Pergamon

Tetrahedron 56 (2000) 8883–8891

TETRAHEDRON

A Chiral Axis due to an Acyclic Imide–Ar Bond: a Study of Steric Effects of Acyl Groups on Racemization

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Received 14 August 2000; accepted 20 September 2000

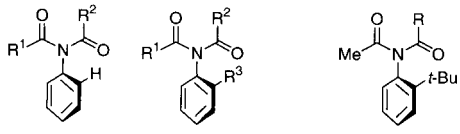
Abstract—Studies on the racemization in a series of optically active compounds **3a**–**e**, including the steric effect of their acyl groups, are described. The first example of optically active compounds **3c** and **3d**, which possess axial chirality based on an acyclic imide–Ar bond, has been reported. A quite interesting result has been revealed, namely, that **3a** bearing a bulky acyl group rather than a relatively small one racemized more easily. To explain this observed phenomenon, ^{13}C NMR experiments and the reaction with benzylamine of **3a**–**e** were undertaken. These results suggested that the *t*-BuCO–N bond in **3a** which racemized easily, is more twisted, compared with the RCO–N bonds in **3b**–**e** which are relatively stable to racemization. Furthermore, the absolute configuration of **3b** and **3c** has been determined to be *R* by the CD spectrum and the X-ray crystallographic analysis of racemic **3f** has been accomplished. © 2000 Published by Elsevier Science Ltd.

Introduction

Optically active biaryl compounds such as binaphthyl and biphenyl derivatives, due to the rotational barrier about the C_{aryl}–C_{aryl} bond, have been well known,[1] but optically active compounds which possess axial chirality based on the N–C bond, have received little attention.[2] After a pioneering report by Curran in 1994,[3] several examples of optically active N–Ar axially chiral cyclic imides and amides, have been reported.[4,5] However, to the best of our knowledge, no optically active compound has been reported that possesses axial chirality based on an acyclic imide N–Ar bond. In the course of our study on the reactivity[6] of the imide in *N*-acyl-*N*-arylacetamides, we became very interested in the imide N–Ar axial chirality of these compounds.[7,8] In this paper, we would like to report the first example of optically active compounds **3c** and **3d** which possess axial chirality based on the acyclic imide N–Ar bond.[7] A quite interesting result is also described, namely, that **3a** bearing a bulky acyl group rather than a relatively small one racemized more easily. Furthermore, the absolute configuration of optically active compounds **3b** and **3c** has been determined by the CD spectrum, and the X-ray crystallographic analysis of racemic **3f**, whose conformation should be similar to that of **3e**, has been accomplished.

Results and Discussion

The imide group and the phenyl ring in **1** are not coplanar in the ground state, but instead twist in order to relieve unfavorable steric interactions between the *ortho*-hydrogen on the phenyl ring and the imide group.[9] Replacing one *ortho*-hydrogen with a bulky group (from **1** to **2**) increases both the imide N–Ar torsion angle and the barrier to rotation through planarity. On the basis of the foregoing concept, we planned to search for an optically active N–Ar axially chiral compound. We chose compound **3** bearing one large (*t*-butyl) and one small (H) *ortho* substituents on the phenyl ring as the candidates, which might retain sufficient rotational barriers to be stable to racemization at room temperature.



1 **2** (R^3 = bulky group)

3a: R = *t*-Bu **3d**: R = Et
3b: R = *i*-Pr **3e**: R = Ph
3c: R = *i*-Bu **3f**: R = 4-trifluoromethylphenyl

Optically active compounds **3a**–**e** were given through the optical resolution of racemic **3a**–**e**, which were prepared by acylation of *N*-(2-*tert*-butylphenyl)acetamide, by HPLC using chiral phase column (DAICEL CHIRALCEL OD, eluent: hexane/isopropanol). At first, the stability to racemization in benzene was investigated with optically active compounds **3a**, **3b** and **3d**.[10,11] The results are shown in

Keywords: N–C axial chirality; atropisomer; acyclic imide; twist; steric effect.

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0040–4020/00/$ - see front matter © 2000 Published by Elsevier Science Ltd.
PII: S0040-4020(00)00852-8

Table 1. Initial study of the stability to racemization with optically active **3a**, **3b**, and **3d** (all reactions were carried out in benzene at 25°C)

Entry	Compound	Results
1	**3a**	0 h, 64% ee; within 30 min, 0% ee
2	**3b**	0 h, 91% ee; after 3 days, 89% ee
3	**3d**	0 h, >99% ee; after 3 days, >99% ee

Table 1. Surprisingly, optically active compound **3a** bearing a bulky *t*-BuCO group racemized rapidly at 25°C within 30 min, affording the racemate (entry 1). Slight racemization of **3b** bearing a sterically medium-sized *i*-PrCO group was observed at 25°C (entry 2). On the other hand, no loss of the optical purity of **3d** bearing a sterically small EtCO group, was observed at 25°C, even after 3 days (entry 3). As an initial result, it was found that **3** bearing a smaller acyl group was more stable to racemization.

With the intention of gaining further insight into the steric effects of acyl groups on racemization, we planned to obtain the kinetic parameters of racemization for **3c** and **3e** bearing *i*-BuCO and PhCO groups, in addition to **3a**, **3b** and **3d** bearing *t*-BuCO, *i*-PrCO and EtCO groups as shown in Table 2. Heating optically active compounds **3b**–**e** in benzene at four different temperatures and measurement of the rate constants for their racemization at each temperature, gave transition-state functions,[12] though, unfortunately, the racemization of **3a** was too rapid at 25°C for the exact rate constant to be determined. The free energies of activation ($\Delta G^{\ddagger}$) at 27°C for racemization of **3b**, **3c**, **3d** and **3e** were 27.0, 30.5, 28.6 and 26.3 kcal/mol, respectively. These values in the $\Delta G^{\ddagger}$ were found to be affected by the steric effect of their acyl groups. Accordingly, **3b** (R=*i*-Pr) and **3e** (R=Ph) bearing relatively large acyl groups rather than a small one (R=*i*-Bu or Et), racemized more easily. To the best of our knowledge, the relatively stable compounds **3c** and **3d** are the first example of optically active compounds which possess axial chirality based on the acyclic imide N–Ar bond. The enthalpies of activation ($\Delta H^{\ddagger}$) for racemization of **3b**, **3c**, **3d** and **3e** were 22.7±1.4, 27.8±0.6, 28.1±0.4 and 25.1±0.2 kcal/mol, respectively. These differences in the $\Delta H^{\ddagger}$ would be mainly due to the destabilization in the ground state. Accordingly, a repulsion between the acetyl C=O and the acyl R group in **3** (Fig. 1), might cause their destabilization. The entropies of activation ($\Delta S^{\ddagger}$) for racemization of **3b**, **3c**, **3d** and **3e** were −13.3±4.5, −8.98±1.92, −1.44±1.27 and −4.05±0.71, respectively. The nearly zero value in the entropy of activation for **3d** is interesting. The $\Delta S^{\ddagger}$ of **3d** would suggest that its racemization occurs with retention of the imide geometry in the ground state. These steric effects prompted us to investigate the relationship between the imide structure in the ground state and the stability to racemization of **3a**–**e**.

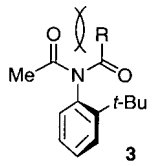

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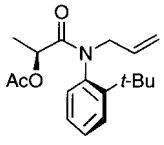
Figure 1.

The assignments of absolute configurations of optically active compounds **3b** and **3c** were achieved by comparison with the CD spectrum of **4** of known configuration,[4c] though the absolute configuration of **3d** and **3e** could not be determined by the CD spectrum. The representative CD spectra of the enantiomers, **3c** and **4**, are shown in Fig. 2. As a result, the absolute configurations of (−)-**3b** and (−)-**3c** with negative values of the specific rotation were determined to be *R* as shown in Fig. 3.



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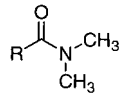
In order to obtain structural information on the imide moieties of **3a**–**e** in the ground state, we undertook a series of ^{13}C NMR experiments as shown in Table 3.[13] The data of the acyl carbonyl signals[14] of **3a**–**e** were corrected by subtracting those of the corresponding planar *N*,*N*-dimethyl carboxyamides **5a**–**f**, to cancel out the substituent effect on the carbonyl group, and the differences were indicated as $\Delta\delta^{13}C$. From these results, it is clear that the $\Delta\delta^{13}C$ value of *t*-butylcarbonyl carbon of **3a** is much larger than those of the acetyl carbonyl carbon in **3a** and the other acyl carbonyl ones of **3b**–**e**. The large difference can be explained as due to the reduction of amide resonance throughout the RCO–N bond rotation. Accordingly, the *t*-BuCO–N bond in **3a** is more twisted than the MeCO–N bond in **3a** and the other RCO–N bonds in **3b**–**e**.



5a: R = *t*-Bu **5d**: R = Et
5b: R = *i*-Pr **5e**: R = Ph
5c: R = *i*-Bu **5f**: R = CH_3

Table 2. Transition-state functions of **3b**–**e** (all reactions were carried out in benzene)

Entry	Compound	$\Delta H^{\ddagger}$[a] (kcal/mol)	$\Delta S^{\ddagger}$[a] (cal/K·mol)	$\Delta G^{\ddagger}$ at 27°C (kcal/mol)
1	**3a**	_[b]	_[b]	_[b]
2	**3b**	22.7±1.4	−13.3±4.5	27.0
3	**3c**	27.8±0.6	−8.94±1.92	30.5
4	**3d**	28.1±0.4	−1.44±1.27	28.6
5	**3e**	25.1±0.2	−4.05±0.71	26.3

[a] The transition-state functions were calculated according to Eyring's equation.
[b] The racemization of **3a** was too rapid at 25°C for the exact rate constant to be determined.

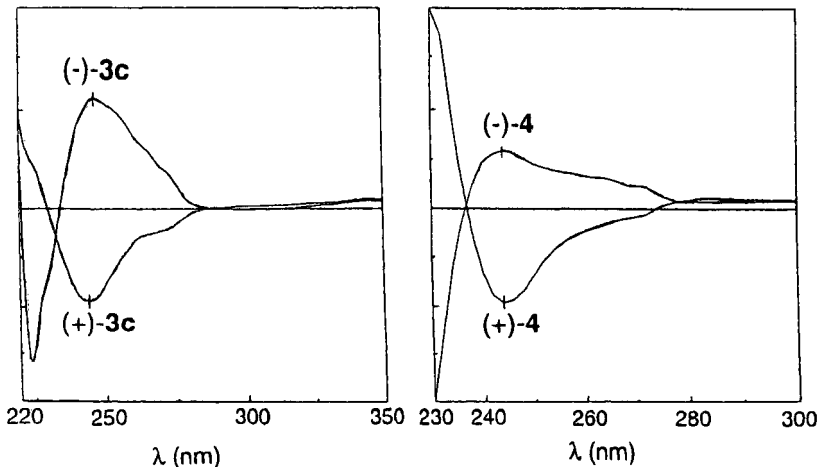
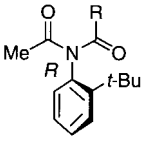


Figure 2. The representative CD spectra of **3c** and **4** in CH_3CN.



(-)-**3b** and (-)-**3c**

Figure 3.

In order to verify the large twist of the *t*-BuCO–N bond in **3a**, we chose to investigate the reactivity of **3a**–**e** with benzylamine (**6**). It has been known that twisted amide groups are more reactive to a nucleophile than the planar ones.[15] The twisted *t*-BuCO–N bond in **3a** is expected to be readily attacked by **6**, whereas the MeCO–N bond in **3a** and the other RCO–N bonds in **3b**–**e** are not. The results are shown in Table 4. As can be seen, only the *t*-BuCO–N bond in **3a** was readily reacted with **6** to give **7** chemoselectively (entry 1). On the contrary, the reactivity of the RCO–N bonds in **3b**–**d** was quite low (entries 2–4), and acetamide **8** was formed selectively. The reaction of **3e** required a prolonged period (10 h, entry 5): the reactivity of this aryl group might be somewhat different from those of the alkyl acyl groups. Again, these results support that the *t*-BuCO–N bond in **3a** is relatively more twisted than the MeCO–N bond in **3a** and the other RCO–N bonds in **3b**–**e**. It is noteworthy that the *t*-BuCO–N bond in **3a**, which racemized easily, is more twisted, compared with the RCO–N bonds in **3b**–**e** which were relatively stable to racemization.

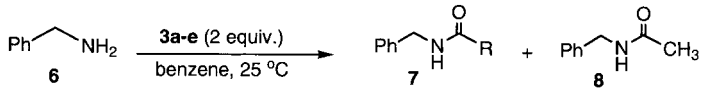
Table 3. ^{13}C NMR chemical shifts (δ, ppm) of acyl carbonyl in **3a**–**e** (recorded at 100 MHz in C_6D_6)

Entry	Compound	δ ^{13}C		$\Delta\delta$ ^{13}C	
		RCO	CH_3CO	RCO	CH_3CO
1	**3a**	184.6 (176.4)[a]	173.2 (169.2)[f]	8.2	4.0
2	**3b**	180.2 (175.9)[b]	173.2 (169.2)[f]	4.3	4.0
3	**3c**	174.6 (170.7)[c]	172.4 (169.2)[f]	3.9	3.2
4	**3d**	176.4 (172.4)[d]	172.8 (169.2)[f]	4.0	3.6
5	**3e**	173.1 (170.8)[e]	173.3 (169.2)[f]	2.3	4.1

[a] The data of **5a**.
[b] The data of **5b**.
[c] The data of **5c**.
[d] The data of **5d**.
[e] The data of **5e**.
[f] The data of **5f**.

The X-ray crystallographic analysis of racemic **3f** was accomplished, though our attempt for **3a**–**e** proved to be unsuccessful. The ORTEP drawing of racemic **3f** is shown in Fig. 4.[16] The 2-*tert*-butylphenyl group and the imide plane were approximately orthogonal. The imide geometry was the *exo–endo* arrangement[17] with acetyl carbonyl *trans* and benzoyl carbonyl *cis* to the 2-*t*-butylphenyl group. The nature of imide nitrogen can be represented in terms of two angle parameters, the summation of the three valence angles around the nitrogen θ, and the twist angle[18] τ of the amide bond calculated by the average of ω_1 ($C^3C^2NC^5$) and ω_2 ($O^2C^2NC^1$), its range[19] being between 0 and 90° (the highest

Table 4. Reaction of **3a**–**e** with benzylamine (**6**)



Entry	Compound	Time (h)	Yield (%) of **7**	Yield (%) of **8**
1	**3a**	3.5	72	0
2	**3b**	7.5[a]	0	8
3	**3c**	7.5[a]	0	5
4	**3d**	7.5[a]	3	8
5	**3e**	10	80	0

[a] The quite slow reaction was observed.

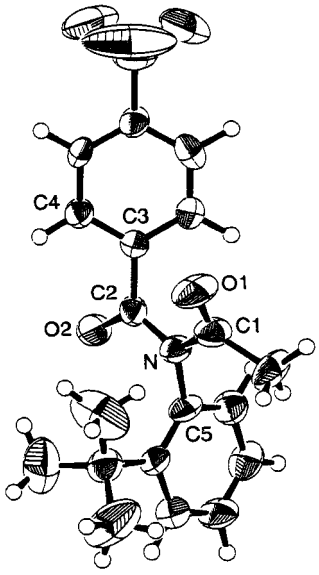


Figure 4. The ORTEP drawing of (±)-**3f**.

τ value[2c] reported for imide is 83.2°). The parameter of racemic **3f** is shown in Table 5. The essentially sp^2 nature of the imide nitrogen was confirmed: θ=359.8° (the angle θ of the ideal sp^2 planar nitrogen atom is 360°). The twist angle τ of **3f** was 18.5°, which was a small value compared with the highest τ value 83.2° reported for imide.[2c]

The racemization of **3** should occur when this N–Ar bond rotates across the *ortho* substituent (**3-A** or **3-B**, Fig. 5). Taking all the experimental results into consideration, one possible reason for the facile racemization of **3a** bearing a *t*-BuCO group would be as follows. Due to the largely twisted *t*-BuCO–N bond in **3a**, **3a** is strongly destabilized in the ground state, compared with **3b**–**e** which were slightly twisted.[20] Therefore, the activation energy of **3a** for racemization is smaller than those of **3b**–**e**, facilitating the racemization of **3a**.

Conclusion

We have demonstrated the first example of optically active compounds **3c** and **3d**, which possess axial chirality based on an acyclic imide N–Ar bond.[21] Furthermore, a quite interesting result has also been found, namely, that **3a** bearing a bulky acyl group rather than a small one racemized more easily. Since the large rotation barrier around the N–Ar bond of imide compounds has been utilized for stereoselective synthesis[3,4] and molecular recognition,[22] our novel findings would be utilized for their further development.

Experimental

All melting points (mp) were determined on a Yanagimoto melting point apparatus and are uncorrected. IR spectra were measured on a JASCO FT/IR-230 diffraction grating IR spectrophotometer. ^{1}H and ^{13}C NMR spectra were measured on a JEOL AL-400 or JEOL EX-400 NMR spectrometer, operating at 400 MHz for ^{1}H NMR and at 100 MHz at ^{13}C NMR. ^{1}H and ^{13}C NMR spectra were reported in δ units, parts per million (ppm) downfield from tetramethylsilane (δ=0). Electron impact (EI) MS spectra were measured on a JEOL JMS-DX-303 instrument. Specific rotations (in deg cm^3 g^{-1} L^{-1}) were determined on a JASCO DIP-1000 digital polarimeter. UV spectra were measured on a Shimadzu UV-265 instrument. Circular dichroisms (CD) were measured on a JASCO J-720W spectropolarimeter. The enantiomeric excess was determined by HPLC analysis.

2-*tert*-Butylaniline, and authentic samples of *N*,*N*-Dimethylisobutyramide (**5b**), *N*,*N*-dimethylpropionamide (**5d**) and *N*,*N*-dimethylacetamide (**5f**) were commercially available. All reagents were available from commercial sources and used without further purification unless otherwise stated. In general, all reactions were carried out in dry solvents under an argon atmosphere. All racemization experiments were performed on Taitec Thermo Minder SM-05 or Toyo Lab Thermo LH-1000. Pyridine was distilled under an argon atmosphere from CaH_2. Benzene was distilled under an argon atmosphere from Na. Benzylamine (**6**) was distilled under an argon atmosphere from Zn powder. Silica gel column chromatography was performed on Kanto Chemical Silica gel 60 (spherical, 100–210 μm).

Table 5. Angle around N, twist angle of aryl bond and selected bond lengths of **3f**

Angle around N θ (°)	Twist angle[a] τ of aryl bond (°)	C^1–N (Å)	C^1=O^1 (Å)	C^2–N (Å)	C^2–O^2 (Å)
359.8	18.5	1.432 (10)[b]	1.199 (9)[b]	1.374 (10)[b]	1.213 (9)[b]

[a] The twist angle τ was calculated by the average of ω_1 ($C^3C^2NC^5$) and ω_2 ($O^2C^2NC^1$).
[b] Standard deviations are shown in parentheses.

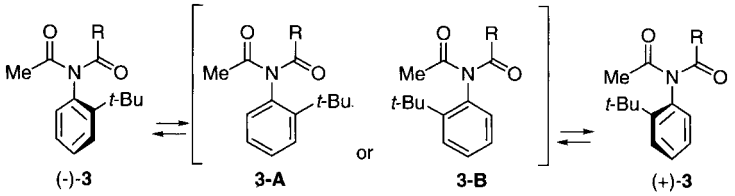


Figure 5.

Syntheses of (±)-3a–f

***N*-(2-*tert*-Butylphenyl)acetamide.** To a stirred solution of 2-*tert*-butylaniline (3.10 mL, 19.9 mmol) in pyridine (58.0 mL) was gradually added acetic anhydride (3.80 mL, 40.0 mmol) at 0°C. The reaction mixture was stirred at 25°C for 15 h, cooled to 0°C, quenched by the addition of 10% aqueous HCl at the same temperature, and extracted with EtOAc. The combined organic extracts were washed with saturated aqueous $NaHCO_3$ and brine, dried over Na_2SO_4 and concentrated using a rotary evaporator to afford the crude product. Purification by recrystallization (benzene–hexane) afforded the analytically pure *N*-(2-*tert*-butylphenyl)acetamide (3.66 g, 96%) as colorless needles of mp 158–158.5°C. R_f value=0.51 (hexane–EtOAc=2:1). IR (KBr): ν=3240, 1642 cm^{-1}. UV (CH_3CN): λ_{max} 225.7 (4170) nm. ^1H NMR ($CDCl_3$): δ=1.41 (s, 9H), 1.89 (s, 3H×1/3), 2.21 (s, 3H×2/3), 7.00–7.29 (m, 3H), 7.36–7.56 (m, 2H), 7.66 (br s, 1H). EI-MS: *m*/*z*=191 (M^+), 176, 149, 134 (bp). Anal. Calcd for $C_{12}H_{17}NO$: C, 75.35; H, 8.96; N, 7.32. Found: C, 75.55; H, 8.74; N, 7.21.

(*RS*)-*N*-(2-*tert*-Butylphenyl)-*N*-pivaloylacetamide [(±)-3a]. To a stirred solution of *N*-(2-*tert*-butylphenyl)acetamide (100 mg, 0.523 mmol) in pyridine (1.10 mL) was gradually added pivaloyl chloride (0.06 mL, 0.487 mmol) at 0°C. The mixture was stirred at 25°C for 3 h, cooled to 0°C, quenched by the addition of H_2O and extracted with EtOAc. The combined organic extracts were washed with brine, dried over Na_2SO_4 and concentrated using a rotary evaporator to afford the crude product. Purification by chromatography on silica gel (hexane–EtOAc=45:1, the silica gel was pretreated with 2% Et_3N in hexane) afforded the analytically pure (±)-**3a** (105 mg, 73%) as a clear colorless oil. R_f value=0.58 (hexane:EtOAc=4:1). IR (KBr): ν=1708, 1696 cm^{-1}. ^1H NMR (C_6D_6): δ=1.28 (s, 9H), 1.41 (s, 9H), 1.71 (s, 3H), 6.68 (dd, *J*=8.7, 1.7 Hz, 1H), 6.86 (ddd, *J*=8.7, 8.7, 1.7 Hz, 1H), 7.00 (ddd, *J*=8.7, 8.7, 1.7 Hz, 1H), 7.27 (dd, *J*=8.7, 1.7 Hz, 1H). ^{13}C NMR (C_6D_6): δ=26.06, 28.29, 31.91, 36.28, 43.95, 126.4, 128.6, 129.9, 132.1, 138.9, 147.6, 173.2 (C=O of acetyl group), 184.6 (C=O of pivaloyl group). EI-MS: *m*/*z*=275 (M^+), 191, 176, 158, 134, 106, 83, 57 (bp). Anal. Calcd for $C_{17}H_{25}NO_2$: C, 74.14; H, 9.15; N, 5.09. Found: C, 74.19; H, 8.96; N, 5.03.

(*RS*)-*N*-(2-*tert*-Butylphenyl)-*N*-isobutyrylacetamide [(±)-3b]. To a stirred solution of *N*-(2-*tert*-butylphenyl)-acetamide (608 mg, 3.18 mmol) in pyridine (9.50 mL) was gradually added isobutyryl chloride (0.68 mL, 6.49 mmol) at 0°C. The reaction mixture was stirred at 25°C for 1 h, cooled to 0°C, quenched by the addition of H_2O at the same temperature and extracted with EtOAc. The combined organic extracts were washed with brine, dried over Na_2SO_4 and concentrated using a rotary evaporator to afford the crude product. Purification by chromatography on silica gel (hexane–EtOAc=10:1, the silica gel was pretreated with 3% Et_3N in hexane) afforded the analytically pure (±)-**3b** (756 mg, 91%) as a clear colorless viscous oil. R_f value=0.52 (hexane–EtOAc=4:1). IR (KBr): ν= 1707 cm^{-1}. UV (CH_3CN): λ_{max} 270.2 (486.7), 250.4 (806.5) nm. ^1H NMR (C_6D_6): δ=1.05 (d, *J*=6.7 Hz, 3H), 1.11 (d, *J*=6.7 Hz, 3H), 1.22 (s, 9H), 2.15 (s, 3H), 3.01 (septet, *J*=6.7 Hz, 1H), 6.64 (dd, *J*=7.7, 1.5 Hz, 1H), 6.91 (ddd, *J*=7.7, 7.7, 1.5 Hz, 1H), 7.04 (ddd, *J*=7.7, 7.7, 1.5 Hz, 1H), 7.29 (dd, *J*=7.7, 1.5 Hz, 1H). ^{13}C NMR (C_6D_6): δ=19.29, 19.84, 27.54, 31.93, 35.46, 36.14, 127.1, 128.9, 129.7, 132.1, 138.0, 147.1, 173.2 (C=O of acetyl group), 180.2 (C=O of isobutyryl group). EI-MS: *m*/*z*=261 (M^+), 191, 176, 158, 134, 106, 83, 57, 43 (bp). Anal. Calcd for $C_{16}H_{23}NO_2$: C, 73.53; H, 8.87; N, 5.36. Found: C, 73.57; H, 9.06; N, 5.43.

(*RS*)-*N*-(2-*tert*-Butylphenyl)-*N*-isovalerylacetamide [(±)-3c]. To a stirred solution of isovaleric acid (0.64 mL, 5.87 mmol) in CH_2Cl_2 (3.70 mL) were added CCl_4 (5.80 mL, 60.1 mmol) and PPh_3 (4.62 g, 17.6 mmol) at 0°C. The reaction mixture was stirred at 25°C for 2.5 h, cooled to 0°C and then, to this mixture were added pyridine (19.6 mL) and *N*-(2-*tert*-butylphenyl)acetamide (1.12 g, 5.86 mmol) at the same temperature. The whole mixture was stirred at 25°C for 1 h, cooled to 0°C, quenched by the addition of H_2O at the same temperature and extracted with EtOAc. The combined organic extracts were washed with brine, dried over Na_2SO_4 and concentrated using a rotary evaporator to afford the crude product. Purification by chromatography on silica gel (hexane–EtOAc=5:1, the silica gel was pretreated with 1% Et_3N in hexane) afforded the analytically pure (±)-**3c** (364 mg, 23%) as a clear colorless oil accompanied with *N*-(2-*tert*-butylphenyl)acetamide (168 mg, 15%). R_f value=0.40 (hexane–EtOAc=3:1). IR (nujol): ν=1710 cm^{-1}. UV (CH_3CN): λ_{max} 270.1 (803.0), 257.6 (1226) nm. ^1H NMR (C_6D_6): δ=0.85 (d, *J*=6.6 Hz, 3H), 0.90 (d, *J*=6.6 Hz, 3H), 1.23 (s, 9H), 2.16 (s, 3H), 2.30–2.49 (m, 3H), 6.58 (dd, *J*=7.8, 1.5 Hz, 1H), 6.91 (ddd, *J*=7.8, 7.8, 1.5 Hz, 1H), 7.03 (ddd, *J*=7.8, 7.8, 1.5 Hz, 1H), 7.29 (dd, *J*=7.8,1.5 Hz, 1H). ^{13}C NMR (C_6D_6): δ=22.59, 22.65, 25.02, 27.51, 31.83, 36.02, 47.84, 126.9, 128.5, 129.5, 131.9, 137.4, 146.5, 172.4 (C=O of acetyl group), 174.6 (C=O of isovaleryl group). EI-MS: *m*/*z*=275 (M^+), 218, 191, 173, 158, 132, 106 (bp). Anal. Calcd for $C_{17}H_{25}NO_2$: C, 74.14; H, 9.15; N, 5.09. Found: C, 74.16; H, 9.28; N, 5.06.

(*RS*)-*N*-(2-*tert*-Butylphenyl)-*N*-propionylacetamide [(±)-3d]. To a stirred solution of *N*-(2-*tert*-butylphenyl)-acetamide (413 mg, 2.16 mmol) in THF (3.0 mL) was gradually added BuLi (1.53 *M* in hexane, 2.10 mL, 3.21 mmol) at 0°C. The mixture was stirred at 25°C for 1.5 h, cooled to 0°C, and then to this mixture was added $(EtCO)_2O$ (1.10 mL, 8.58 mmol) at the same temperature. The whole mixture was stirred at 25°C for 26 h, cooled to 0°C, quenched by the addition of H_2O at the same temperature and extracted with EtOAc. The combined organic extracts were washed with saturated aqueous $NaHCO_3$ and brine, dried over Na_2SO_4 and concentrated using a rotary evaporator to afford the crude product. Purification by chromatography on silica gel (hexane–EtOAc=20:1, the silica gel was pretreated with 3% Et_3N in hexane) afforded the analytically pure (±)-**3d** (315 mg, 59%) as a clear pale yellow oil. R_f value=0.43 (hexane–EtOAc=4:1). IR (KBr): ν=1709 cm^{-1}. ^1H NMR (C_6D_6): δ=1.02 (t, *J*=7.3 Hz, 3H), 1.19 (s, 9H), 2.20 (s, 3H), 2.34 (q, *J*=7.3 Hz, 2H), 6.53 (dd, *J*=8.0, 1.5 Hz, 1H), 6.91 (ddd, *J*=8.0, 8.0, 1.5 Hz, 1H), 7.04 (ddd, *J*=8.0, 8.0, 1.5 Hz, 1H), 7.28 (dd, *J*=8.0, 1.5 Hz, 1H). ^{13}C NMR (C_6D_6): δ=8.94, 27.54, 31.77, 32.72, 36.03, 127.2, 128.9, 129.7, 132.2, 137.8, 146.7, 172.8 (C=O of

acetyl group), 176.4 (C=O of propionyl group). EI-MS: m/z=247 (M^+), 214, 191, 177, 173, 134 (bp). Anal. Calcd for $C_{15}H_{21}NO_2$: C, 72.84; H, 8.56; N, 5.66. Found: C, 72.76; H, 8.71; N, 5.64.

(*RS*)-*N*-(2-*tert*-Butylphenyl)-*N*-benzoylacetamide [(±)-3e]. To a stirred solution of *N*-(2-*tert*-butylphenyl)acetamide (100 mg, 0.523 mmol) in pyridine (1.70 mL) was gradually added benzoyl chloride (0.13 mL, 1.12 mmol) at 0°C. The reaction mixture was stirred at 25°C for 11 h, cooled to 0°C, quenched by the addition of H_2O at the same temperature and extracted with EtOAc. The combined organic extracts were washed with brine, dried over Na_2SO_4 and concentrated using a rotary evaporator to afford the crude product. Purification by chromatography on silica gel (hexane–EtOAc=5:1, the silica gel was pretreated with 1% Et_3N in hexane) afforded the analytically pure (±)-**3e** (145 mg, 94%) as a colorless solid. Recrystallization (benzene–hexane) afforded colorless prisms of mp 83–84°C. R_f value=0.35 (hexane–EtOAc=4:1). IR (KBr): ν=1687 cm^{-1}. ^1H NMR (C_6D_6): δ=1.30 (s, 9H), 1.86 (s, 3H), 6.79 (dd, J=7.3, 1.5 Hz, 1H), 6.90 (ddd, J=7.3, 7.3, 1.5 Hz, 1H), 7.00–7.05 (m, 4H), 7.28 (dd, J=7.3, 1.5 Hz, 1H), 7.71–7.74 (m, 2H). ^{13}C NMR (C_6D_6): δ=26.15, 31.77, 36.06, 127.2, 128.1, 129.0, 129.2, 129.6, 131.3, 132.8, 136.9, 137.9, 147.3, 173.1 (C=O of benzoyl group), 173.3 (C=O of acetyl group). EI-MS: m/z=295 (M^+), 253, 239, 197, 149, 135, 93, 77 (bp). Anal. Calcd for $C_{19}H_{21}NO_2$: C, 77.26; H, 7.17; N, 4.74. Found: C, 77.25; H, 7.19; N, 4.73.

(*RS*)-*N*-(2-*tert*-Butylphenyl)-*N*-(4-trifluorometylbenzoyl)-acetamide [(±)-3f]. To a stirred solution of *N*-(2-*tert*-butylphenyl)acetamide (1.07 g, 5.59 mmol) in pyridine (16.0 mL) was added 4-trifluorometylbenzoyl chloride (1.60 mL, 10.8 mmol) at 0°C. The reaction mixture was stirred at 25°C for 5 h, cooled to 0°C, quenched by the addition of H_2O at the same temperature and extracted with EtOAc. The combined organic extracts were washed with saturated aqueous $NaHCO_3$ and brine, dried over Na_2SO_4 and concentrated using a rotary evaporator to afford the crude product. Purification by chromatography on silica gel (hexane–EtOAc=7:1, the silica gel was pretreated with 3% Et_3N in hexane) afforded the analytically pure (±)-**3f** (1.82 g, 90%) as a colorless solid. Recrystallization (benzene–hexane) afforded colorless plates of mp 125–126°C. R_f value=0.67 (hexane–EtOAc=2:1). IR (nujol): ν=1678, 1722 cm^{-1}. ^1H NMR (C_6D_6): δ=1.26 (s, 9H), 1.73 (s, 3H), 6.70 (dd, J=7.7, 1.5 Hz, 1H), 6.91 (ddd, J=7.7, 7.7, 1.5 Hz, 1H), 7.03 (ddd, J=7.7, 7.7, 1.5 Hz, 1H), 7.25–7.29 (m, 3H), 7.53 (d, J=8.1 Hz, 2H). ^{13}C NMR (C_6D_6): δ=25.76, 31.65, 35.97, 124.1 (q, J=272 Hz), 124.9 (q, J=3.3 Hz), 127.1, 128.6, 129.0, 129.4, 132.1, 132.1 (q, J=32.5 Hz), 136.9, 140.0, 146.8, 171.4 (C=O of 4-trifluoromethylbenzoyl group), 172.6 (C=O of acetyl group). EI-MS: m/z=363 (M^+), 265, 149, 83 (bp). Anal. Calcd for $C_{20}H_{20}O_2NF_3$: C, 66.11; H, 5.55; N, 3.85. Found: C, 66.14; H, 5.58; N, 3.93.

Optical resolution of (±)-3a–e

Optical resolutions of (±)-**3a–e** were performed by HPLC using a chiral phase column (DAICEL CHIRALCEL OD: 25 cm×1 cm i.d.).

(*S*)-*N*-(2-*tert*-Butylphenyl)-*N*-isobutyrylacetamide [(+)-3b]. Retention Time=22 min (eluent: hexane–isopropanol=450:1). $[\alpha]_D^{27}$=+23° (c 0.57, benzene, >99% ee). CD (CH_3CN): λ_{ext} 247.0 (−1.32) nm. Other spectral data of (+)-**3b** were identical with those of (±)-**3b**.

(*R*)-*N*-(2-*tert*-Butylphenyl)-*N*-isobutyrylacetamide [(−)-3b]. Retention Time=29 min (eluent: hexane–isopropanol=450:1). $[\alpha]_D^{27}$=−23° (c 0.87, benzene, >99% ee). CD (CH_3CN): λ_{ext} 246.0 (+1.23) nm. Other spectral data of (−)-**3b** were identical with those of (±)-**3b**.

(*S*)-*N*-(2-*tert*-Butylphenyl)-*N*-isovalerylacetamide [(+)-3c]. Retention Time=24 min (eluent: hexane–isopropanol=450:1). $[\alpha]_D^{27}$=+16° (c 1.05, benzene, >99% ee). CD (CH_3CN): λ_{ext} 244.0 (−0.36) nm. Other spectral data of (+)-**3c** were identical with those of (±)-**3c**.

(*R*)-*N*-(2-*tert*-Butylphenyl)-*N*-isovalerylacetamide [(−)-3c]. Retention Time=31 min (eluent: hexane–isopropanol=450:1). $[\alpha]_D^{27}$=−19° (c 1.06, benzene, >99% ee). CD (CH_3CN): λ_{ext} 246.5 (+0.42) nm. Other spectral data of (−)-**3c** were identical with those of (±)-**3c**.

(+)-*N*-(2-*tert*-Butylphenyl)-*N*-propionylacetamide [(+)-3d]. Retention Time=39 min (eluent: hexane–isopropanol=450:1). $[\alpha]_D^{27}$=+14° (c 0.57, benzene, >99% ee). Other spectral data of (+)-**3d** were identical with those of (±)-**3d**.

(−)-*N*-(2-*tert*-Butylphenyl)-*N*-propionylacetamide [(−)-3d]. Retention Time=42 min (eluent: hexane–isopropanol=450:1). $[\alpha]_D^{27}$=−15° (c 1.10, benzene, >99% ee). Other spectral data of (−)-**3d** were identical with those of (±)-**3d**.

(−)-*N*-(2-*tert*-Butylphenyl)-*N*-benzoylacetamide [(−)-3e]. Retention Time=32 min (eluent: hexane–isopropanol=150:1). $[\alpha]_D^{27}$=−28° (c 0.45, benzene, >99% ee). CD (CH_3CN): λ_{ext} 240.0 (+2.33), 223.0 (−2.48) nm. Other spectral data of (−)-**3d** were identical with those of (±)-**3e**.

(+)-*N*-(2-*tert*-Butylphenyl)-*N*-benzoylacetamide [(+)-3e]. Retention Time=40 min (eluent: hexane–isopropanol=150:1). $[\alpha]_D^{27}$=+29° (c 1.38, benzene, >99% ee). CD (CH_3CN): λ_{ext} 240.0 (−2.12), 220.0 (+2.97) nm. Other spectral data of (+)-**3e** were identical with those of (±)-**3e**.

General procedure for racemization experiment of 3b–e

A solution of optically active **3b–e** (8.89×10^{-3} mmol) in benzene (3.0 mL) was stirred at four different temperatures (sealed-tube experiments). The rate constants for their racemization were measured in the 15–70% range of reaction conversion.

The rate constants of **3b–e** are shown below.

3b. k (40°C)=1.22±0.09×10^{-6} s^{-1}, k (47°C)=2.44±0.06×10^{-6} s^{-1}, k (54°C)=5.54±0.36×10^{-6} s^{-1}, k (61°C)=12.8±1.0×10^{-6} s^{-1}.

3c. k (40°C)=1.50±0.02×10^{-7} s^{-1}, k (50°C)=6.35±0.14×

10^{-7} s^{-1}, k (57°C)=14.9±0.1×10^{-7} s^{-1}, k (64°C)=40.4±0.1×10^{-7} s^{-1}.

3d. k (49°C)=3.08±0.10×10^{-7} s^{-1}, k (56°C)=8.36±0.22×10^{-7} s^{-1}, k (63°C)=20.9±0.1×10^{-7} s^{-1}, k (70°C)=48.5±0.1×10^{-7} s^{-1}.

3e. k (33°C)=1.02±0.02×10^{-6} s^{-1}, k (40°C)=2.73±0.09×10^{-6} s^{-1}, k (51°C)=10.9±0.2×10^{-6} s^{-1}, k (58°C)=25.0±0.4×10^{-6} s^{-1}.

(R_a, 2*S*)-*N*-Allyl-*N*-(2-*tert*-butylphenyl)-2-acetoxypropionamide [(+)-4] and (S_a, 2*S*)-*N*-allyl-*N*-(2-*tert*-butylphenyl)-2-acetoxypropionamide [(−)-4]. (+)-4 and (−)-4 were prepared according to the published procedure.[4c]

(+)-4. The physical data shown below were comparable to those reported.[4c] A colorless solid of mp 40–43°C. Reported mp 44°C. $[\alpha]_D^{25}$=+51.0° (*c* 1.0, $CHCl_3$). Reported $[\alpha]_D^{25}$=+55.0° (*c* 1.0, $CHCl_3$). IR (KBr): ν=1742, 1663 cm^{-1}. ^1H NMR ($CDCl_3$): δ=1.29 (d, *J*=6.4 Hz, 3H), 1.38 (s, 9H), 1.98 (s, 3H), 3.36 (dd, *J*=14.1, 8.1 Hz, 1H), 4.95 (tdd, *J*=14.1, 4.9, 1.5 Hz, 1H), 5.02 (q, *J*=6.4 Hz, 1H), 5.11 (md, *J*=17.0 Hz, 1H), 5.18 (dd, *J*=10.2, 0.8 Hz, 1H), 5.99 (dddd, *J*=17.0, 10.2, 8.1, 4.9 Hz, 1H), 7.06 (dd, *J*=7.8, 1.6 Hz, 1H), 7.15 (dt, *J*=7.8, 1.5 Hz, 1H), 7.32 (ddd, *J*=7.8, 7.2, 1.5 Hz, 1H), 7.56 (dd, *J*=7.2, 1.6 Hz, 1H). ^{13}C NMR ($CDCl_3$): δ=15.79, 20.82, 32.27, 36.11, 54.65, 67.55, 118.6, 126.1, 128.6, 129.9, 131.7, 137.7, 145.8, 168.9, 169.1. EI-MS: *m*/*z*=304 (M^++1), 303 (M^+), 245 (bp).

[(−)-4]. The physical data shown below were comparable to those reported.[4c] A colorless solid of mp 92–95°C. Reported mp 94–95°C. $[\alpha]_D^{25}$=−92.0° (*c* 1.0, $CHCl_3$). Reported $[\alpha]_D^{25}$=−99. 0° (*c* 1.0, $CHCl_3$). IR (KBr): ν=1736, 1670 cm^{-1}. ^1H NMR ($CDCl_3$): δ=1.30 (d, *J*=6.5 Hz, 3H), 1.35 (s, 9H), 2.02 (s, 3H), 3.34 (dd, *J*=14.1, 8.2 Hz, 1H), 4.95 (tdd, *J*=14.1, 5.0, 1.3 Hz, 1H), 5.08 (q, *J*=6.5 Hz, 1H), 5.09 (md, *J*=17.1 Hz, 1H), 5.18 (d, *J*=10.4 Hz, 1H), 5.98 (m, 1H), 6.92 (dd, *J*=7.8, 1.5 Hz, 1H), 7.19 (dt, *J*=7.4, 1.4 Hz, 1H), 7.34 (ddd, *J*=7.4, 1.5 Hz, 1H), 7.58 (dd, *J*=8.2, 1.5 Hz, 1H). ^{13}C NMR ($CDCl_3$): δ=17.19, 20.99, 31.64, 36.17, 54.47, 67.77, 119.0, 126.4, 128.8, 130.2, 131.4, 131.8, 137.7, 146.2, 169.5, 169.6. EI-MS: *m*/*z*=304 (M^++1), 303 (M^+), 247, 204 (bp).

General procedure for preparation of 5a, 5c and 5e

To a stirred solution of *N*,*N*-dimethylamine hydrochloride (4.65 g, 57.0 mmol) in benzene (6.20 mL) were added Et_3N (8.30 mL, 59.5 mol) and acyl chloride (2.85 mmol) at 0°C. The reaction mixture was stirred at 25°C for 4 h, cooled to 0°C, quenched by the addition of 10% aqueous HCl at the same temperature and extracted with EtOAc. The combined organic extracts were washed with saturated aqueous $NaHCO_3$ and brine, dried over Na_2SO_4, and concentrated using a rotary evaporator to afford the crude product. Purification by chromatography on silica gel afforded the desired compound.

***N*,*N*-Dimethylpivalamide (5a).** Yield 44%. A colorless oil. R_f value=0.26 (EtOAc-hexane=3:1). IR (KBr): ν=1627 cm^{-1}. ^1H NMR (C_6D_6): δ=1.15 (s, 9H), 2.57 (s, 3H×2). ^{13}C NMR (C_6D_6): δ=28.33, 37.80, 38.54, 176.4 (C=O). EI-MS: *m*/*z*=129 (M^+), 114, 87, 74, 47 (bp). Anal. Calcd for $C_7H_{15}NO$: C, 65.07; H, 11.70; N, 10.84. Found: C, 64.86; H, 11.86; N, 10.37.

***N*,*N*-Dimethylisovaleramide (5c).** Yield 35%. A colorless oil. R_f value=0.36 (EtOAc-hexane=3:1). IR (nujol): ν=1644 cm^{-1}. ^1H NMR (C_6D_6): δ=0.95 (d, *J*=6.6 Hz, 3H×2), 1.87 (d, *J* = 6.6 Hz, 2H), 2.21 (s, 3H), 2.29 (tq, *J*=6.6, 6.6 Hz, 1H), 2.67 (s, 3H). ^{13}C NMR (C_6D_6): δ=22.92, 25.54, 34.78, 36.29, 42.05, 170.7 (C=O). EI-MS *m*/*z*: 129 (M^+), 84, 72, 58 (bp). Anal. Calcd for $C_7H_{15}NO$: C, 65.07; H, 11.70; N, 10.84. Found: C, 64.68; H, 12.09; N, 10.46.

***N*,*N*-Dimethylbenzamide (5e).** Yield 75%. A colorless oil. R_f value=0.49 (EtOAc-hexane=2:1). IR (KBr): ν=1632 cm^{-1}. ^1H NMR (C_6D_6): δ=2.32 (s, 3H), 2.75 (s, 3H), 7.05–7.07 (m, 3H), 7.30–7.33 (m, 2H). ^{13}C NMR (C_6D_6): δ=34.97, 38.72, 127.7, 128.5, 129.3, 137.4, 170.8 (C=O). EI-MS: *m*/*z*=149 (M^+), 135, 105, 83 (bp). Anal. Calcd for $C_9H_{11}NO$: C, 72.46; H, 7.43; N, 9.39. Found: C, 72.17; H, 7.57; N, 9.68.

Representative procedure for reaction of 3a–e with benzylamine (6) corresponding to entry 1 in Table 4

To a stirred solution of **3a** (151 mg, 0.549 mmol) in benzene (0.55 mL) was added benzylamine (**6**) (3.66 M in benzene, 75.0 μL, 0.275 mmol) at 0°C. The reaction mixture was stirred at 25°C for 3.5 h, cooled to 0°C, quenched by the addition of 10% aqueous HCl at the same temperature and extracted with EtOAc. The combined organic extracts were washed with saturated aqueous $NaHCO_3$ and brine, and dried over Na_2SO_4. Evaporation of the solvent yielded the colorless residue (143 mg). Purification by chromatography on silica gel (benzene-EtOAc=8:1) and subsequent PTLC (hexane: EtOAc=10:1) afforded *N*-benzylpivalamide (37.8 mg, 72%) as a colorless solid and *N*-(2-*tert*-butylphenyl)acetamide (99.9 mg, 95%) as a colorless solid. No *N*-benzylacetamide (**8**) was detected by TLC and ^1H NMR of the crude product.

***N*-Benzylpivalamide.** The physical data shown below were comparable to those reported.[23] A colorless solid of mp 82–82.5°C. Reported mp 82–83°C. R_f value=0.35 (hexane–EtOAc=4:1). IR (nujol): ν=3297, 1633 cm^{-1}. ^1H NMR ($CDCl_3$): δ=1.23 (s, 9H), 4.43 (d, *J*=5.7 Hz, 2H), 5.93 (br s, 1H), 7.24–7.35 (m, 5H). ^{13}C NMR ($CDCl_3$): δ=27.56, 38.62, 43.48, 127.1, 127.3, 128.4, 138.3, 177.8. EI-MS: *m*/*z*=191 (M^+), 149, 106, 91 (bp).

The physical data of other amides in entries 2–5, Table 4, are shown below.

Entries 2–4. *N*-Benzylacetamide (8). The physical data shown below were comparable to those reported.[23] A colorless solid of mp 58–59°C. Reported mp 61–62°C. R_f value=0.25 (hexane–EtOAc=1:1). IR (nujol): ν=3289, 1633 cm^{-1}. ^1H NMR ($CDCl_3$): δ=2.01 (s, 3H), 4.41 (d, *J*=5.7 Hz, 2H), 5.90 (br s, 1H), 7.26–7.35 (m, 5H). ^{13}C NMR ($CDCl_3$): δ=23.09, 43.58, 127.1, 127.5, 128.3, 137.9, 169.6. EI-MS: *m*/*z*=149 (M^+), 148, 108, 106 (bp).

Entry 4. *N*-Benzylpropionamide. The physical data shown below were comparable to those reported.[23] A colorless solid of mp 51–51.5°C. Reported mp 48–49.5°C. R_f value=0.42 (hexane–EtOAc=1:1). IR (nujol): ν=3292, 1637 cm^{-1}. ^1H NMR ($CDCl_3$): δ=1.18 (t, J=7.5 Hz, 3H), 2.24 (q, J=7.5 Hz, 2H), 4.43 (d, J=5.7 Hz, 2H), 5.81 (br s, 1H), 7.25–7.36 (m, 5H). ^{13}C NMR ($CDCl_3$): δ=9.85, 29.58, 43.43, 127.1, 127.4, 128.3, 138.1, 173.2. EI-MS: m/z=163 (M^+), 107, 106, 91 (bp).

Entry 5. *N*-Benzylbenzamide. The physical data shown below were comparable to those reported.[6b] A colorless solid of mp 108–109°C. Reported mp 107–109°C. R_f value=0.28 (hexane–EtOAc=4:1). IR (nujol): ν=3290, 1638 cm^{-1}. ^1H NMR ($CDCl_3$): δ=4.65 (dd, J=5.7, 1.8 Hz, 2H), 6.49 (br s, 1H), 7.27–7.50 (m, 8H), 7.78–7.81 (m, 2H). ^{13}C NMR ($CDCl_3$): δ=43.96, 126.7, 127.2, 127.5, 128.2, 128.4, 131.5, 134.0, 137.9, 167.0. EI-MS: m/z=211 (M^+), 105, 91, 77 (bp).

The physical data of other resulting anilides in entries 2–4, Table 4, are shown below.

Entry 2. *N*-(2-*tert*-butylphenyl)isobutyramide. A colorless solid of mp 140–141.5°C. R_f value=0.55 (hexane–EtOAc=2:1). IR (nujol): ν=3259, 1651 cm^{-1}. ^1H NMR ($CDCl_3$): δ=1.31 (d, J=6.8 Hz, 3H×2), 1.42 (s, 9H), 2.57 (septet, J=6.8 Hz, 1H), 7.13–7.26 (m, 3H), 7.38 (d, J=7.7 Hz, 1H), 7.62 (d, J=7.7 Hz, 1H). ^{13}C NMR ($CDCl_3$): δ=19.51, 30.63, 34.49, 36.63, 125.6, 126.1, 126.4, 127.5, 135.0, 141.9, 174.4. EI-MS: m/z=219 (M^+), 162, 149, 134 (bp). Anal. Calcd for $C_{14}H_{21}NO$: C, 76.67; H, 9.65; N, 6.39. Found: C, 76.55; H, 9.78; N, 6.48.

Entry 3. *N*-(2-*tert*-Butylphenyl)isovaleramide. A colorless solid of mp 118–119°C. R_f value=0.55 (hexane–EtOAc=2:1). IR (nujol): ν=3213, 1650 cm^{-1}. ^1H NMR ($CDCl_3$): δ=1.04 (d, J=5.1 Hz, 3H×2), 1.41 (s, 9H), 2.26–2.34 (m, 3H), 7.14–7.26 (m, 3H), 7.38 (d, J=7.7 Hz, 1H), 7.60 (d, J=7.7 Hz, 1H). ^{13}C NMR ($CDCl_3$): δ=22.56, 26.14, 30.68, 34.48, 47.11, 125.7, 126.2, 126.5, 127.5, 134.9, 141.9, 170.3. EI-MS: m/z=233 (M^+), 176, 149, 134 (bp). Anal. Calcd for $C_{15}H_{23}NO$: C, 77.21; H, 9.93; N, 6.00. Found: C, 77.02; H, 9.93; N, 6.03.

Entry 4. *N*-(2-*tert*-Butylphenyl)propionamide. A colorless solid of mp 102–103°C. R_f value=0.32 (hexane–EtOAc=2:1). IR (nujol): ν=3244, 1645 cm^{-1}. ^1H NMR ($CDCl_3$): δ=1.23 (t, J=7.3 Hz, 3H), 1.40 (s, 9H), 2.43 (q, J=7.3 Hz, 3H), 7.15–7.26 (m, 3H), 7.38 (d, J=7.6 Hz, 1H), 7.55 (d, J=7.6 Hz, 1H). ^{13}C NMR ($CDCl_3$): δ=9.73, 30.66, 35.51, 125.8, 126.2, 126.5, 127.8, 134.9, 142.2, 171.5. EI-MS: m/z=205 (M^+), 148, 84, 57 (bp). Anal. Calcd for $C_{13}H_{19}NO$: C, 76.06; H, 9.33; N, 6.82. Found: C, 75.77; H, 9.42; N, 6.75.

Crystal data for 3f

$C_{20}H_{20}O_2NF_3$, M=363.38, monoclinic, a=8.815(2) Å, b=9.900(2) Å, c=21.953(5) Å, β=97.671(4)°, V=1898.5(6) $Å^3$, space group $P2_1/n$ (#14), Z=4, D_{calc}=1.271 g cm^{-3}. Crystal dimensions 0.42×0.33×0.22 mm, μ(MoKα)=1.01 cm^{-1}. Data collection and processing: CCD diffractometer, graphite monochromated MoKα (λ=0.71069 Å) radiation, 11603 reflections measured, giving 877 with $I>3.00\sigma$ (I).

Structure analysis and refinement

The structure was solved by direct methods using DIFABS[24] and was refined by full-matrix least-squares techniques using DIRDIF94.[25] The non-hydrogen atoms were refined anisotropically. The final residuals for reflections with $I>3.00\sigma$ (I) were R=0.061, R_w=0.062.

Acknowledgements

This study was financially supported by a Grant-in-Aid for Scientific Research from the Ministry of Education, Science and Culture, Japan, a Sasakawa Scientific Research Grant from The Japan Science Society, and the Mitsubishi Chemical Corporation Fund.

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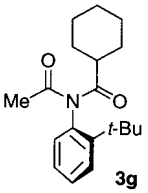
10. The use of other solvents such as DMF and CH_3CN instead of benzene, led to the decomposition of **3**.
11. The optical resolution of racemic **3g** bearing a cyclohexanecarbonyl group could not be achieved by using HPLC on a chiral stationary phase. This disappointing result could be due to decomposition of **3g** by a chiral column.



3g

12. According to Eyring's equation, $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ of **3b**–**e** were calculated. For Eyring's equation, see: Cagle, Jr., F. W.; Eyring, H. *J. Am. Chem. Soc.* **1951**, *73*, 5628–5630.
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16. The $\Delta\delta^{13}C$ values (Table 6) of arylcarbonyl and acetylcarbonyl carbon of **3f** were 0.7 and 3.4.
17. In the case of a simple acyclic imide, the *endo–exo* arrangement of imide carbonyl groups would be the generally preferred conformation, see: Noe, E. A.; Raban, M. *J. Am. Chem. Soc.* **1975**, *97*, 5811–5820.
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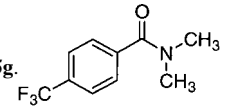
19. Twist angle τ is defined as follows: $\tau = 1/2\ (\omega_1 + \omega_2)$. According to the definition, the τ value lies in the range between -180 and 180°. However, the larger the distortion, the nearer the value lies to 90 or -90°; on the other hand, the smaller the distortion, the nearer the value lies to 0, 180°, or -180°. Therefore, in order to avoid confusion regarding the magnitude of τ, we represented the twist angle as $|\tau|$ (for $0° \leq |\tau| \leq 90°$) or $180-|\tau|$ (for $90° \leq |\tau|$).
20. Facile racemization of 8-diphenylphosphinoyl-8′-methoxy-1,1′-binaphthyl due to its large strain energy, has been reported, see: Fuji, K.; Sakurai, M.; Tohkai, N.; Kuroda, A.; Kawabata, T.; Fukuzawa, Y.; Kinoshita, T.; Tada, T. *Chem. Commun.* **1996**, 1609–1610.
21. Instead of the optical resolution of racemic **3d**, optically active **3d** could be obtained by asymmetric synthesis as shown in. Quite recently, the similar asymmetric synthesis of anilides has been reported by Simpkins et al., see: Ref. [4f] Scheme 1.

Table 6. ^{13}C NMR chemical shift (δ, ppm) of acyl carbonyl (recorded at 100 MHz in C_6D_6)

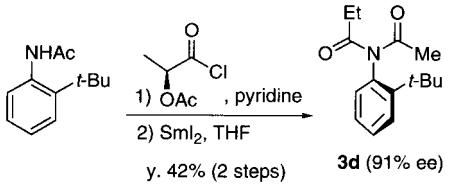
Compound	$\delta^{13}C$		$\Delta\delta^{13}C$	
	RCO	CH_3CO	RCO	CH_3CO
3f	169.9 (169.2)[a]	172.6 (169.2)[b]	0.7	3.4

[a] The data of **5g**.



5g

[b] The data of **5f**.



3d (91% ee)

Scheme 1. Asymmetric synthesis of **3d**.

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