryloxy)-ethyl]-2,4-dimethylbenzene (29b): colorless oil; 11% yield; IR ($CHCl_3$) 2976, 1735, 1473, 1388, 1259, 1158, 1044, 871 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.42 (s, 1H), 6.93 (s, 1H), 6.02 (q, $J = 6.8$ Hz, 2H), 2.54 (sept, $J = 6.8$ Hz, 2H), 2.32 (s, 6H), 1.49 (d, $J = 6.4$ Hz, 6H), 1.18 (d, $J = 6.8$ Hz, 3H), 1.15 (d, $J = 6.8$ Hz, 3H); MS *m*/*z* 334 (M^+, 1.1), 246 (96), 159 (100), 158 (96); HRMS *m*/*z* calcd for $C_{16}H_{22}O_2$ ($M^+ - C_4H_8O_2$) 246.1620, found 246.1586.

Data for 1-[(1*R*)-(isobutyryloxy)ethyl]-4-[(1*S*)-hydroxyethyl]-benzene (30a): colorless oil; 69% yield; IR (neat) 3449, 2977, 1735, 1513, 1470, 1388, 1261, 1158, 1061, 833 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.34 (s, 1H), 7.26 (s, 1H), 6.02 (q, $J = 6.8$ Hz, 1H), 5.10 (q, $J = 6.4$ Hz, 1H), 2.58 (sept, $J = 6.8$ Hz, 1H), 2.32 (s, 3H), 2.29 (s, 3H), 1.50 (d, $J = 6.4$ Hz, 3H), 1.47 (d, $J = 6.4$ Hz, 3H) 1.20 (d, $J = 6.8$ Hz, 3H), 1.17 (d, $J = 6.8$ Hz, 3H); MS *m*/*z* 236 (M^+, 31), 148 (38) 43 (100); HRMS *m*/*z* calcd for $C_{14}H_{20}O_3$ 236.1412, found 236.1380.

Data for 1-[(1*R*)-(isobutyryloxy)ethyl]-4-[(1*S*)-(isobutyryloxy)-ethyl]benzene (30b): colorless oil; 24% yield; IR (neat) 2079, 1734, 1472, 1387, 1258, 1157, 1021, 831 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.32 (s, 2H), 5.86 (q, $J = 6.8$ Hz, 2H), 2.56 (sept, $J = 6.8$ Hz, 2H), 1.50 (d, $J = 6.8$ Hz, 6H) 1.18 (d, $J = 6.8$ Hz, 3H), 1.16 (d, $J = 6.8$ Hz, 3H); MS *m*/*z* 306 (M^+, 2.0), 218 (137) 148 (100), 130 (14); HRMS *m*/*z* calcd for $C_{14}H_{18}O_2$ ($M^+ - C_4H_8O_2$) 218.1307, found 218.1277.

Preparation of (*R*)-1-[2-[1-(Isobutyryloxy)ethyl]phenyl]ethanone (31). To a solution of monoester **27a** (37 mg, 0.156 mmol) in dry CH_2Cl_2 (3.2 mL) was added Dess−Martin periodinane (79.7 mg, 0.188 mmol). The solution was stirred for 1 h, and the precipitate was filtered. Concentration of the filtrate gave a crude product, which was purified by preparative TLC (hexane:AcOEt = 4:1) to afford pure **31** (36 mg): oil; IR (neat) 2976, 1735, 1686, 1573, 1487, 1356, 1252, 1060, 763 cm^{-1}; ^1H NMR (400 Hz, $CDCl_3$) δ 1.13 (d, $J = 6.8$ Hz, 3H), 1.15 (d, $J = 6.8$ Hz, 3H), 1.57 (d, $J = 6.4$ Hz, 3H), 2.54 (sept, $J = 6.8$ Hz, 1H) 2.64 (s, 3H), 6.22 (q, $J = 6.4$ Hz, 1H), 7.33 (dt, $J = 1.2$, 6.8 Hz, 1H), 7.49 (dt, $J = 1.2$, 6.8 Hz, 1H), 7.56 (dd, $J = 1.2$, 6.8 Hz, 1H), 7.64 (dd, $J = 1.2$, 6.8 Hz, 1H); MS *m*/*z* 163 ($M^+ - 71$, 100), 147 (51), 146 (32), 129 (25), 71 (15); HRMS *m*/*z* calcd for $C_{10}H_{11}O_2$ ($M^+ - C_4H_7O$) 163.0759, found 163.0685; $[\alpha]_D^{26.5}$ +3.6 (*c* 0.95, $CHCl_3$).

Preparation of (*R*)-1-[4-(1-Hydroxyethyl)phenyl]ethanone (32). To a solution of monoester **30a** (22 mg, 0.1 mmol) in CH_2Cl_2 (4 mL) was added Dess−Martin periodinane (43 mg, 0.1 mmol). After being stirred for 30 min, the reaction mixture was concentrated. The residue was purified by preparative TLC (hexane:AcOEt = 3:1) to give 1-[4-[1-(isobutyryloxy)ethyl]phenyl]ethanone (20 mg), which was hydrolyzed with 2 N NaOH/MeOH to give **32**: colorless oil; 91% yield for two steps; ^1H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, $J = 6.8$ Hz, 1H), 7.47 (d, $J = 7.8$ Hz, 1H), 4.98 (q, $J = 6.8$ Hz, 1H), 2.61 (s, 3H), 151 (d, $J = 6.8$ Hz, 3H); $[\alpha]_D^{24}$ +41.7 (*c* 0.69, $CHCl_3$).

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Supporting Information Available: Details of the kinetic resolution of *sec*-alcohols, ^1H NMR spectra for **1a**−**1d**, **2**−**4**, **5a**, **5b**, **6**, **7**, **20**, **21**, **23**, **24**, **25b**, **26a**−**30a**, **26b**−**30b**, and **31**, ^1H NMR chemical shift data for **1a**, **5**, **6**, and **7** and $\Delta\delta$ values, ^1H NMR spectra for NOE experiments, X-ray crystallographic data and CIF files for **1d** and **5b**, Cartesian coordinates of conformers **A** and **B** from optimized DFT calculations, and conformer distribution predicted by AM1 calculations. This material is available free of charge via the Internet at http://pubs.acs.org.

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