Super Acid-Induced Pummerer-Type Cyclization Reaction: Improvement in the Synthesis of Chiral 1,3-Dimethyl-1,2,3,4-tetrahydroisoquinolines

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Improved synthesis of four stereoisomeric chiral 1,3-dimethyl-1,2,3,4-tetrahydroisoquinolines (1a, b, ent-1a, b) was achieved *via* the super acid-induced cyclization of chiral *N*-[1-methyl-2-(phenylsulfinyl)ethyl]-*N*-(1-phenylethyl)formamides (4a, b, ent-4a, b) using the Pummerer-type cyclization reaction as a key step. The cyclization leading to the isoquinoline ring proceeded in a quantitative manner when trifluoromethane sulfonic acid (TFSA) was used as the super acid, although Friedel–Crafts-type alkylation of 4-phenylsulfanyl TIQ derivatives (5) with benzene used as the solvent accompanied cyclization to yield the 4-phenyl-TIQs (7). The byproduct (7) was exclusively formed when a large excess amount of TFSA was used.

Key words super acid; Pummerer reaction; 1,3-dimethyl-1,2,3,4-tetrahydroisoquinoline; trifluoromethane sulfonic acid; chiral synthesis; parkinsonism

It is well known that the sulfonium ion formed *in situ* from a sulfoxide by the action of anhydrides such as trifluoroacetic anhydride (TFAA) is a powerful electrophile reacting with nucleophilic carbon species (Pummerer reaction).[1] Recently, we explored the Pummerer-type cyclization reaction of simple alkyl sulfoxides and developed an efficient method for the preparation of *N*-heterocycles with isoquinoline, quinoline, and benzazepine ring systems.[2] During the study, we discovered that boron trifluoride diethyl etherate ($BF_3 \cdot Et_2O$), when used together with TFAA, dramatically facilitated the cyclization reaction.[3—9] The high efficiency of this reaction was encountered particularly in the cyclization for substrates with a weak nucleophilic aromatic π-bond, which in the absence of the Lewis acid undergoes no cyclization.[3]

Recently, we succeeded in the syntheses of four stereoisomeric chiral 1,3-dimethyl-1,2,3,4-tetrahydroisoquinolines (1,3-DiMeTIQs) (**1a**, **ent-1a**, **1b**, **ent-1b**).[10] 1,3-DiMeTIQ was detected in the brain of chronic ethanol-intoxicated rats subjected to repeated amphetamine administrations and confirmed to cause behavior abnormalities similar to parkinsonism.[11] In the syntheses, we used the $BF_3 \cdot Et_2O$-catalyzed Pummerer reaction of the sulfoxide (**4**) as a key step, which, however, gave a poor result, producing the corresponding TIQ (**5**) in low yields (Chart 1).[10] In this paper, we report the Pummerer-type cyclization reaction of **4** promoted by trifluoromethane sulfonic acid (TFSA), a super strong acid, which may improve the cyclization reaction leading to 1,3-DiMeTIQ (**1**).

Results and Discussion

Chiral sulfoxides, substrates of the Pummerer reactions, were prepared starting from (*R*)- and (*S*)-1-phenylethylamines (**2**, **ent-2**) according to the methods reported in the previous paper (Chart 2).[10] Condensation of **2** and **ent-2** with phenylsulfanylacetone in titanium(IV) isopropoxide followed by reduction with $NaBH_4$ gave four stereoisomeric sulfides (**3a**, **ent-3a**, **3b**, **ent-3b**) in an optically pure form, as shown in Chart 2. Formylation of the sulfides followed by oxidation with $NaIO_4$ yielded the sulfoxides (**4a**, **ent-4a**, **4b**, **ent-4b**).

The super acid-promoted Pummerer reaction of **4a** was carried out as follows (Chart 3). A solution of **4a** in benzene was treated with 5 molar equivalent of TFAA at room temperature for 1 h under an argon atmosphere, and then to this solution 5 molar equivalent of TFSA was added. The reaction mixture was allowed to react at room temperature for a further 1 h. Separation of crude products with medium-pressure liquid chromatography over silica gel yielded two 2-formyl-4-phenylsulfanyl-1,3-DiMeTIQs (**5aA**) (66%) and (**5aB**) (19%), and 2-formyl-4-phenyl-1,3-DiMeTIQ (**7aA**) (10%). The spectral and analytical data of **5aA** and **5aB** indicated that they are epimers in terms of the stereochemistry of the phenylsulfanyl group at the C_4-position, although the stereochemistries could not be determined since the coupling constants between C_4-H and C_3-H of **5aA** and **5bB** showed similar values (J=2 Hz). The structure of **7aA** was deduced from the mass spectroscopic, ^{1}H- and ^{13}C-NMR data, and the stereochemistry of the phenyl group at the C_4 position was determined to be *trans* to the C_3-methyl group from the coupling constant (J=8 Hz) between C_3-H and C_4-H.

To simplify the product analysis, the Pummerer products were purified after reductive elimination of the phenylsulfanyl group. The benzene solution of **4a** was treated with TFAA (5 mol eq) and TFSA (5 mol eq) followed by reduction with $NaBH_4$–$NiCl_2$ to yield 2-formyl-1,3-DiMeTIQ (**6a**) and **7aA** in yields of 79% and 5%, respectively, as shown in Table 1 (entry 1). This result demonstrated that the TFSA-promoted Pummerer reaction of **4a** induced the cyclization leading to the isoquinoline ring in a highly effective manner, although the 4-phenyl-TIQ derivative (**7aA**) was a byproduct.

A similar reaction of **4a** on using 7 molar equivalent of TFSA decreased the formation of **6a** (68%) and increased that of **7aA** (16%) (Table 1, entry 2). On the reaction of **4a** using a large excess amount of TFSA (21 mol eq), **6a** was not obtained, but instead 4-phenylTIQ (**7aA**) and its stereoisomer (**7aB**) were obtained in yields of 87% and 9%, respectively (Table 1, entry 3). The results clearly demonstrate that the 4-phenylsulfanyl TIQ derivative initially formed by the Pummerer reaction undergoes an intermolecular alkylation reaction (Friedel–Crafts reaction) with benzene used as the solvent to give 4-phenylTIQ, and that the increasing acidity in the reaction medium facilitates this undesirable reaction.

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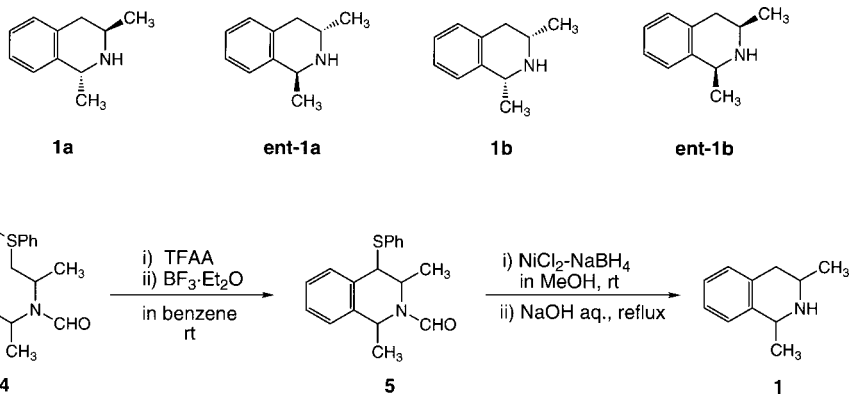

Chart 1

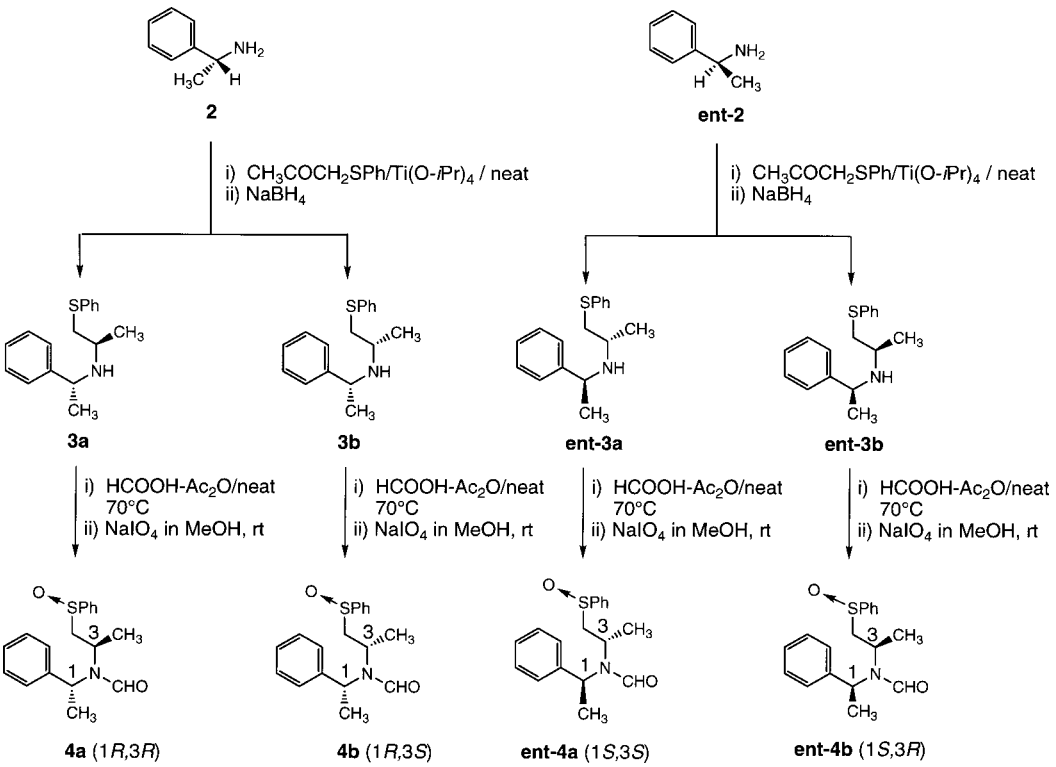

Chart 2

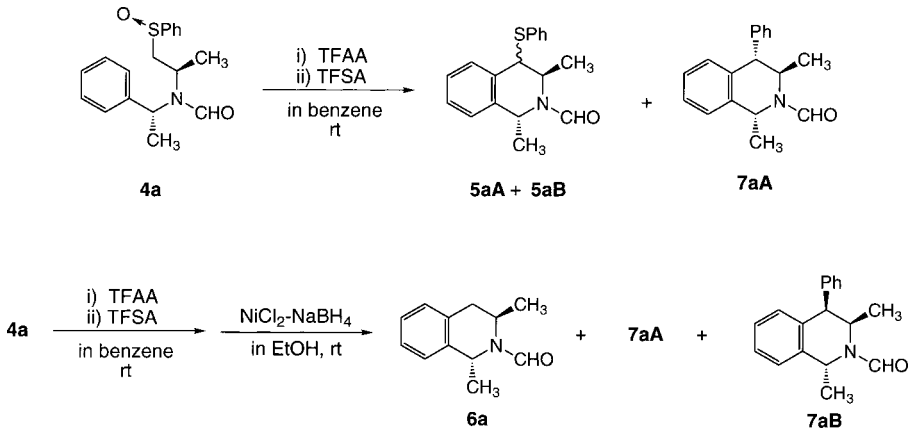

Chart 3

Several attempts to avoid this alkylation reaction using other solvents such as tetrahydrofuran (THF) and dichloromethane failed, and no characterizable products were obtained.

The sulfoxide (**ent-4a**), an enantiomer of **4a**, in the TFSA-promoted Pummerer reaction, gave similar results to those of **4a**, as shown in Table 1 (entries 4, 5, 6), (Chart 4). The reaction of the sulfoxide (**4b**), a diastereoisomer of **4a**, yielded the 2-formyl-1,3-DiMeTIQ (**6b**) and the 4-phenyl-DiMeTIQ (**7bB**). In the reaction using 5 molar equivalent of TFSA, **6b** was obtained as the major product (53% yield) and **7bB** as the minor one (9%) (Table 1, entry 7). The reaction with 7 molar equivalent of TFSA increased both the formation of **6b** (56% yield) and **7bB** (23% yield) (Table 1, entry 8). The reaction using 21 molar equivalent of TFSA also enhanced the Friedel–Crafts reaction to yield **7bB** in an exclusive manner (91%) (Table 1, entry 9). The sulfoxide (**ent-4b**) in the reactions gave similar results to those of the enantiomer (**4b**), thus producing the corresponding 1,3-DiMeTIQ (**ent-6b**) and 4-Ph-1,3-DiMeTIQ (**ent-7bA**), as shown in Table 1 (entries 10, 11, 12).

Table 1. TFSA-Promoted Pummerer-Type Cyclization Reaction of the Chiral Sulfoxides (**4**)

Entry	Sulfoxide (**4**)	Reagents (mol eq)		Yield (%) of products	
		TFAA	TFSA	1,3-diMeTIQ (**6**)	4-Ph-1,3-diMeTIQ (**7**)
1	**4a**	5	5	79 (**6a**)	5 (**7aA**)
2	**4a**	5	7	68 (**6a**)	16 (**7aA**)
3	**4a**	5	21	—	87 (**7aA**), 9 (**7aB**)
4	**ent-4a**	5	5	76 (**ent-6a**)	5 (**ent-7aB**)
5	**ent-4a**	5	7	67 (**ent-6a**)	17 (**ent-7aB**)
6	**ent-4a**	5	21	7 (**ent-6a**)	73 (**ent-7aB**), 12 (**ent-7aA**)
7	**4b**	5	5	53 (**6b**)	9 (**7bB**)
8	**4b**	5	7	56 (**6b**)	23 (**7bB**)
9	**4b**	5	21	4 (**6b**)	91 (**7bB**)
10	**ent-4b**	5	5	54 (**ent-6b**)	5 (**ent-7bA**)
11	**ent-4b**	5	7	56 (**ent-6b**)	36 (**ent-7bA**)
12	**ent-4b**	5	21	4 (**ent-6b**)	95 (**ent-7bA**)

Alkaline hydrolysis of the *N*-formyl-1,3-DiMeTIQs (**6a**, **ent-6a**, **6b**, **ent-6b**) yielded the corresponding chiral 1,3-DiMeTIQs (**1a**, **ent-1a**, **1b**, **ent-1b**). Similarly, *N*-formyl-4-Ph-1,3-DiMeTIQs (**7aA**, **ent-7aB**, **7bB**, **ent-7bA**) yielded the 4-Ph-1,3-DiMeTIQs (**8aA**, **ent-8aB**, **8bB**, **ent-8bA**).

These results demonstrated that the super acid TFSA greatly facilitates the Pummerer-type cyclization reaction leading to the isoquinoline ring system, although the Friedel–Crafts reaction of the Pummerer product with benzene occurred. The fact that the increased acidity of the reaction medium dramatically enhanced the cationic cyclization in the Pummerer reaction suggested that the reaction can involve a dicationic intermediate like the super acid-catalyzed Pictet–Spengler reaction reported by Yokoyama and collaborators.[12] For example, as shown in Chart 5, the sulfonium–carbenium dication (**10**) can be generated by the protonation to the cationic sulfur atom of the sulfonium ion (**9**). The dicationic species may be a true electrophile in this cyclization reaction. Mechanistic studies are now under way.

Experimental

Unless otherwise noted, the following procedures were adopted. Melting points were recorded on a Yanagimoto SP-M1 hot-stage melting point apparatus and are uncorrected. IR spectra were measured as films for oils and gums, and KBr disks for solids with a HORIBA FT-710 spectrophotometer, and the values are given in cm^{-1}. NMR spectra were measured on a JEOL JNM-AL300 (^{1}H-NMR: 300 MHz, ^{13}C-NMR: 75 MHz) NMR spectrometer in $CDCl_3$ with tetramethylsilane as an internal standard and the chemical shifts are given in δ values. Low-resolution electron-impact ionization mass spectra (LR-EIMS) were recorded on JEOL JMS-AM20 mass spectrometer at 70 eV using direct inlet probe. High-resolution EIMS (HR-EIMS) and low-resolution chemical ionization mass spectra (LR-CIMS) were measured on a JEOL JMS-D300 mass spectrometer at 70 eV (EIMS) or at 270 eV

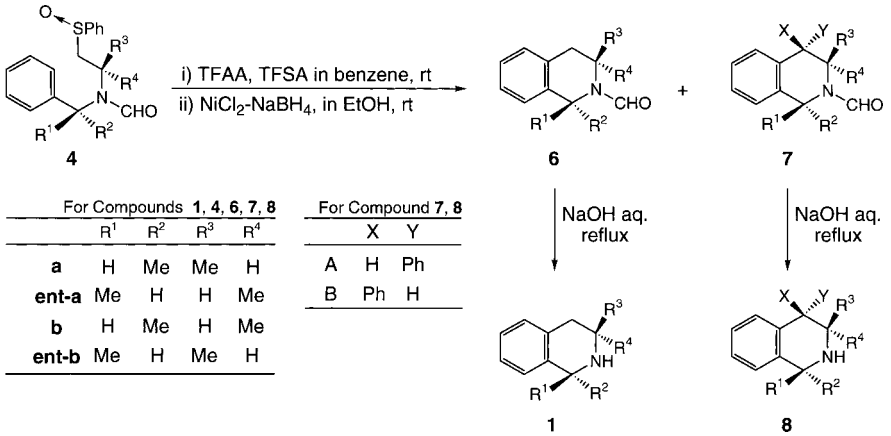

Chart 4

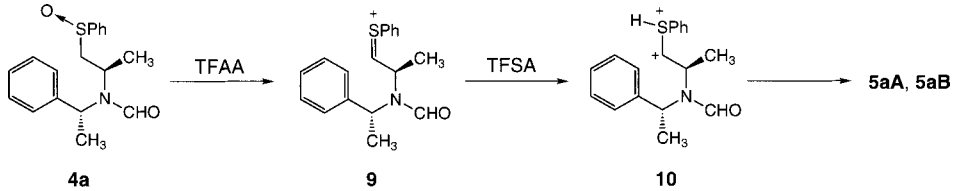

Chart 5

[CIMS, reactant gas: *iso*-butane] using a direct inlet probe. Elemental analysis were recorded on a Yanaco CHN-corder MT-3. Optical rotations were determined using a JASCO DIP-1000 digital polarimeter in MeOH. CD spectra were measured on a JASCO J-600 spectrometer in MeOH. TLC was performed on Merck precoated Silica gel 60 F_{254} plates. Column chromatography was carried out with silica gel (Wakogel C-200) or aluminium oxide (Alumium oxide 90, Merck). Medium-pressure liquid chromatography (MPLC) was performed on a Kusano CIG prepacked column. The chiral HPLC analysis were performed on a chiral column of Sumichiral OA 4700 [25 cm×4 mm i.d., room temperature, mobile phase, hexane–EtOH–trifluoroacetic acid (960 : 40 : 4); flow rate, 1.5 ml/min]. The organic extract from each reaction mixture was washed with brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo* to dryness.

Spectral Data of 3, ent-3, 4 and ent-4[13] (1*R*)-*N*-[(1*R*)-1-Methyl-2-(phenylsulfanyl)ethyl]-1-phenylethylamine (**3a**): A colorless oil. HCl salt, colorless needles recrystallized from Et_2O–EtOH, mp 165 °C (sublimation). IR: 2962, 1583. ^{1}H-NMR: 1.07 (3H, d, J=6 Hz, C1′-CH_3), 1.27 (3H, d, J=6 Hz, C1-CH_3), 2.7—2.9 (1H, m, C1′-H), 2.94 (1H, dd, J=6, 13 Hz, C2′-H), 3.04 (1H, dd, J=5, 13 Hz, C2′-H), 3.82 (1H, q, J=7 Hz, C1-H), 7.1—7.3 (10H, m, Ph-H×2). ^{13}C-NMR: 21.1 (C1′-CH_3), 24.7 (C1-CH_3), 40.3 (C2′), 49.7 (C1′), 55.3 (C1), 125.9 (Ph-CH), 126.5 (2×Ph-CH), 126.8 (Ph-CH), 128.4 (2×Ph-CH), 128.8 (2×Ph-CH), 129.3 (2×Ph-CH), 136.8 (Ph-C), 145.9 (Ph-C). LR-CIMS *m/z*: 272 (MH^+, base peak. $[\alpha]_D^{24}$=+76.4° (*c*=1.04%). Chiral-HPLC: 17.4 min.

(1*R*)-*N*-[(1*S*)-1-Methyl-2-(phenylsulfanyl)ethyl]-1-phenylethylamine (**3b**): A colorless oil. HCl salt recrystallized from Et_2O–EtOH, mp 167—170 °C. IR: 2962, 1583. ^{1}H-NMR: 1.09 (3H, d, J=6 Hz, C1′-CH_3), 1.35 (3H, d, J=7 Hz, C1-CH_3), 2.6—2.7 (1H, m, C1′-H), 2.83 (1H, dd, J=7, 13 Hz, C2′-H), 2.93 (1H, dd, J=5, 13 Hz, C2′-H), 3.87 (1H, q, J=7 Hz, C1-H), 7.1—7.3 (10H, m, Ph-H×2). ^{13}C-NMR: 19.8 (C1′-CH_3), 24.9 (C1-CH_3), 41.7 (C2′), 48.4 (C1′), 55.0 (C1), 125.9 (Ph-CH), 126.4 (2×Ph-CH), 126.8 (Ph-CH), 128.4 (2×Ph-CH), 128.8 (2×Ph-CH), 129.3 (2×Ph-CH), 136.2 (Ph-C), 145.2 (Ph-C). LR-CIMS *m/z*: 272 (MH^+, base peak). $[\alpha]_D^{24}$=+79.6° (*c*=0.87%). Chiral-HPLC: 12.5 min.

(1*S*)-*N*-[(1*S*)-1-Methyl-2-(phenylsulfanyl)ethyl]-1-phenylethylamine (**ent-3a**): A colorless oil. IR: 2962, 1583. ^{1}H-NMR: 1.07 (3H, d, J=6 Hz, C1′-CH_3), 1.27 (3H, d, J=6 Hz, C1-CH_3), 2.7—2.9 (1H, m, C1′-H), 2.94 (1H, dd, J=6, 13 Hz, C2′-H), 3.04 (1H, dd, J=5, 13 Hz, C2′-H), 3.82 (1H, q, J=7 Hz, C1-H), 7.1—7.3 (10H, m, Ph-H×2). ^{13}C-NMR: 21.1 (C1′-CH_3), 24.7 (C1-CH_3), 40.3 (C2′), 49.7 (C1′), 55.3 (C1), 125.9 (Ph-CH), 126.5 (2×Ph-CH), 126.8 (Ph-CH), 128.4 (2×Ph-CH), 128.8 (2×Ph-CH), 129.3 (2×Ph-CH), 136.8 (Ph-C), 145.9 (Ph-C). LR-EIMS *m/z*: 271 (M^+), 113 (base peak). HR-EIMS *m/z* (M^+): Calcd for $C_{17}H_{21}NS$: 271.1343. Found: 271.1388. $[\alpha]_D^{24}$=−77.0° (*c*=0.80%). Chiral-HPLC: 6.8 min.

(*S*)-*N*-[(1*R*)-1-Methyl-2-(phenylsulfanyl)ethyl]-1-phenylethylamine (**ent-3b**): A colorless oil. IR: 2964, 1583. ^{1}H-NMR: 1.09 (3H, d, J=6 Hz, C1′-CH_3), 1.35 (3H, d, J=7 Hz, C1-CH_3), 2.6—2.7 (1H, m, C1′-H), 2.83 (1H, dd, J=7, 13 Hz, C2′-H), 2.93 (1H, dd, J=5, 13 Hz, C2′-H), 3.87 (1H, q, J=7 Hz, C1-H), 7.1—7.3 (10H, m, Ph-H×2). ^{13}C-NMR: 19.8 (C1′-CH_3), 24.9 (C1-CH_3), 41.7 (C2′), 48.4 (C1′), 55.0 (C1), 125.9 (Ph-CH), 126.4 (2×Ph-CH), 126.8 (Ph-CH), 128.4 (2×Ph-CH), 128.8 (2×Ph-CH), 129.3 (2×Ph-CH), 136.2 (Ph-C), 145.2 (Ph-C). LR-CIMS *m/z*: 272 (MH^+, base peak). $[\alpha]_D^{24}$=−77.5° (*c*=0.97%). Chiral-HPLC: 7.3 min.

N-[(1*R*)-1-Methyl-2-(phenylsulfinyl)ethyl]-*N*-[(1*R*)-1-phenylethyl]formamide (**4a**): Colorless needles recrystallized from AcOEt–hexane, mp 91—93 °C. IR: 1664. ^{1}H-NMR: 1.3—1.8 (6H, m, 2×CH_3), 2.5—2.9 (1H, m, C2′-H), 3.3—3.9 (2H, m, C1′-H, C2′-H), 4.76 (1H, q, J=7 Hz, C1-H), 7.1—7.3 (10H, m, 2×Ph-H), 8.31 (1H, s, CHO). LR-CIMS *m/z*: 316 (MH^+, base peak). *Anal.* Calcd for $C_{18}H_{21}NO_2S$: C, 68.54; H, 6.71; N, 4.44. Found: C, 68.61; H, 6.85; N, 4.41.

N-[(1*S*)-1-Methyl-2-(phenylsulfinyl)ethyl]-*N*-[(1*R*)-1-phenylethyl]formamide (**4b**): A colorless gum. IR: 1664. ^{1}H-NMR: 0.90, 1.24 (total 3H, each d, J=6 Hz, C1′-CH_3), 1.65, 1.83 (total 3H, each d, J=7 Hz, C1-CH_3), 2.8—3.0, 3.5—4.1 (total 3H, m, C1′-H, C2′-H), 4.8—4.9 (1H, m, C1-H), 7.3—7.6 (10H, m, 2×Ph-H), 8.31, 8.44 (total 1H, each s, CHO). LR-CIMS *m/z*: 316 (MH^+), 190 (base peak).

N-[(1*S*)-1-Methyl-2-(phenylsulfinyl)ethyl]-*N*-[(1*S*)-1-phenylethyl]formamide (**ent-4a**): Colorless needles recrystallized from AcOEt–hexane, mp 93—95 °C. IR: 1664. ^{1}H-NMR: 1.3—1.8 (6H, m, 2×CH_3), 2.5—2.9 (1H, m, C2′-H), 3.3—3.9 (2H, m, C1′-H, C2′-H), 4.76 (1H, q, J=7 Hz, C1-H), 7.1—7.3 (10H, m, 2×Ph-H), 8.31 (1H, s, CHO). LR-CIMS *m/z*: 316 (MH^+, base peak).

N-[(1*R*)-1-Methyl-2-(phenylsulfinyl)ethyl]-*N*-[(1*S*)-1-phenylethyl]formamide (**ent-4b**): A colorless gum. IR: 1664. ^{1}H-NMR: 0.90, 1.24 (total 3H, each d, J=6 Hz, C1′-CH_3), 1.65, 1.83 (total 3H, each d, J=7 Hz, C1-CH_3), 2.8—3.0, 3.5—4.1 (total 3H, m, C1′-H, C2′-H), 4.8—4.9 (1H, m, C1-H), 7.3—7.6 (10H, m, 2×Ph-H), 8.31, 8.44 (total 1H, each s, CHO). LR-CIMS *m/z*: 316 (MH^+), 190 (base peak).

Pummerer Reaction of *N*-[(1*R*)-1-Methyl-2-(phenylsulfinyl)ethyl]-*N*-[(1*R*)-1-phenylethyl]formamides (4a) TFAA (1.665 g, 7.93 mmol) was added to a solution of **4a** (500 mg, 1.59 mmol) in benzene (50 ml) at root temperature, and the mixture was stirred under an argon atmosphere. After the mixture was stirred for 1 h, TFSA (1.190 g, 7.93 mmol) was added, and the reaction mixture was further stirred at the same temperature for 1 h. To this reaction mixture, 5% NaOH solution (50 ml) was added and the mixture was extracted with benzene. The residue was purified by MPLC (benzene : acetone=5 : 1) to give **5aA** (312 mg, 66%), **5aB** (76 mg, 19%), and **7aA** (42 mg, 10%).

(1*R*,3*R*)-2-Formyl-1,3-dimethyl-4-phenylsulfanyl-1,2,3,4-tetrahydroisoquinoline (**5aA**): Colorless prisms, recrystallized from AcOEt–hexane, mp 101—103 °C. IR: 1676. ^{1}H-NMR: 0.98, 1.10 (total 3H, each d, J=7 Hz, C3-CH_3), 1.74, 1.85 (total 3H, each d, J=7 Hz, C1-CH_3), 4.05, 4.89 (total 1H, each dd, J=2, 7 Hz, C3-H), 4.17, 4.23 (total 1H, each d, J=2 Hz, C4-H), 4.85, 5.05 (total 1H, q, J=7 Hz, C1-H), 7.2—7.5 (9H, m, Ph-H, SPh-H). 8.18, 8.57 (total 1H, each s, CHO). LR-EIMS *m/z*: 297 (M^+), 188 (base peak). HR-EIMS *m/z* (M^+): Calcd for $C_{18}H_{19}NOS$: 297.1188. Found: 297.1187.

(1*R*,3*R*)-2-Formyl-1,3-dimethyl-4-phenylsulfanyl-1,2,3,4-tetrahydroisoquinoline (**5aB**): A colorless gum. IR: 1655. ^{1}H-NMR: 1.43 (3H, d, J=7 Hz, C1-CH_3), 1.55 (3H, d, J=7 Hz, C3-CH_3), 4.18 (1H, dq, J=2, 7 Hz, C3-H), 4.35 (1H, d, J=2 Hz, C4-H), 5.37 (1H, q, J=7 Hz, C1-H), 7.2—7.5 (9H, m, Ph-H, SPh-H). 8.35 (1H, s, CHO). LR-CIMS *m/z*: 298 (MH^+, base peak).

(1*R*,3*R*,4*S*)-2-Formyl-1,3-dimethyl-4-phenyl-1,2,3,4-tetrahydroisoquinoline (**7aA**): Colorless prisms, recrystallized from AcOEt–hexane, mp 109—111 °C. IR: 1654. ^{1}H-NMR: 1.20, 1.31 (total 3H, each d, J=7 Hz, C3-CH_3), 1.45, 1.56 (total 3H, each d, J=7 Hz, C1-CH_3), 3.83 (1H, d, J=8 Hz, C4-H), 3.9—4.1, 5.1 (total 1H, each m, C3-H), 4.77, 5.70 (total 1H, each q, J=7 Hz, C1-H), 6.7—7.5 (9H, m, 2×Ph-H). 8.37, 8.40 (total 1H, each s, CHO). LR-EIMS *m/z*: 265 (M^+), 177 (base peak). HR-EIMS *m/z* (M^+): Calcd for $C_{18}H_{19}N_2O$: 265.1467. Found: 265.1467. $[\alpha]_D^{25}$=−56.7° (*c*=1.01%).

Pummerer Reaction and Reductive Desulfurization of Pummerer Products: Typical Procedure i) TFAA (1.665 g, 7.93 mmol) was added to a solution of **4a** (500 mg, 1.59 mmol) in benzene (50 ml) at room temperature, and the mixture was stirred under an argon atmosphere for 1 h. To this reaction mixture TFSA (1.190 g, 7.93 mmol) was added, and the mixture was further stirred at the same temperature for 1 h. To this reaction mixture, 5% NaOH aqueous solution (50 ml) was added and the mixture was extracted with benzene. The residue was dissolved in EtOH (200 ml) and $NiCl_2 \cdot 6H_2O$ (1.13 g, 7 mmol) in EtOH (200 ml) solution was added to this solution under ice cooling. $NaBH_4$ (1.7 g, 21 mol) was added in small portions to stirred mixture at 0 °C, and the mixture was stirred at room temperature for 2 h. Ice water was added to the reaction mixture and then the precipitate was removed by filtration. The filtrate was concentrated *in vacuo*. The residue was extracted with $CHCl_3$. The residue was purified by MPLC (benzene–acetone 5 : 1) to give **6a** (237 mg, 79%) and **7aA** (21 mg, 5%) (Table 1, entry 1).

(1*R*,3*R*)-2-Formyl-1,3-dimethyl-1,2,3,4-tetrahydroisoquinoline (**6a**): Colorless prisms, recrystallized from AcOEt–hexane, mp 67—70 °C. IR: 1660. ^{1}H-NMR: 1.0—1.5 (6H, m, C1-CH_3, C3-CH_3), 2.6—2.7 (1H, m, C4-H), 3.1—3.2 (1H, m, C4-H), 4.0—4.1, 4.6—4.7 (total 1H, each m, C3-H), 4.75, 5.37 (total 1H, each q, J=7 Hz, C1-H), 7.1—7.3 (4H, m, Ph-H), 8.32, 8.35 (total 1H, each s, CHO). LR-EIMS *m/z*: 189 (M^+), 91 (base peak). HR-EIMS *m/z* (M^+): Calcd for $C_{12}H_{15}NO$: 189.1154. Found: 189.1157. *Anal.* Calcd for $C_{12}H_{15}NO$: C, 76.16; H, 7.99; N, 7.40. Found: C, 76.17; H, 8.15; N, 7.36. $[\alpha]_D^{25}$=24.1° (*c*=0.82%).

ii) The reaction was proceeded under using excess amount of TFSA (5.1 g, 33.3 mmol) to give **7aA** (367 mg, 87%) and **7aB** (38 mg, 9%) (Table 1, entry 3).

(1*R*,3*R*,4*R*)-2-Formyl-1,3-dimethyl-4-phenyl-1,2,3,4-tetrahydroisoquinoline (**7aB**): Colorless prisms, recrystallized from AcOEt–hexane, mp 135—138 °C. IR: 1658. ^{1}H-NMR: 1.26 (3H, d, J=7 Hz, C3-CH_3), 1.56 (3H, d, J=7 Hz, C1-CH_3), 4.00 (1H, d, J=3 Hz, C4-H), 4.16 (1H, dq, J=3, 7 Hz, C3-H), 5.84 (1H, q, J=7 Hz, C1-H), 6.9—7.3 (9H, m, 2×Ph-H) 7.76 (1H, s, CHO). ^{13}C-NMR: 16.4 (C3-CH_3), 21.5 (C1-CH_3), 47.9 (C1), 49.0 (C3), 51.2 (C4), 126.8 (Ph-CH), 128.1 (3×Ph-CH), 128.2 (2×Ph-CH), 129.9 (3×Ph-CH), 136.8 (Ph-C), 137.1 (Ph-C), 139.2 (Ph-C), 159.9 (CHO). LR-EIMS *m/z*: 265 (M^+), 177 (base peak). HR-EIMS *m/z* (M^+): Calcd for $C_{18}H_{19}N_2O$:

265.1467. Found: 265.1461. $[\alpha]_D^{25}=-208.4°$ ($c=0.32\%$).

Similarly, **ent-4a** (3.0 g, 9.52 mmol) was treated with TFAA (9.99 g, 47.6 mol) and TFSA (30.6 g, 0.2 mol) under similar condition described above. The reduction of this reaction mixture in EtOH with $NiCl_2\cdot 6H_2O$ (1.13 g, 7 mmol) and $NaBH_4$ (1.7 g, 21 mol) gave **ent-6a** (128 mg, 7%), **ent-7aA** (293 mg, 12%), and **ent-7aB** (1.832 g, 73%) (Table 1, entry 6).

(1*S*,3*S*)-2-Formyl-1,3-dimethyl-1,2,3,4-tetrahydroisoquinoline (**ent-6a**): Colorless prisms, recrystallized from AcOEt–hexane, mp 74—76 °C. IR: 1660. ^{1}H-NMR: 1.0—1.5 (6H, m, C1-CH_3, C3-CH_3), 2.6—2.7 (1H, m, C4-H), 3.1—3.2 (1H, m, C4-H), 4.0—4.1, 4.6—4.7 (total 1H, each m, C3-H) 4.75, 5.37 (total 1H, each q, J=7 Hz, C1-H), 7.1—7.3 (4H, m, Ph-H) 8.32, 8.35 (total 1H, each s, CHO). LR-EIMS *m/z*: 189 (M^+), 91 (base peak). HR-EIMS *m/z* (M^+): Calcd for $C_{12}H_{15}NO$: 189.1154. Found: 189.1157. *Anal.* Calcd for $C_{12}H_{15}NO$: C, 76.16; H, 7.99; N, 7.40. Found: C, 76.17; H, 8.15; N, 7.36. $[\alpha]_D^{25}=-23.5°$ ($c=1.00\%$).

(1*S*,3*S*,4*S*)-2-Formyl-1,3-dimethyl-4-phenyl-1,2,3,4-tetrahydroisoquinoline (**ent-7aA**): Colorless prisms, recrystallized from AcOEt–hexane, mp 154—156 °C. IR: 1662. ^{1}H-NMR: 1.26, (3H, d, J=7 Hz, C3-CH_3), 1.56 (3H, d, J=7 Hz, C1-CH_3), 4.00 (1H, d, J=3 Hz, C4-H), 4.16 (1H, dq, J=3, 7 Hz, C3-H), 5.84 (1H, q, J=7 Hz, C1-H), 6.9—7.3 (9H, m, 2×Ph-H) 7.76 (1H, s, CHO). LR-EIMS *m/z*: 265 (M^+), 179 (base peak). HR-EIMS *m/z* (M^+): Calcd for $C_{18}H_{19}N_2O$: 265.1467. Found: 265.1476. $[\alpha]_D^{25}=212.6°$ ($c=1.00\%$).

(1*S*,3*S*,4*R*)-2-Formyl-1,3-dimethyl-4-phenyl-1,2,3,4-tetrahydroisoquinoline (**ent-7aB**): Colorless prisms, recrystallized from AcOEt–hexane, mp 108—110 °C. IR: 1655. ^{1}H-NMR: 1.20, 1.31 (total 3H, each d, J=7 Hz, C3-CH_3), 1.45, 1.56 (total 3H, each d, J=7 Hz, C1-CH_3), 3.83 (1H, d, J=8 Hz, C4-H), 3.9—4.1, 5.1 (total 1H, each m, C3-H), 4.77, 5.70 (total 1H, each q, J=7 Hz, C1-H), 6.7—7.5 (9H, m, 2×Ph-H). 8.37, 8.40 (total 1H, each s, CHO). LR-EIMS *m/z*: 265 (M^+), 177 (base peak). HR-EIMS *m/z* (M^+): Calcd for $C_{18}H_{19}N_2O$: 265.1467. Found: 265.1479. $[\alpha]_D^{25}=-91.0°$ ($c=1.00\%$).

Similarly, **4b** (8.0 g, 25 mmol) was treated with TFAA (26.7 g, 0.125 mol) and TFSA (27.2 g, 0.175 mol) under similar conditions as described above. The reduction of this reaction mixture in EtOH with $NiCl_2\cdot 6H_2O$ (1.13 g, 7 mmol) and $NaBH_4$ (1.7 g, 21 mol) gave **6b** (2.65 g, 56%), **7bB** (1.55 g, 23%) (Table 1, entry 8).

(1*R*,3*S*)-2-Formyl-1,3-dimethyl-1,2,3,4-tetrahydroisoquinoline (**6b**): Colorless prisms, recrystallized from AcOEt–hexane, mp 59—61 °C. IR: 1660. ^{1}H-NMR: 1.33, 1.36 (total 3H, each d, J=7 Hz, C3-CH_3) 1.59, 1.60 (total 3H, each d, J=7 Hz, C1-CH_3), 2.7—2.8 (1H, m, C4-H), 3.1—3.2 (1H, m, C4-H), 4.1—4.2, 4.6—4.7 (total 1H, each m, C3-H), 4.78, 5.38 (total 1H, each q, J=7 Hz, C1-H), 7.1—7.3 (4H, m, Ph-H) 8.23, 8.29 (total 1H, each s, CHO). LR-EIMS *m/z*: 189(M^+), 174 (base peak). HR-EIMS *m/z* (M^+): Calcd for $C_{12}H_{15}NO$: 189.1154. Found: 189.1154. $[\alpha]_D^{25}=-80.8°$ ($c=0.65\%$).

(1*R*,3*S*,4*R*)-2-Formyl-1,3-dimethyl-4-phenyl-1,2,3,4-tetrahydroisoquinoline (**7bB**): Colorless prisms, recrystallized from AcOEt–hexane, mp 97—100 °C. IR: 1668. ^{1}H-NMR: 1.37, 1.44 (total 3H, each d, J=7 Hz, C3-CH_3), 1.6—1.7 (3H, m, C1-CH_3), 3.9—4.0, 4.8—4.9 (total 1H, each m, C3-H), 4.08 (1H, s, C4-H), 4.90, 5.48 (total 1H, each q, J=7 Hz, C1-H), 6.8—7.4 (9H, m, 2×Ph-H), 7.62, 8.25 (total 1H, each s, CHO). LR-EIMS *m/z*: 265 (M^+), 179 (base peak). HR-EIMS *m/z* (M^+): Calcd for $C_{18}H_{19}N_2O$: 265.1467. Found: 265.1484. $[\alpha]_D^{25}=-160.0°$ ($c=1.00\%$).

Similarly, **ent-4b** (500 mg, 1.59 mmol) was treated with TFAA (1.66 g, 11.13 mmol) and TFSA (27.2 g, 0.175 mol) under similar conditions as described above. The reduction of this reaction mixture in EtOH with $NiCl_2\cdot 6H_2O$ (1.13 g, 7 mmol) and $NaBH_4$ (1.7 g, 21 mol) gave **ent-6b** (167 mg, 56%), and **ent-7bA** (152 mg, 36%) (Table 1, entry 11).

(1*S*,3*R*)-2-Formyl-1,3-dimethyl-1,2,3,4-tetrahydroisoquinoline (**ent-6b**): Colorless prisms, recrystallized from AcOEt–hexane, mp 62—65 °C. IR: 1660. ^{1}H-NMR: 1.33, 1.36 (total 3H, each d, J=7 Hz, C3-CH_3) 1.59, 1.60 (total 3H, each d, J=7 Hz, C1-CH_3), 2.7—2.8 (1H, m, C4-H), 3.1—3.2 (1H, m, C4-H), 4.1—4.2, 4.6—4.7 (total 1H, each m, C3-H), 4.78, 5.38 (total 1H, each q, J=7 Hz, C1-H), 7.1—7.3 (4H, m, Ph-H) 8.23, 8.29 (total 1H, each s, CHO). LR-EIMS *m/z*: 189 (M^+), 174 (base peak). HR-EIMS *m/z* (M^+): Calcd for $C_{12}H_{15}NO$: 189.1154. Found: 189.1157. $[\alpha]_D^{25}=83.2°$ ($c=1.00\%$).

(1*S*,3*R*,4*S*)-2-Formyl-1,3-dimethyl-4-phenyl-1,2,3,4-tetrahydroisoquinoline (**ent-7bA**): Colorless prisms, recrystallized from AcOEt–ether, mp 98—101 °C. IR: 1670. ^{1}H-NMR: 1.21, 1.44 (total 3H, each d, J=7 Hz, C3-CH_3), 1.6—1.7 (3H, m, C1-CH_3), 3.9—4.0, 4.8—4.9 (total 1H, each m, C3-H), 4.08 (1H, s, C4-H), 4.90, 5.48 (total 1H, each q, J=7 Hz, C1-H), 6.8—7.4 (9H, m, 2×Ph-H). 7.62, 8.25 (total 1H, each s, CHO). LR-EIMS *m/z*: 265 (M^+), 179 (base peak). HR-EIMS *m/z* (M^+): Calcd for $C_{18}H_{19}N_2O$: 265.1467. Found: 265.1484. *Anal.* Calcd for $C_{18}H_{19}N_2O$: C, 91.47; H, 7.22; N, 5.28. Found: C, 81.65; H, 7.31; N, 5.50. $[\alpha]_D^{25}=157.3°$ ($c=1.00\%$).

Hydrolysis of 2-Formyl-1,3-DiMeTIQs (6a, ent-6a, 6b, ent-6b): Typical Procedure A solution of **6a** (426 mg, 2.25 mmol) in EtOH (40 ml) and 20% NaOH aqueous solution (40 ml) was refluxed for 17 h under an argon atmosphere. The reaction mixture was diluted with water and extracted with $CHCl_3$. The residue was purified by column chromatography over aluminum oxide with AcOEt–hexane (1 : 2) to give **1** (265 mg, 73%) as a pale yellow oil. Similarly, the isomers (**6b**—**d**) gave 1,3-DiMeTIQs (**ent-1**, **2**, **ent-2**), respectively.

(1*R*,3*R*)-1,3-Dimethyl-1,2,3,4-tetrahydroisoquinoline (**1a**): A pale yellow oil. HCl salt, colorless prisms, recrystallized from EtOH, mp 249 °C (sublimation). ^{1}H-NMR: 1.21 (3H, d, J=7 Hz, C3-CH_3), 1.45 (3H, d, J=7 Hz, C1-CH_3), 2.46 (1H, dd, J=10, 16 Hz, C4-H), 2.79 (1H, dd, J=4, 16 Hz, C4-H), 3.3 (1H, m, C3-H), 4.23 (1H, q, J=7 Hz, C1-H), 7.0—7.2 (4H, m, Ph-H). ^{13}C-NMR: 22.4 (C3-CH_3), 24.2 (C1-CH_3), 37.5 (C4), 42.7 (C3), 50.8 (C1), 125.6 (C6), 125.9 (C7), 126.7 (C5), 129.1 (C8), 134.4 (C4a), 134.0 (C8a). HR-EIMS *m/z* (M^+): Calcd for $C_{11}H_{15}N$: 161.1202. Found: 161.1195. *Anal.* Calcd for $C_{11}H_{16}ClN$ (HCl salt): C, 66.83; H, 8.16; N, 7.08. Found: C, 66.68; H, 8.26; N, 7.03. $[\alpha]_D^{26}=-45.9°$ (HCl salt, $c=1.00\%$). CD (HCl salt, $c=2.54\times10^{-3}$ M) $[\theta]^{25}$ (nm): −300 (269), −310 (263).

(1*S*,3*S*)-1,3-Dimethyl-1,2,3,4-tetrahydroisoquinoline (**ent-1a**): Yield 70%. A pale yellow oil. HCl salt, colorless prisms, recrystallized from EtOH, mp 252 °C (sublimation). ^{1}H-NMR: 1.21 (3H, d, J=7 Hz, C3-CH_3), 1.45 (3H, d, J=7 Hz, C1-CH_3), 2.46 (1H, dd, J=10, 16 Hz, C4-H), 2.79 (1H, dd, J=4, 16 Hz, C4-H), 3.3 (1H, m, C3-H), 4.23 (1H, q, J=7 Hz, C1-H), 7.0—7.2 (4H, m, Ph-H). ^{13}C-NMR: 22.4 (C3-CH_3), 24.2 (C1-CH_3), 37.5 (C4), 42.7 (C3), 50.8 (C1), 125.6 (C6), 125.9 (C7), 126.7 (C5), 129.1 (C8), 134.4 (C4a), 134.0 (C8a). HR-EIMS *m/z* (M^+): Calcd for $C_{11}H_{15}N$: 161.1202. Found: 161.1184. *Anal.* Calcd for $C_{11}H_{16}ClN$ (HCl salt): C, 66.83; H, 8.16; N, 7.08. Found: C, 66.73; H, 8.21; N, 7.04. $[\alpha]_D^{28}=+49.2°$ (HCl salt, $c=1.03\%$). CD (HCl salt, $c=2.64\times10^{-3}$ M) $[\theta]^{25}$ (nm): 293 (270), 316 (263).

(1*R*,3*S*)-1,3-Dimethyl-1,2,3,4-tetrahydroisoquinoline (**1b**): Yield 72%. A pale yellow oil. HCl salt, colorless needles, recrystallized from EtOH, mp 248 °C (sublimation). ^{1}H-NMR: 1.24 (3H, d, J=7 Hz, C3-CH_3), 1.48 (3H, d, J=7 Hz, C1-CH_3), 2.56 (1H, dd, J=10, 16 Hz, C4-H), 2.75 (1H, dd, J=4, 16 Hz, C4-H), 3.0—3.1 (1H, m, C3-H), 4.16 (1H, q, J=7 Hz, C1-H), 7.1—7.2 (4H, m, Ph-H). ^{13}C-NMR: 22.3 (C3-CH_3), 22.7 (C1-CH_3), 38.4 (C4), 49.0 (C3), 52.6 (C1), 125.2 (C6), 125.9 (C7), 125.9 (C5), 128.9 (C8), 135.1 (C4a), 139.9 (C8a). HR-EIMS *m/z* (M^+): Calcd for $C_{11}H_{15}N$: 161.1202. Found: 161.1188. *Anal.* Calcd for $C_{11}H_{16}ClN$ (HCl salt): C, 66.83; H, 8.16; N, 7.08. Found: C, 66.75; H, 8.21; N, 7.06. $[\alpha]_D^{26}=+129.9°$ (HCl salt, $c=1.02\%$). CD (HCl salt, $c=2.48\times10^{-3}$ M) $[\theta]^{25}$ (nm): −230 (272), −200 (263).

(1*S*,3*R*)-1,3-Dimethyl-1,2,3,4-tetrahydroisoquinoline (**ent-1b**): Yield 72%. A pale yellow oil. HCl salt, colorless needles, recrystallized from EtOH, mp 247 °C (sublimation). ^{1}H-NMR: 1.24 (3H, d, J=7 Hz, C3-CH_3), 1.48 (3H, d, J=7 Hz, C1-CH_3), 2.56 (1H, dd, J=10, 16 Hz, C4-H), 2.75 (1H, dd, J=4, 16 Hz, C4-H), 3.0—3.1 (1H, m, C3-H), 4.16 (1H, q, J=7 Hz, C1-H), 7.1—7.2 (4H, m, Ph-H). ^{13}C-NMR: 22.3 (C3-CH_3), 22.7 (C1-CH_3), 38.4 (C4), 49.0 (C3), 52.6 (C1), 125.2 (C6), 125.9 (C7), 125.9 (C5), 128.9 (C8), 135.1 (C4a), 139.9 (C8a). LR-CIMS *m/z*: 162 (MH^+, base peak). *Anal.* Calcd for $C_{11}H_{16}ClN$ (HCl salt): C, 66.83; H, 8.16; N, 7.08. Found: C, 66.89; H, 8.24; N, 7.11. $[\alpha]_D^{24}=-119.3°$ (HCl salt, $c=0.99\%$). CD (HCl salt, $c=2.49\times10^{-3}$ M) $[\theta]^{25}$ (nm): 230 (272), 200 (263).

Hydrolysis of 2-Formyl-4-Phenyl-1,3-DiMeTIQs (7aA, ent-7aB, 7bB, ent-7bA): Typical Procedure A solution of **7aA** (235 mg, 0.887 mmol) in EtOH (20 ml) and 20% NaOH aqueous solution (20 ml) was refluxed for 17 h under an argon atmosphere. The reaction mixture was diluted with water and extracted with $CHCl_3$. The residue was purified by column chromatography over aluminum oxide with AcOEt–hexane (1 : 2) to give **8aA** (207 mg, 99%) as a pale yellow oil. Similarly, the isomers (**ent-7aB**, **7bB**, **ent-7bA**) gave 4-phenyl-1,3-DiMeTIQs (**ent-8aB**, **8bB**, **ent-8bA**), respectively.

(1*R*,3*R*,4*S*)-1,3-Dimethyl-4-phenyl-1,2,3,4-tetrahydroisoquinoline (**8aA**): HCl salt, pale yellow prisms, recrystallized from AcOEt–hexane, mp 127—129 °C. ^{1}H-NMR: 1.11 (3H, d, J=6 Hz, C3-CH_3), 1.58 (3H, d, J=7 Hz, C1-CH_3), 3.3—3.4 (1H, m, C3-H), 3.64 (1H, d, J=8 Hz, C4-H), 4.27 (1H, q, J=7 Hz, C1-H), 6.7—7.3 (9H, m, Ar-H, Ph-H). ^{13}C-NMR: 20.6 (C3-CH_3), 24.1 (C1-CH_3), 50.4 (C4), 50.7 (C1), 53.2 (C3), 125.9 (C6), 126.1 (C7), 126.2 (C5), 126.4 (C8), 128.4 (2×PhCH), 129.4 (2×PhCH), 130.3 (PhCH), 137.5 (C4a), 140.4 (C8a), 144.7 (PhC). LR-EIMS *m/z*: 237 (M^+), 179 (base peak). HR-EIMS *m/z* (M^+): Calcd for $C_{17}H_{19}N$: 237.1516. Found: 237.1516.

$[\alpha]_D^{24}=+53.1°$ (HCl salt, $c=0.86\%$). CD (HCl salt, $c=7.91\times10^{-4}$ M) $[\theta]^{25}$ (nm): 1500 (268), 1900 (263), −25000 (224).

(1*S*,3*S*,4*R*)-1,3-Dimethyl-4-phenyl-1,2,3,4-tetrahydroisoquinoline (**ent-8aB**): 177 mg (99%) was obtained from **ent-7aB** (200 mg, 0.755 mmol) as a pale yellow oil, HCl salt, pale yellow prisms, recrystallized from AcOEt–hexane, mp 127—129 °C. ^{1}H-NMR: 1.11 (3H, d, $J=6$ Hz, C3-CH_3), 1.58 (3H, d, $J=7$ Hz, C1-CH_3), 3.3—3.4 (1H, m, C3-H), 3.64 (1H, d, $J=8$ Hz, C4-H), 4.27 (1H, q, $J=7$ Hz, C1-H), 6.7—7.3 (9H, m, Ar-H, Ph-H). ^{13}C-NMR: 20.6 (C3-CH_3), 24.1 (C1-CH_3), 50.4 (C4), 50.7 (C1), 53.2 (C3), 125.9 (C6), 126.1 (C7), 126.2 (C5), 126.4(C8), 128.4 (2×PhCH), 129.4 (2×PhCH), 130.3 (PhCH), 137.5 (C4a), 140.4 (C8a), 144.7 (PhC). LR-EI-MS *m*/*z*: 237 (M^+), 179 (base peak). HR-EIMS *m*/*z* (M^+): Calcd for $C_{17}H_{19}N$: 237.1516. Found: 237.1516. $[\alpha]_D^{24}=-62.1°$ (HCl salt, $c=0.86\%$). CD (HCl salt $c=7.17\times10^{-4}$ M) $[\theta]^{25}$ (nm): −1100 (268), −1800 (261), 28600 (224).

(1*R*,3*S*,4*R*)-1,3-Dimethyl-4-phenyl-1,2,3,4-tetrahydroisoquinoline (**8bB**): 561 mg (48%) was obtained from **7bB** (1.3 g, 4.95 mmol) as colorless prisms, recrystallized from AcOEt–hexane, mp 57—59 °C, HCl salt, pale yellow prisms, recrystallized from AcOEt–hexane, mp 253—256 °C. ^{1}H-NMR: 1.07 (3H, d, $J=6$ Hz, C3-CH_3), 1.53 (3H, d, $J=7$ Hz, C1-CH_3), 3.1—3.2 (1H, m, C3-H), 3.70 (1H, d, $J=8$ Hz, C4-H), 4.33 (1H, q, $J=7$ Hz, C1-H), 6.7—7.3 (9H, m, Ar-H, Ph-H). ^{13}C-NMR: 20.9 (C3-CH_3), 22.4 (C1-CH_3), 52.6 (C4), 54.7 (C1), 56.5 (C3), 124.5 (C6), 125.9 (C7), 126.1 (C5), 126.4 (C8), 128.4 (2×PhCH), 129.7 (2×PhCH), 129.9 (PhCH), 139.1 (C4a), 140.2 (C8a), 144.2 (PhC). LR-EIMS *m*/*z*: 237 (M^+), 179 (base peak). HR-EIMS *m*/*z* (M^+): Calcd for $C_{17}H_{19}N$: 237.1516. Found: 237.1499. $[\alpha]_D^{28}=-30.84°$ (HCl salt, $c=1.00\%$). CD (HCl salt $c=7.50\times10^{-4}$ M) $[\theta]^{25}$ (nm): −3000 (268), −3400 (261), 22600 (226).

(1*S*,3*R*,4*S*)-1,3-Dimethyl-4-phenyl-1,2,3,4-tetrahydroisoquinoline (**ent-8bA**): 97 mg (48%) was obtained from **ent-7bA** (233 mg, 0.88 mmol) as colorless prisms, recrystallized from AcOEt–hexane, mp 57—59 °C, HCl salt, pale yellow prisms, recrystallized from AcOEt–hexane, mp 253—256 °C. ^{1}H-NMR: 1.07 (3H, d, $J=6$ Hz, C3-CH_3), 1.53 (3H, d, $J=7$ Hz, C1-CH_3), 3.1—3.2 (1H, m, C3-H), 3.70 (1H, d, $J=8$ Hz, C4-H), 4.33 (1H, q, $J=7$ Hz, C1-H), 6.7—7.3 (9H, m, Ar-H, Ph-H). ^{13}C-NMR: 20.9 (C3-CH_3), 22.4 (C1-CH_3), 52.6 (C4), 54.7 (C1), 56.5 (C3), 124.5 (C6), 125.9 (C7), 126.1 (C5), 126.4 (C8), 128.4 (2×PhCH), 129.7 (2×PhCH), 129.9 (PhCH), 139.1 (C4a), 140.2 (C8a), 144.2 (PhC). LR-EIMS *m*/*z*: 237 (M^+), 179 (base peak). HR-EIMS *m*/*z* (M^+): Calcd for $C_{17}H_{19}N$: 237.1516. Found: 237.1499. $[\alpha]_D^{28}=+34.32°$ (HCl salt $c=1.00\%$). CD (HCl salt $c=1.82\times10^{-3}$ M) $[\theta]^{25}$ (nm): 2400 (269), 3000 (261), −15000 (227).

References and Notes

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13) The spectral data including the $[\alpha]_D$ values of the compounds (**1a**, **ent-1a**, **1b**, **ent-1b**, **3a**, **ent-3a**, **3b**, **ent-3b**, **4a**, **ent-4a**, **4b**, **ent-4b**) and the CD values of the TIQs (**1a**, **ent-1a**, **1b**, **ent-1b**) reported in ref. 4 are found have errors in the description and therefore should be discarded. [Errata: *Chem. Pharm. Bull.*, **50**, 1641—1642 (2002)].