

## Preparation of Optically Active Amines by a Combination of Gabriel Synthesis and Optical Resolution. X-Ray Crystal Structure of the Adduct between (-)-10,10'-Dihydroxy-9,9'-biphenanthryl and *N*-(1-*tert*-Butyl-2-oxoazetidin-3-yl)phthalimide

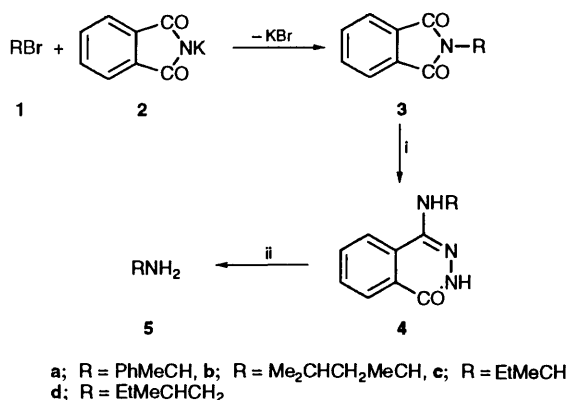
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Phthalimides which have a chiral alkyl group on the nitrogen atom, and which can easily be derived from potassium phthalimide and a chiral alkyl halide, were resolved by complexation with an optically active host compound. Decomposition, with hydrazine, of the resolved phthalimides gave optically active amines. Chiral recognition in an inclusion crystal of optically active *N*-azetidinone-substituted phthalimide and the optically active 10,10'-dihydroxy-9,9'-biphenanthryl host compound was studied by X-ray structure analysis.

The Gabriel synthesis is a classical but useful preparatory method for primary amines.<sup>1</sup> As shown in Scheme 1, reaction of an alkyl bromide **1** with potassium phthalimide **2** gives the corresponding *N*-alkylphthalimide **3**, which upon treatment with hydrazine followed by KOH affords the primary amine **5** via the intermediate **4**. When a chiral alkyl halide is used in the Gabriel synthesis, a chiral primary amine is obtained. However, preparation of optically active alkyl halides is not easy. We found that imides **3** which had a chiral alkyl group could be resolved by complexation with an optically active host compound. Finally, we established a new preparative method for optically active primary amines by a combination of Gabriel synthesis and optical resolution of an *N*-alkylphthalimide derivative.



Scheme 1 Reagents: i, NH<sub>2</sub>NH<sub>2</sub>; ii, KOH

### Results and Discussion

The phthalimides **3a-d** which have a chiral alkyl group on the nitrogen atom were prepared from potassium phthalimide **2** and the corresponding chiral alkyl bromide by the reported procedure.<sup>1</sup> Optical resolution of compounds **3a-d** was carried out by complexation with the optically active host compound (*S,S*)-(-)-1,6-bis-(*o*-chlorophenyl)-1,6-diphenylhexa-2,4-diyne-1,6-diol **6**<sup>3</sup> or (-)-10,10'-dihydroxy-9,9'-biphenanthryl **7**<sup>4</sup> by the reported procedure.<sup>5</sup> For example, when a solution of compound **6** and two mol equiv. of ( $\pm$ )-**3a** in diethyl ether-light petroleum was kept at room temperature for 12 h, a crystalline 1:1 inclusion complex of compounds **6** and (+)-**3a** was

Table 1  $[\alpha]_D$  Values and ees of compounds **5a-d**

Compound	$[\alpha]_D/10^{-1}$ deg cm <sup>2</sup> g <sup>-1</sup> ( <i>c</i> in EtOH)	Ee (%)
<b>5a</b>	+ 13 (0.3)	50
<b>5b-HCl</b>	- 54 (0.3)	30
<b>5c</b>	+ 4.3 (0.5)	30
<b>5d-HCl</b>	- 32 (0.1)	<i>a</i>

<sup>a</sup> Optical purity was not determined.

obtained. Two recrystallisations of the crude crystals from diethyl ether-light petroleum gave pure crystals which, upon distillation *in vacuo* gave compound (+)-**3a** of 55% enantiomeric excess (ee), in 10% yield. Decomposition of imide (+)-**3a** with hydrazine gave amine (+)-**5a** of 55% ee in 40% yield. By the same procedure, optically active amines **5b-d** were obtained (Table 1).

The preparation method of optically active amines was applied to aminoazetidinone. Reaction of 1-*tert*-butyl-3-chloroazetidin-2-one **8** with the salt **2** gave the phthalimide **9**. Optical resolution of ( $\pm$ )-**9** was achieved efficiently by complexation with the chiral host **7**. When a solution of diol **7** and two mol equiv. of ( $\pm$ )-**9** in benzene-hexane (1:1) was kept at room temperature for 12 h, a crystalline 1:1 inclusion complex (**11**) of diol **7** and (-)-**9** was obtained. After one recrystallisation from benzene-hexane, the crystals were chromatographed on silica gel to give complex **11** consisting of imide (-)-**9** of 100% ee and diol **7** in 63% yield as crystals. Decomposition of the complex **11** with hydrazine gave optically pure (-)-3-amino-1-*tert*-butylazetidin-2-one **10** in 44% yield. Chiral recognition in the inclusion crystal **11** was very efficient.

The preparation method is also applicable to primary diamines. Reaction of substrate **2** with 1,3-dibromobutane **12** gave the diphtalimide **13**. Optical resolution of ( $\pm$ )-**13** was achieved efficiently by complexation with diol **6** to give optically pure (-)-**13** in 42% yield. Decomposition of optically pure (-)-**13** gave optically pure (-)-butane-1,3-diamine **14** in 50% yield. However, reaction of 1,2-dichloropropane **15** with substrate **2** gave *N*-(2-chloropropyl)phthalimide **16** but not the diphtalimide derivative. Furthermore, although ( $\pm$ )-**16** was resolved efficiently by complexation with diol **7** decomposition (with hydrazine) of the resolved product **16** into the corresponding optically active amine, 2-chloropropylamine, failed.

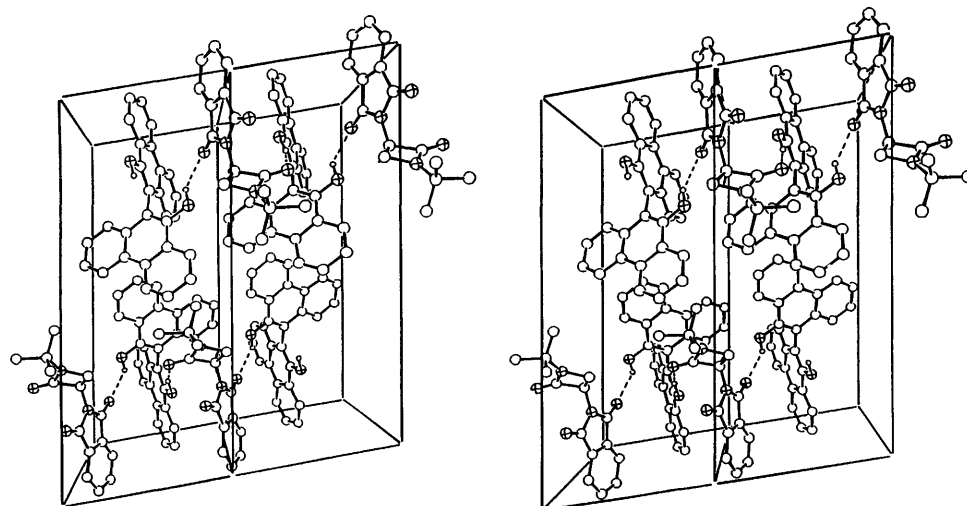
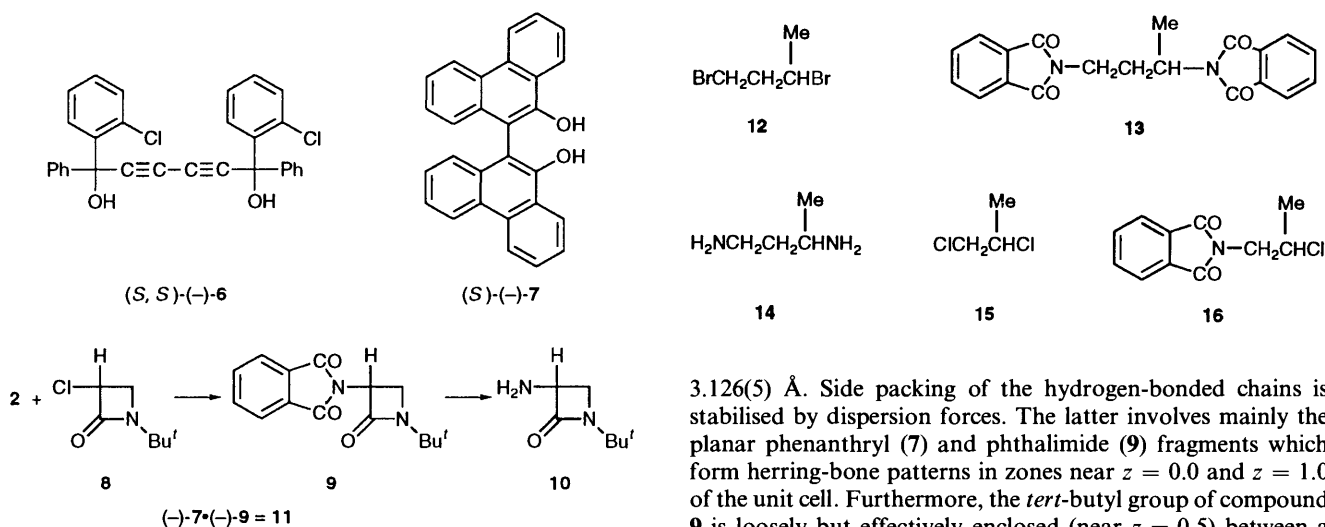


Fig. 1 The crystal structure of adduct **11**, viewed approximately down the *b*-axis (*c* is vertical). Two unit cells displaced along *a* are shown to illustrate better the continuous hydrogen-bonding scheme (marked by broken lines); the heteroatoms are indicated by crossed circles.



In order to investigate the mechanism of the efficient chiral recognition between the optically active host (**6** or **7**) and the phthalimide derivative in their inclusion compounds, an X-ray crystal structure study of the 1:1 inclusion complex **11** of compounds **7** and  $(-)\text{-}9$  was carried out.

Fig. 1 illustrates the crystal structure of complex **11**. It shows that the two rigid phenanthryl rings in compound **7** are nearly perpendicular to one another, thus allowing a co-ordinative association from both sides of the molecule with two different neighbouring species. The second molecular component of the solid complex, compound **9** also contains differently oriented multiple polar sites available for hydrogen bonding. Optimisation of these H-bonds in the crystalline phase leads to the formation of continuous chains of strongly co-ordinated molecules. The two components are arranged in an alternating manner along these chains along the *a*-axis of the crystal. Adjacent arrays of H-linked molecules are related to each other by the screw two-fold symmetry. The two hydroxy-group sites of diol **7** and two out of the three carbonyl sites of compound **9**, as proton donors and proton acceptor respectively, are involved in the hydrogen bonds: the observed  $\text{OH} \cdots \text{O}$  distances are 2.74(4) and 2.858(5) Å. The third carbonyl (of the phthalimide fragment) is not involved in co-ordinative interactions: however, it lies in proximity to the aryl group of a neighbouring molecule **9** from an adjacent unit cell at  $\text{C}=\text{O} \cdots \text{C}$  (aryl)

3.126(5) Å. Side packing of the hydrogen-bonded chains is stabilised by dispersion forces. The latter involves mainly the planar phenanthryl (**7**) and phthalimide (**9**) fragments which form herring-bone patterns in zones near  $z = 0.0$  and  $z = 1.0$  of the unit cell. Furthermore, the *tert*-butyl group of compound **9** is loosely but effectively enclosed (near  $z = 0.5$ ) between a second phenanthryl residue from the diol molecule it co-ordinates to and an additional phenanthryl moiety (from an adjacent chain) to the former by the screw symmetry (Fig. 1).

It should be pointed out that all attempts to prepare single crystals of the other diastereoisomer of this complex have failed thus far, suggesting for the latter a lower degree of spatial complementarity of the corresponding components in the organised solid phase. The energetically favoured formation of the chiral lattice chains of strongly linked molecules considerably limits the flexibility of the chiral lattice which forms, while enhancing the significance of steric fit between the complexing components. In the solid structure of complex **11**, the chiral phthalimide entities are surrounded by an asymmetric environment of rigid biphenanthryl groups. Accommodation of the  $(+)\text{-}9$  enantiomer in a similar crystal lattice with diol **7** appears clearly less favoured, requiring location of the bulky *tert*-butyl substituent in a smaller intermolecular space and/or disruption of the hydrogen-bonding scheme. The structural features observed in this study are consistent with those observed earlier in resolved solid complexes of diol **7** with other molecular components containing an asymmetric carbon.<sup>4,6,7</sup>

## Experimental

**General Procedures.**—All IR spectra of oily and crystalline samples were measured in neat samples and Nujol mulls,

respectively. All  $^1\text{H}$  NMR spectra were measured in  $\text{CDCl}_3$  solution. Optical rotations were measured on a digital polarimeter, JASCO DIP-140, and are given in units of  $10^{-1}$  deg  $\text{cm}^2 \text{g}^{-1}$ . All optical purities were determined by HPLC using a column containing an optically active solid phase, Chiralcel OC,\* unless otherwise noted. Light petroleum refers to the fraction boiling in the range 40–80 °C.

**Synthesis and Resolution of N-(1-Phenylethyl)phthalimide 3a.**—A solution of compound **2**<sup>2</sup> (10 g, 54 mmol) and (1-bromoethyl)benzene **1a** (10 g, 54 mmol) in dimethylformamide (DMF) (30  $\text{cm}^3$ ) was heated under reflux for 1 h. The reaction mixture was poured into ice–water and was extracted with  $\text{CHCl}_3$  (150  $\text{cm}^3$ ). The extract was washed successively with dil. KOH, water, dil. HCl, and water, dried over  $\text{Na}_2\text{SO}_4$ , and evaporated to leave an oily product, which upon distillation gave crude ( $\pm$ )-**3a** (9.5 g, 70%). When a solution of ( $\pm$ )-**3a** (5.8 g, 23 mmol) and diol **6** (5.6 g, 12 mmol) in diethyl ether (10  $\text{cm}^3$ ) was kept at room temperature for 12 h, a 1 : 1 inclusion complex of compounds **6** and (+)-**3a** was obtained as crystals, after two recrystallisations from diethyl ether–light petroleum (2.0 g, 24%), m.p. 92–93 °C;  $\nu_{\text{max}}/\text{cm}^{-1}$  3350, 1770 and 1700;  $\delta_{\text{H}}$  7.6 (22 H, m, ArH), 5.5 (1 H, m, CH), 3.4 (2 H, s, OH) and 1.9 (3 H, d, Me) (Found: C, 75.3; H, 4.6; N, 1.6. Calc. for  $\text{C}_{46}\text{H}_{33}\text{Cl}_2\text{NO}_4$ : C, 75.20; H, 4.53; N, 1.91%).

When the 1 : 1 inclusion crystals (2 g) were dissolved in benzene (10  $\text{cm}^3$ )–hexane (30  $\text{cm}^3$ ), diol **6** crystallised out as needles. After separation of diol **6** by filtration, the benzene–hexane solution was evaporated to leave (+)-**3a** as an oil, which upon purification by chromatography on silica gel with  $\text{CCl}_4$  as eluent, finally gave imide (+)-**3a** of 55% ee (0.3 g, 10%),  $[\alpha]_{\text{D}} + 35.8$  ( $c$  0.5, EtOH).

The hexane solution left after filtration of the 1 : 1 inclusion crystals (see above) was evaporated and the residue was chromatographed on silica gel to give imide (–)-**3a** of 32% ee (2.7 g, 92%),  $[\alpha]_{\text{D}} - 21.5$  ( $c$  0.5, EtOH). The optical purity of imides (+)-**3a** and (–)-**3a** was determined by measurement of their  $^1\text{H}$  NMR spectra in the presence of the chiral shift reagent europium tris(heptafluorobutyl) camphorate),  $\text{Eu}(\text{hfc})_3$ .

**Synthesis and Resolution of N-(1,3-Dimethylbutyl)phthalimide 3b.**—From 2-bromo-4-methylpentane **1b** and compound **2**, ( $\pm$ )-**3b** was obtained by the same procedure used for the preparation of compound **3a** as an oil (51%). When a solution of ( $\pm$ )-**3b** (3 g, 13 mmol) and diol **6** (1.6 g, 3.3 mmol) in diethyl ether (5  $\text{cm}^3$ )–light petroleum (5  $\text{cm}^3$ ) was kept at room temperature for 12 h, a 1 : 2 inclusion complex of **6** and (+)-**3b** was obtained as crystals, after two recrystallisations from diethyl ether–light petroleum (2 g, 57%), m.p. 88–90 °C;  $\nu_{\text{max}}/\text{cm}^{-1}$  3430, 1685 and 1760;  $\delta_{\text{H}}$  7.5 (26 H, m, ArH), 4.5 (10 H, m,  $\text{CH}_2$ , Me) and 0.9 (12 H, m, Me) (Found: C, 73.8; H, 5.9; N, 2.7. Calc. for  $\text{C}_{29}\text{H}_{27}\text{ClNO}_3$ : C, 73.64; H, 5.75; N, 2.96%).

When the inclusion crystals were treated by the same procedure as employed for the 1 : 1 inclusion complex of **6** and (+)-**3a**, compound (+)-**3b** of 30% ee was obtained as an oil in 56% yield  $\{[\alpha]_{\text{D}} + 3.8$  ( $c$  0.8, EtOH) $\}$ .

**Synthesis and Resolution of N-(1-Methylpropyl)phthalimide 3c.**—From 2-bromobutane **1c** and compound **2**, ( $\pm$ )-**3c** was prepared by the same procedure used for the preparation of compound **3a** as an oil in 68% yield. Treatment of ( $\pm$ )-**3c** with diol **6** by the same procedure as employed for ( $\pm$ )-**3a** gave a 1 : 1 inclusion complex of compounds **6** and (+)-**3c** as crystals in 60% yield, m.p. 98–103 °C;  $\nu_{\text{max}}/\text{cm}^{-1}$  1740, 1440 and 1680;  $\delta_{\text{H}}$  7.6 (22

H, m, ArH), 4.3 (1 H, m, CH), 3.3 (2 H, s, OH), 1.9 (2 H, m,  $\text{CH}_2$ ), 1.4 (3 H, d, Me) and 0.9 (3 H, t, Me) (Found: C, 73.7; H, 5.0; N, 1.8. Calc. for  $\text{C}_{42}\text{H}_{33}\text{Cl}_2\text{NO}_4$ : C, 73.47; H, 4.84; N, 2.04%).

When the inclusion crystals were treated by the same procedure as employed for the 1 : 1 inclusion complex of **6** and (+)-**3a**, compound (+)-**3c** of 30% ee was obtained as an oil in 74% yield  $\{[\alpha]_{\text{D}} + 11.8$  ( $c$  0.7, EtOH) $\}$ .

**Synthesis and Resolution of N-(2-Methylbutyl)phthalimide 3d.**—From 1-bromo-2-methylbutane **1d** and compound **2**, ( $\pm$ )-**3d** was prepared by the same procedure as used for the preparation of compound **3a** as an oil in 70% yield. Treatment of ( $\pm$ )-**3d** with diol **6** by the same procedure as employed for ( $\pm$ )-**3a** gave a 2 : 1 inclusion complex of compounds **6** and (+)-**3d** as crystals in 75% yield, m.p. 102–103 °C;  $\nu_{\text{max}}/\text{cm}^{-1}$  3350, 1755 and 1690;  $\delta_{\text{H}}$  7.6 (50 H, m, ArH), 3.5 (2 H, d,  $\text{CH}_2$ ), 3.2 (4 H, s, OH), 1.9 (1 H, m, CH) and 1.1 (8 H, m,  $\text{CH}_2$ , Me) (Found: C, 74.1; H, 4.7; N, 1.0. Calc. for  $\text{C}_{73}\text{H}_{55}\text{Cl}_4\text{NO}_6$ : C, 74.05; H, 4.68; N, 1.18%).

When the inclusion crystals were treated by the same procedure as employed for the 1 : 1 inclusion complex of compounds **6** and (+)-**3a**, compound (+)-**3d** was obtained as an oil in 56% yield  $\{[\alpha]_{\text{D}} + 1.0$  ( $c$  1.0, EtOH) $\}$ . However, the optical purity of (+)-**3d** was not determined.

**Decomposition, with Hydrazine, of N-Alkylphthalimides to Amines.**—A solution of compound (+)-**3a** of 55% ee (0.26 g, 1.04 mmol) in EtOH (10  $\text{cm}^3$ ) containing 95% hydrazine (0.06 g) was heated under reflux for 2 h. The crystalline solid left after evaporation of the solvent under reduced pressure was combined with 3 mol  $\text{dm}^{-3}$  HCl (20  $\text{cm}^3$ ) and heated in a water-bath for 5 min. The precipitate formed was removed by filtration and the filtrate was concentrated by evaporation to give the HCl salt of (+)-1-phenylethylamine **5a**. Acidification of the salt with dil. HCl gave (+)-**5a** of 50% ee in 40% yield  $\{[\alpha]_{\text{D}} + 13$  ( $c$  0.3, EtOH) $\}$ . The optical purity of the amine (+)-**5a** was determined by measurement of its  $^1\text{H}$  NMR spectrum in the presence of the chiral shift reagent (–)-2,2'-dihydroxy-1,1'-binaphthyl,<sup>8</sup>  $\nu_{\text{max}}/\text{cm}^{-1}$  3350;  $\delta_{\text{H}}$  7.3 (5 H, m, ArH), 4.1 (1 H, m, CH), 1.8 (2 H, s,  $\text{NH}_2$ ) and 1.4 (3 H, d, Me).

Decomposition of compound (+)-**3b** of 30% ee with hydrazine gave (+)-1,3-dimethylbutylamine of 30% ee in 20% yield  $\{[\alpha]_{\text{D}} + 4.3$  ( $c$  0.5, EtOH) $\}$ ;  $\nu_{\text{max}}/\text{cm}^{-1}$  3300;  $\delta_{\text{H}}$  3.8 (1 H, m, CH) and 1.3 (14 H, m,  $\text{NH}_2$ , CH,  $\text{CH}_2$  and Me).

Decomposition of compound (+)-**3c** of 30% ee and compound (+)-**3d** of unknown optical purity with hydrazine gave amines (+)-**5c** of 30% ee and (+)-**5d** of unknown optical purity, respectively. Since amines **5c** and **5d** are volatile, these were isolated as their HCl salts, (+)-**5c**·HCl {81% yield,  $[\alpha]_{\text{D}} - 54$  ( $c$  0.3, EtOH)} and (+)-**5d**·HCl {46% yield,  $[\alpha]_{\text{D}} - 32$  ( $c$  0.1, MeOH)}.

**Synthesis and Resolution of N-(1-tert-Butyl-2-oxoazetid-3-yl)phthalimide 9.**—A solution of 1-tert-butyl-3-chloroazetid-2-one **8**<sup>9,10</sup> (2.63 g, 16.3 mmol) and compound **2** (3.3 g, 17.8 mmol) in DMF (30  $\text{cm}^3$ ) was heated under reflux for 3 h. The reaction mixture was poured into ice–water, and extracted with  $\text{CHCl}_3$ . The extract was washed successively with dil. KOH, water, dil. HCl, and water, dried over  $\text{Na}_2\text{SO}_4$ , and evaporated to leave a crystalline product. Column chromatography of the product on silica gel with  $\text{CHCl}_3$  as eluent gave ( $\pm$ )-**9** in a pure state as crystals (2.32 g, 52%), m.p. 143–145 °C;  $\nu_{\text{max}}/\text{cm}^{-1}$  1720 and 1710;  $\delta_{\text{H}}$  7.8 (4 H, m, ArH), 5.3 (1 H, m, CH), 3.6 (2 H, m,  $\text{CH}_2$ ) and 1.4 (9 H, s, Bu') (Found: C, 65.8; H, 6.1; N, 10.2. Calc. for  $\text{C}_{15}\text{H}_{16}\text{N}_2\text{O}_3$ : C, 66.16; H, 5.92; N, 10.29%).

When a solution of ( $\pm$ )-**9** (0.8 g, 2.94 mmol) and diol **7** (0.57 g, 1.48 mmol) in benzene (10  $\text{cm}^3$ )–hexane (10  $\text{cm}^3$ ) was kept at

\* Chiralcel OC is available from Daicel Chemical Industries Ltd., Himeji, Japan.

room temperature for 12 h, a 1:1 inclusion complex **11** of compound **7** and (–)-**9** was formed as needles, after recrystallisation from benzene–hexane (0.63 g, 65%), m.p. 185–187 °C;  $\nu_{\max}/\text{cm}^{-1}$  3400, 1740 and 1710;  $\delta_{\text{H}}$  8.0 (2 H, m, ArH), 5.6 (2 H, OH), 3.5 (2 H, m, CH<sub>2</sub>) and 1.4 (9 H, s, Bu<sup>t</sup>) (Found: C, 78.2; H, 5.25; N, 4.0. Calc. for C<sub>43</sub>H<sub>34</sub>N<sub>2</sub>O<sub>5</sub>: C, 78.40; H, 5.20; N, 4.25%).

Chromatography of the 1:1 inclusion complex on silica gel with CHCl<sub>3</sub>–CCl<sub>4</sub> (1:2) as eluent gave compound (–)-**9** of 100% ee in 63% yield as crystals, m.p. 154–155 °C;  $[\alpha]_{\text{D}} -43$  (c 0.2, CHCl<sub>3</sub>);  $\nu_{\max}/\text{cm}^{-1}$  1780 and 1730;  $\delta_{\text{H}}$  7.8 (4 H, m, ArH), 5.3 (1 H, m, CH), 3.6 (2 H, m, CH<sub>2</sub>) and 1.4 (9 H, s, Bu<sup>t</sup>) (Found: C, 65.9; H, 6.1; N, 10.2. Calc. for C<sub>15</sub>H<sub>16</sub>N<sub>2</sub>O<sub>3</sub>: C, 66.16; H, 5.92; N, 10.29%).

**Decomposition, with Hydrazine, of Imide (–)-9 into (–)-3-Amino-1-tert-butylazetid-2-one 10.**—A solution of amide (–)-**9** (0.66 g) in EtOH (50 cm<sup>3</sup>) containing 95% hydrazine (0.16 g) was heated under reflux for 2 h. The crystalline solid left after evaporation of the solvent under reduced pressure was combined with 3 mol dm<sup>–3</sup> HCl (15 cm<sup>3</sup>) and the mixture was stirred for 2 h. The precipitate thus formed was removed by filtration and the filtrate was neutralised with 1 mol dm<sup>–3</sup> NaOH and extracted with benzene. The extract was dried over NaOH and evaporated to give (–)-**10** of 100% ee (0.12 g, 44%),  $[\alpha]_{\text{D}} -18$  (c 0.2, CHCl<sub>3</sub>);  $\nu_{\max}/\text{cm}^{-1}$  3370 and 1730;  $\delta_{\text{H}}$  4.0 (1 H, m, CH), 3.5 (1 H, m, CH), 2.9 (1 H, m, CH), 1.7 (2 H, m, NH<sub>2</sub>) and 1.3 (9 H, s, Bu<sup>t</sup>). The optical purity of (–)-**10** was determined by measurement of <sup>1</sup>H NMR spectrum in the presence of Eu(hfc)<sub>3</sub>.

**Synthesis and Resolution of 1,3-Diphthalimidobutane 13.**—A solution of compound **2** (10 g, 54 mmol) and 1,3-dibromobutane **12** (5.84 g, 27 mmol) in DMF (30 cm<sup>3</sup>) was heated under reflux for 2 h. The reaction mixture was poured into ice–water and was extracted with CHCl<sub>3</sub> (150 cm<sup>3</sup>). The extract was washed successively with dil. KOH, water, dil. HCl, and water, dried over Na<sub>2</sub>SO<sub>4</sub>, and evaporated to leave a crystalline product, which upon recrystallisation from benzene gave (±)-**13** as crystals (11.9 g, 63%), m.p. 128–130 °C;  $\nu_{\max}/\text{cm}^{-1}$  1760 and 1710;  $\delta_{\text{H}}$  7.7 (8 H, m, ArH), 4.3 (1 H, m, CH), 3.7 (2 H, m, CH<sub>2</sub>), 2.4 (2 H, m, CH<sub>2</sub>) and 1.5 (3 H, d, Me) (Found: C, 68.9; H, 4.6; N, 7.9. Calc. for C<sub>20</sub>H<sub>16</sub>N<sub>2</sub>O<sub>4</sub>: C, 68.96; H, 4.63; N, 8.04%).

When a solution of diimide (±)-**13** (2 g, 5.8 mmol) and diol **6** (1.4 g, 2.9 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (10 cm<sup>3</sup>)–hexane (10 cm<sup>3</sup>) was kept at room temperature for 12 h, a 2:2:1 inclusion complex of compounds (–)-**13**, **6**, and CH<sub>2</sub>Cl<sub>2</sub> was formed as fine needles, after recrystallisation from CH<sub>2</sub>Cl<sub>2</sub> (2 g, 79%), m.p. 124–126 °C;  $\nu_{\max}/\text{cm}^{-1}$  3340, 1760 and 1700;  $\delta_{\text{H}}$  7.5 (26 H, m, ArH), 5.3 (1 H, s, CH<sub>2</sub>Cl<sub>2</sub>), 4.4 (1 H, m, CH), 3.7 (4 H, m, CH<sub>2</sub>, OH), 2.4 (2 H, m, CH<sub>2</sub>) and 1.5 (3 H, d, Me) (Found: C, 69.3; H, 4.3; N, 3.0. Calc. for C<sub>101</sub>H<sub>74</sub>Cl<sub>6</sub>N<sub>4</sub>O<sub>12</sub>: C, 69.38; H, 4.27; N, 3.20%).

When a solution of the 2:2:1 inclusion complex of compounds (–)-**13**, **6**, and CH<sub>2</sub>Cl<sub>2</sub> in tetrahydrofuran (THF)–hexane was kept at room temperature for 24 h, (–)-**13** of 100% ee crystallised out as crystals, after recrystallisation from THF–hexane, in 42% yield, m.p. 138–140 °C;  $[\alpha]_{\text{D}} -2.6$  (c 0.8, CHCl<sub>3</sub>);  $\nu_{\max}/\text{cm}^{-1}$  1770 and 1705;  $\delta_{\text{H}}$  7.7 (8 H, m, ArH), 4.3 (1 H, m, CH), 3.7 (2 H, m, CH<sub>2</sub>), 2.4 (2 H, m, CH<sub>2</sub>) and 1.5 (2 H, d, Me) (Found: C, 69.3; H, 4.6; N, 8.0. Calc. for C<sub>20</sub>H<sub>16</sub>N<sub>2</sub>O<sub>4</sub>: C, 68.96; H, 4.63; N, 8.04%).

**Decomposition with Hydrazine, of Diimide (–)-13 into (–)-Butane-1,3-diamine 14.**—A solution of compound (–)-**13** of 100% ee (1 g, 2.9 mmol) in EtOH (10 cm<sup>3</sup>) containing 95% hydrazine (0.3 g) was heated under reflux for 3 h. The crystalline solid left after evaporation of the solvent was combined with 3

mol dm<sup>–3</sup> HCl (25 cm<sup>3</sup>) and heated in a water-bath for 5 min. The precipitate thus formed was removed by filtration and the filtrate was neutralised with dil. KOH and extracted with diethyl ether. The extract was dried over KOH and evaporated to give amine (–)-**14** of 100% ee as an oil, after chromatography on silica gel (0.12 g, 50%),  $[\alpha]_{\text{D}} -6.1$  (c 0.5, EtOH);  $\nu_{\max}/\text{cm}^{-1}$  3200;  $\delta_{\text{H}}$  2.9 (3 H, m, CH, CH<sub>2</sub>), 1.6 (4 H, m, CH<sub>2</sub>, NH<sub>2</sub>) and 1.3 (3 H, d, Me). The optical purity of amine (–)-**14** was determined by measurement of its <sup>1</sup>H NMR spectrum in the presence of both diol **6** and Eu(hfc)<sub>3</sub>. It has been reported that diol **6** works as a chiral shift reagent.<sup>11</sup> However, when both diol **6** and Eu(hfc)<sub>3</sub> were used together, the efficiency of diol **6** as a chiral shift reagent increased.

**Synthesis and Resolution of N-(2-Chloropropyl)phthalimide 16.**—A solution of **2** (10 g, 54 mmol) and 1,2-dichloropropane **15** (20 g, 180 mmol) in DMF (20 cm<sup>3</sup>) was heated under reflux for 3 h. The reaction mixture was poured into ice–water, and extracted with CHCl<sub>3</sub> (150 cm<sup>3</sup>). The extract was washed successively with dil. KOH, water, dil. HCl, and water, dried over Na<sub>2</sub>SO<sub>4</sub>, and evaporated to leave a crystalline solid. Column chromatography of the crude product on silica gel with CHCl<sub>3</sub> as eluent gave compound (±)-**16** as crystals (2.0 g, 17%), m.p. 86–89 °C;  $\nu_{\max}/\text{cm}^{-1}$  1775 and 1700;  $\delta_{\text{H}}$  7.9 (4 H, m, ArH), 4.5 (1 H, m, CH), 4.0 (2 H, m, CH<sub>2</sub>) and 1.7 (3 H, d, Me) (Found: C, 59.2; H, 4.4; N, 5.9. Calc. for C<sub>11</sub>H<sub>10</sub>ClNO<sub>2</sub>: C, 59.07; H, 4.51; N, 6.26%).

When a solution of (±)-**16** (1.8 g, 3.6 mmol) and diol **7** (0.7 g, 1.8 mmol) in benzene (20 cm<sup>3</sup>)–hexane (20 cm<sup>3</sup>) was kept at room temperature for 12 h, a 1:1 inclusion complex of diol **7** and imide (+)-**16** was formed as needles, after recrystallisation from benzene (1.4 g, 88%), m.p. 166–168 °C;  $\nu_{\max}/\text{cm}^{-1}$  3380, 1760 and 1700;  $\delta_{\text{H}}$  8.0 (20 H, m, ArH), 5.8 (2 H, s, OH), 4.3 (1 H, m, CH), 3.7 (2 H, m, CH<sub>2</sub>) and 1.5 (3 H, d, Me) (Found: C, 76.8; H, 4.65; N, 2.0. Calc. for C<sub>39</sub>H<sub>28</sub>ClNO<sub>4</sub>: C, 76.79; H, 4.63; N, 2.30%).

Chromatography of the 1:1 inclusion complex of compounds **7** and (+)-**16** on silica gel with CHCl<sub>3</sub>–CCl<sub>4</sub> (1:2) as eluent gave imide (+)-**16** of 100% ee in 56% yield as crystals, m.p. 102–105 °C;  $[\alpha]_{\text{D}} +17$  (c 0.6, CHCl<sub>3</sub>);  $\nu_{\max}/\text{cm}^{-1}$  1780 and 1700;  $\delta_{\text{H}}$  7.8 (4 H, m, ArH), 4.4 (1 H, m, CH), 3.9 (2 H, m, CH<sub>2</sub>) and 1.6 (3 H, d, Me) (Found: C, 59.2; H, 4.5; N, 6.0. Calc. for C<sub>11</sub>H<sub>10</sub>ClNO<sub>2</sub>: C, 59.07; H, 4.51; N, 6.26%).

**Crystal Structure Analysis of Adduct 11.**—The X-ray diffraction measurements were carried out at room temperature (~ 298 K) on an automated and upgraded Picker diffractometer equipped with a graphite monochromator, using Mo-K $\alpha$  ( $\lambda$  0.7107 Å) radiation. Intensity data were collected out to  $2\theta = 50^\circ$  by the  $\omega$ - $2\theta$  scan mode at a constant scan speed of 4.5 deg min<sup>–1</sup>. Possible deterioration of the analysed crystal was tested for by detecting periodically the intensities of three standard reflections from different zones of the reciprocal space, and was found to be negligible during the experiment. A total of 2844 unique reflections with positive intensities were recorded. No corrections for absorption or secondary extinction effects were applied.

**Crystal data:** C<sub>28</sub>H<sub>18</sub>O<sub>2</sub>·C<sub>15</sub>H<sub>16</sub>N<sub>2</sub>O<sub>3</sub>, *M<sub>r</sub>* 658.75, monoclinic, space group *P*2<sub>1</sub>, *a* = 7.499(1), *b* = 12.920(1), *c* = 17.931(1) Å,  $\beta$  = 99.71(1)°, *V* = 1712.4 Å<sup>3</sup>, *Z* = 2, *D*<sub>calc</sub> = 1.278 g cm<sup>–3</sup>, *F*(000) = 692,  $\mu$ (Mo-K $\alpha$ ) = 0.78 cm<sup>–1</sup>.

The structure was solved by direct methods (SHELXS-86),<sup>12</sup> and refined by full-matrix least-squares (SHELX-76),<sup>13</sup> including the positional and anisotropic thermal parameters of the non-hydrogen atoms. Most of the hydrogens were introduced in calculated positions; those attached to the hydroxy group O-atoms in diol **7** and to the chiral carbon in imide **9** were located directly in difference-Fourier maps. The terminal *tert*-butyl

group of compound **9** exhibits in the crystal a significant rotational disorder (of an apparently dynamic rather than static nature) about the C–N bond, as is reflected in the relatively large parameters of thermal motion associated with the three peripheral C-atoms ( $U_{eq}$  ranging from 0.18 to 0.20 Å<sup>2</sup>); the individual atomic parameters related to this group are, therefore, characterised by low precision. The final refinement, minimising  $w(\Delta F)^2$  where  $w = 1/\sigma^2(F_o)$ , converged at  $R = 0.048$  and  $wR = 0.052$  for 2220 observations having  $I > 3\sigma(I)$ . At convergence, the peaks and troughs of the difference density map did not exceed 0.18 and  $-0.19$  e Å<sup>-3</sup>, respectively, confirming the correctness of the structural model.

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