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Asymmetric cycloaddition of anthrone with *N*-substituted maleimides with C_2-chiral pyrrolidines

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Abstract: Base-catalyzed asymmetric cycloaddition of anthrone with achiral and chiral *N*-substituted maleimides was carried out in the presence of C_2-chiral pyrrolidines in almost quantitative yields. Chiral, non-racemic [4+2] adducts up to 61% ee were produced with achiral *N*-methyl and *N*-benzylmaleimide using the chiral catalysts. De's of the adducts up to 38% were observed in the cases of chiral *N*-substituted maleimides and achiral pyrrolidine, in which the absolute configuration of the major product was established by X-ray analysis. The combination of chiral maleimides and chiral catalysts afforded the adducts having up to 80% de. © 1997 Published by Elsevier Science Ltd. All rights reserved.

The asymmetric Diels–Alder reaction has been studied extensively and recognized as an efficient method creating up to four chiral centers at one time. Almost all investigations are focused on the use of stereogenic auxiliaries bound to one of the reactants[1] and both stoichiometric and catalytic amounts of chiral Lewis acids.[2] On the other hand, only a few reports of base-catalyzed asymmetric [4+2] cycloaddition closely related to the Diels–Alder reaction have been published with anthrone[3] and 3-hydroxy-2-pyronone.[4] We now describe the asymmetric cycloaddition with C_2-chiral pyrrolidines which have been successfully employed as chiral auxiliaries in various types of asymmetric syntheses.[5] Moreover, double asymmetric synthesis using chiral catalysts and chiral *N*-substituted maleimides is discussed.

Except commercially available *N*-methylmaleimide **1a**, *N*-substituted maleimides **1b–1e** were synthesized from maleic anhydride and corresponding amines by the action of acetic anhydride and sodium acetate in good yields.[6] Among several pyrrolidine derivatives, the C_2-chiral base[7] depicted below exhibited good catalytic activity in $CHCl_3$ while the reaction was very sluggish with *N*-substituted pyrrolidines. As to the catalysts shown in Table 1, the reaction conditions were optimized varying solvents. Moderate enantioselectivity was observed in $CHCl_3$, CH_2Cl_2, and toluene, and the ee's of the products were almost same in these solvents. The enantioselectivity dropped considerably in more polar solvents such as 1,2-dimethoxyethane and acetonitrile. The substrates were consumed much faster in MeOH to yield racemic **3a** along with racemic Michael adduct [the *N*-methyl analog of (*S*)-**4**]. Temperature and amounts of bases affected the velocity of the reaction, while stereoselectivity did not change substantially. Among the bases tested, bis(hydroxymethyl) derivative (*S,S*)-**2d** toward both *N*-methyl **1a** and *N*-benzylmaleimide **1b** gave the highest ee's (entries 4, 6) which were higher than those with (*S*)-prolinol at 20°C (47% ee) and comparable with those with quinidine at −50°C (61% ee) reported by Kagan.[3] The increase of selectivity by using (*S,S*)-**2d** in place of (*S*)-prolinol can be ascribed to the function of reducing the number of possible competing, diastereomeric transition state.[5c] The enantioselectivity was lower with *O*-protected bases **2a–2c** (entries 1–3, 5).

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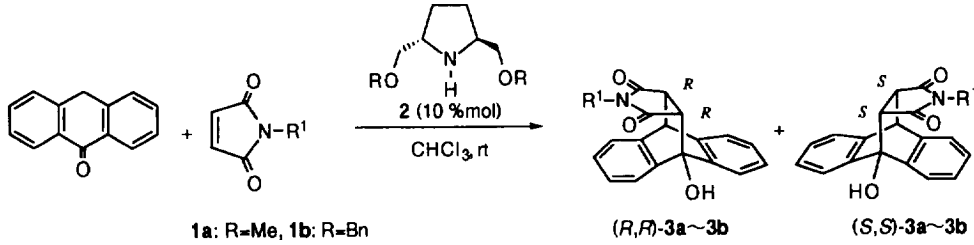
Table 1. Asymmetric cycloaddition of *N*-methyl and *N*-benzylmaleimide catalyzed by C_2-pyrrolidines.

entry	maleimide		catalyst		adduct			
	compd	R^1	compd	R	major isomer	yield (%)	$[\alpha]_D^{25}$ ($CHCl_3$)	ee(%) [b]
1	**1a**	Me	(*S,S*)-**2a**	Me	(*R,R*)-**3a**[a]	86	-15.0	21
2	**1a**	Me	(*S,S*)-**2b**	MOM	(*R,R*)-**3a**[a]	87	-25.0	35
3	**1a**	Me	(*S,S*)-**2c**	Bn	(*R,R*)-**3a**[a]	87	-20.0	28
4	**1a**	Me	(*S,S*)-**2d**	H	(*R,R*)-**3a**[a]	88	-43.3	61
5	**1b**	Bn	(*S,S*)-**2b**	MOM	(*R,R*)-**3b**[c]	99	-19.4	38
6	**1b**	Bn	(*S,S*)-**2d**	H	(*R,R*)-**3b**[c]	92	-31.7	59

[a] Based on the reported maximum rotation of (*S,S*)-**2a**: $[\alpha]_D$ -71.3 (*c* 0.5, $CHCl_3$); Riant, O.; Kagan, H. B. *Tetrahedron*, **1994**, *50*, 4543. [b] Determined by HPLC; Sumipax OA-2000 (200 mm x 4 mm), eluent: hexane / CH_2ClCH_2Cl / EtOH = 450 / 50 / 2, 2.0 mL/min, detection: 245 nm, retention time (*R,R*)-**3a**: 21.5 min, (*S,S*)-**3a**: 19.6 min, (*R,R*)-**3b**: 21.5 min, (*S,S*)-**3b**: 19.8 min. [c] The *R,R* configuration was assigned to (-)-**3b** based on the observation that the major enantiomers of both (-)-**3b** and (*R,R*)-**3a** elute slower on the chiral HPLC (note *b*), as well as on the fact that they have the same sign of specific rotation.



1a: R=Me, **1b**: R=Bn (*R,R*)-**3a**~**3b** (*S,S*)-**3a**~**3b**

In order to attain higher stereoselectivity, we undertook double asymmetric synthesis using *N*-substituted maleimides **1c**–**1e** and chiral catalyst **2d** (R=H) as well as **2b** (R=MOM) which exhibited the highest enantioselectivity among the *O*-protected pyrrolidines. Achiral unsubstituted pyrrolidine was also employed as the reference of the double asymmetric synthesis (Table 2, entries 1, 6, 8), where diastereoselectivity of 36–38% de was observed.[8] The absolute configuration of **3c**–**3e** was established by X-ray analysis of (S)-**4** (*vide infra*). The combinations of (*S*)-**1c**/(*S,S*)-**2b** and (*S*)-**1c**/(*S,S*)-**2d** were the matched pairs (entries 2 and 4), while the combinations of (*S*)-**1c**/(*R,R*)-**2b** and (*S*)-**1c**/(*R,R*)-**2d** were the mismatched pairs (entries 3 and 5).[9] As to chiral maleimides (*S*)-**1d** and (*S*)-**1e**, only the matched combinations were undertaken to improve diastereoselectivity (entries 7 and 9). Among them, the maximum de of 80% was observed with (*S*)-**1c**/(*S,S*)-**2d** (entry 4). In the case of (*R,R*)-**3d**, single crystallization from EtOAc/hexane afforded the diastereomerically pure product.

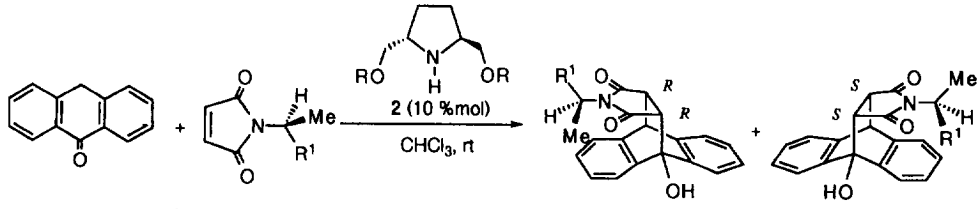
Table 2. Double asymmetric synthesis with chiral *N*-substituted maleimides and C_2-pyrrolidines.

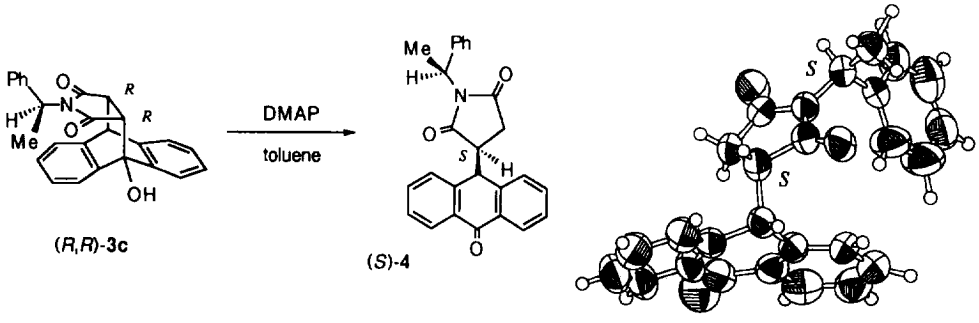
entry	maleimide		catalyst		time (h)	adduct			estimation[d]	
	compd	R^1	compd	R		major isomer	%yield	%de	config	%de
1	(*S*)-**1c**	Ph	pyrrolidine	—	2	(*R,R*)-**3c**	88	38[a]	—	—
2	(*S*)-**1c**	Ph	(*S,S*)-**2b**	MOM	5	(*R,R*)-**3c**	90	70[a]	*R,R*	63
3	(*S*)-**1c**	Ph	(*R,R*)-**2b**	MOM	5	(*S,S*)-**3c**	86	12[a]	*R,R*	1
4	(*S*)-**1c**	Ph	(*S,S*)-**2d**	H	5	(*R,R*)-**3c**	90	80[a]	*R,R*	80
5	(*S*)-**1c**	Ph	(*R,R*)-**2d**	H	5	(*S,S*)-**3c**	87	58[a]	*S,S*	27
6	(*S*)-**1d**	1-Naph	pyrrolidine	—	48	(*R,R*)-**3d**	85	36[b]	—	—
7	(*S*)-**1d**	1-Naph	(*S,S*)-**2d**	H	48	(*R,R*)-**3d**	86	76[b]	*R,R*	80
8	(*S*)-**1e**	(*p*-NO_2)Ph	pyrrolidine	—	2	(*R,R*)-**3e**	88	36[c]	—	—
9	(*S*)-**1e**	(*p*-NO_2)Ph	(*S,S*)-**2d**	H	2	(*R,R*)-**3e**	90	60[c]	*R,R*	80

[a] Determined by ^{1}H-NMR monitoring Me signal of **3c** (*RR*-isomer, 1.16 ppm; *SS*-isomer, 1.26 ppm).
[b] Determined by ^{1}H-NMR monitoring Me signal of **3d** (*RR*-isomer, 1.10 ppm; *SS*-isomer, 1.20 ppm).
[c] Determined by ^{1}H-NMR monitoring Me signal of **3e** (*RR*-isomer, 1.33 ppm; *SS*-isomer, 1.39 ppm).
[d] Calculated with

$$de_{double} = \left(\frac{1+ee_{cat}}{1-ee_{cat}} \cdot \frac{1+de_{maleimide}}{1-de_{maleimide}} - 1\right) \Big/ \left(\frac{1+ee_{cat}}{1-ee_{cat}} \cdot \frac{1+de_{maleimide}}{1-de_{maleimide}} + 1\right)$$

derived from $\Delta\Delta G^{\ddagger}_{double} = \Delta\Delta G^{\ddagger}_{cat} + \Delta\Delta G^{\ddagger}_{maleimide}$ and $\Delta\Delta G^{\ddagger} = -RT\ln[(1+ee)/(1-ee)]$, where positive and negative values of ee and de correspond to predominant products of *RR*- and *SS*-isomers, respectively.





The stereochemical bias of the double asymmetric induction can be estimated by the

equation in the note *d* of Table 2 which is derived from the hypothetical relationship of $\Delta\Delta G^{\ddagger}_{double}=\Delta\Delta G^{\ddagger}_{cat}+\Delta\Delta G^{\ddagger}_{maleimide}$ ($\Delta\Delta G^{\ddagger}=\Delta G^{\ddagger}_{R} - \Delta G^{\ddagger}_{S}$).[10] The estimates in Table 2 are consistent with those yielded from the rule of thumb proposed by Masamune.[9,11]

The absolute configuration of (*R*,*R*)-**3c** was assigned from the single crystal X-ray analysis of imide (*S*)-**4** derived from (*R*,*R*)-**3**. The de of (*S*)-**4** was improved to 100% by recrystallization. The *S*-configuration of succinimide ring was not assigned experimentally but safely chosen on the basis of that for (*S*)-1-phenylethylamine moiety in the molecule because the reactions of the maleimide synthesis, the cycloaddition, and the following transformation do not jeopardize the stereogenic center of (*S*)-1-phenylethylamine. The change in *R*,*S*-notation of **3c** and **4** is due to the change of the priority order of the substituents and the spatial orientation around stereogenic centres is the same. The *R*,*R*-configuration was also assigned to the major isomers of **3d** and **3e** based on the observation that their methyl signals as that of (*R*,*R*)-**3c** appeared at higher field on ^{1}H-NMR (Table 2, note *a–c*).

In conclusion, this report describes asymmetric [4+2] addition between anthrone and achiral/chiral *N*-substituted maleimides with C_2-chiral pyrrolidines in which the maximum selectivity of 80% de is observed. The C_2-chiral bases were also applied to the related asymmetric reaction with 3-hydroxy-2-pyronone, and the lower enantioselectivity than that with anthrone was observed.

Experimental

All mps (measured on a Yanagimoto micro melting point apparatus) are uncorrected. ^{1}H- and ^{13}C-NMR spectra were recorded in $CDCl_3$ with a JEOL-EX-270. *J* values are given in Hz. IR spectra were recorded with a Horiba FT-300 spectrophotometer. Elementary analyses were determined on a Yanaco MT-5. Optical rotation was measured with a Jasco DIP-140 polarimeter (with a 1 dm cell). HPLC analyses were done on a set of Jasco 880-PU and Jasco 875-UV.

Typical procedure for synthesis of N-*substituted maleimides: synthesis of* N-*benzylmaleimide* (***1b***)

To a refluxed solution of maleic anhydride (4.9 g, 50 mmol), benzylamine (5.5 g, 51 mmol) in ether (150 mL) was added dropwise. After 2 h, the mixture was evaporated. Acetic anhydride (150 mL) and sodium acetate (1.5 g) were added to the residue. After refluxing 2 h, the mixture was evaporated. The residue was dissolved in EtOAc (250 mL) and the mixture was filtered. The filtrate was washed with saturated NaCl, dried (Na_2SO_4), and evaporated. The residue was purified by silica gel flash chromatography (20% EtOAc in hexane) to give **1b** (3.8 g, 41% yield): colorless solid; mp 69–70 °C; ^{1}H NMR ($CDCl_3$) δ 4.67 (s, 2H), 6.69 (s, 2H), 7.28–7.33 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 41.3, 127.8, 128.3, 128.6, 134.1, 136.1, 170.4; Anal. Calcd for $C_{11}H_9NO_2$: C, 70.58; H, 4.85; N, 7.48. Found: C, 70.69; H, 4.83; N, 7.43.

*(S)-*N*-(1-Phenylethyl)maleimide (S)-**1c***

86% yield; colorless oil; $[\alpha]_D^{20}$ −87.4 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 1.82 (d, *J*=7.6, 3H), 5.36 (q, *J*=7.3, 1H), 6.62 (s, 2H), 7.25–7.43 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 17.6, 49.6, 127.2, 127.7, 128.5, 134.0, 140.3, 170.5; Anal. Calcd for $C_{12}H_{11}NO_2$: C, 71.63; H, 5.51; N, 6.96; Found: C, 71.15; H, 5.47; N, 6.91.

*(S)-*N*-[1-(1-Naphthyl)ethyl]maleimide (S)-**1d***

71% yield; colorless oil; $[\alpha]_D^{20}$ −185.5 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 1.93 (d, *J*=7.3, 3H), 6.13 (q, *J*=7.3, 1H), 6.58 (s, 2H), 7.23–7.57 (m, 3H), 7.78–7.90 (m, 3H), 8.08–8.13 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 18.0, 45.3, 122.7, 125.0, 125.5, 125.8, 126.6, 128.6, 128.9, 131.0, 133.7, 133.9, 134.5, 170.5; Anal. Calcd for $C_{16}H_{13}NO_2$: C, 76.48; H, 5.21; N, 5.57; Found: C, 76.23; H, 5.12; N, 5.56.

*(S)-*N*-[1-(*p*-Nitrophenyl)ethyl]maleimide (S)-**1e***

47% yield; colorless solid; mp 85–86 °C; $[\alpha]_D^{20}$ −101.3 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 1.86 (d, *J*=7.3, 3H), 5.39 (q, *J*=7.3, 1H), 6.71 (s, 2H), 7.54–7.63 (m, 2H), 8.14–8.24 (m, 2H); ^{13}C NMR

($CDCl_3$) δ 17.3, 48.7, 123.7, 128.1, 129.4, 134.1, 147.1, 147.3, 170.1; Anal. Calcd for $C_{12}H_{10}N_2O_4$: C, 58.54; H, 4.09; N, 11.38; Found: C, 58.49; H, 3.93; N, 11.32.

General procedure for base-catalyzed asymmetric cycloaddition of anthrone and N-substituted maleimides

A mixture of anthrone (194 mg, 1.0 mmol), an *N*-substituted maleimide (1.0 mmol), an amine (0.1 mmol) and a solvent (10 mL) was stirred at rt during which the reaction conversion was assessed by TLC. After completion of the reaction, the mixture was diluted with CH_2Cl_2 (20 mL). The solution was washed successively with 0.5 M HCl and saturated NaCl, dried (Na_2SO_4), and evaporated. The residue was purified by silica gel flash chromatography (15% EtOAc in hexane).

*(R,R)-**3a** (61% ee)*

Colorless solid; mp 189–190 °C [lit.[3b]: mp 194–197 °C (racemate)]; $[\alpha]_D^{25}$ −43.3 (*c* 0.5, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 2.49 (s, 3H), 3.10 (d, *J*=8.4, 1H), 3.30 (dd, *J*=3.5, 8.4, 1H), 4.52 (s, 1H), 4.72 (d, *J*=3.5, 1H), 7.10–7.75 (m, 8H); ^{13}C NMR ($CDCl_3$) δ 24.2, 44.5, 47.6, 50.7, 120.7, 120.8, 123.6, 124.4, 126.7, 126.8, 127.0, 127.2, 136.4, 138.9, 140.6, 142.4, 176.4, 177.8; IR (nujol) 3392, 1773, 1700, 1680; Anal. Calcd for $C_{19}H_{15}NO_3$: C, 74.74; H, 4.95; N, 4.59; Found: C, 74.87; H, 4.83; N, 4.60.

*(R,R)-**3b** (59% ee)*

Colorless solid; mp 211–213 °C; $[\alpha]_D^{25}$ −31.7 (*c* 1.1, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 3.11 (d, *J*=8.91, 1H), 3.31 (dd, *J*=3.51, 3.78, 1H), 4.26 (s, 2H), 4.42 (s, 1H), 4.70 (d, *J*=3.24, 1H), 6.70 (d, *J*=5.94, 2H), 6.98–7.40 (m, 10H), 7.66 (d, *J*=7.29, 1H); ^{13}C NMR ($CDCl_3$) δ 42.2, 44.4, 47.5, 50.6, 120.7, 123.6, 124.4, 127.2, 134.5, 136.4, 139.3, 140.6, 142.7, 176.0, 177.5; IR (nujol) 3359, 1767, 1680; Anal. Calcd for $C_{25}H_{19}NO_3$: C, 78.72; H, 5.02; N, 3.67; Found: C, 78.77; H, 4.99; N, 3.67.

*(R,R)-**3c** (80% de)*

Colorless solid; mp 165–166 °C; ^1H NMR ($CDCl_3$) δ 1.16 (d, *J*=7.3, 2.7H, *RR*-isomer), 1.26 (d, *J*=7.3, 0.3H, *SS*-isomer), 2.97 (d, *J*=8.4, 0.9H, *RR*-isomer), 3.06 (d, *J*=8.4, 0.1H, *SS*-isomer), 3.23 (dd, *J*=3.8, 8.9, 0.1H, *SS*-isomer), 3.27 (dd, *J*=3.8, 8.9, 0.9H, *RR*-isomer), 4.48 (s, 0.1H, *SS*-isomer), 4.56 (s, 0.9H, *RR*-isomer), 4.69 (d, *J*=3.5, 1H), 4.96 (q, *J*=7.6, 1H), 6.95–7.69 (m, 13H); ^{13}C NMR ($CDCl_3$) δ 15.7, 44.5, 47.1, 49.8, 50.0, 120.7, 121.0, 123.6, 124.5, 126.6, 126.7, 127.0, 127.1, 127.2, 127.5, 128.2, 136.5, 138.2, 139.1, 140.9, 142.6, 176.0, 177.7; IR (nujol) 3366, 1770, 1689; Anal. Calcd for $C_{26}H_{21}NO_3$: C, 78.97; H, 5.35; N, 3.54; Found: C, 78.61; H, 5.23; N, 3.21.

*(R,R)-**3d** (100% de)*

Colorless solid; mp 191–192 °C; $[\alpha]_D^{20}$ −77.0 (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.10 (d, *J*=6.8, 3H), 2.85 (d, *J*=8.9, 1H), 3.28 (dd, *J*=3.8, 8.6, 1H), 4.49 (s, 1H), 4.76 (d, *J*=3.24, 1H), 5.71 (q, *J*=7.0, 1H), 7.05–7.78 (m, 15H); ^{13}C NMR ($CDCl_3$) δ 15.8, 44.7, 46.1, 47.0, 49.8, 77.1, 120.7, 121.1, 122.6, 123.6, 124.4, 124.7, 125.5, 126.2, 126.6, 126.7, 126.8, 127.0, 128.8, 128.9, 131.1, 132.7, 133.6, 136.5, 139.0, 141.0, 142.5, 176.3, 178.0; IR (nujol) 3444, 1760, 1684; Anal. Calcd for $C_{30}H_{23}NO_3$: C, 80.88; H, 5.20; N, 3.14; Found: C, 81.13; H, 5.45; N, 3.35.

*(R,R)-**3d** (80% de)*

^1H NMR ($CDCl_3$) δ 1.10 (d, *J*=6.8, 2.7H, *RR*-isomer), 1.20 (d, *J*=6.8, 0.3H, *SS*-isomer), 2.85 (d, *J*=8.9, 1H), 3.28 (dd, *J*=3.8, 8.6, 1H), 4.49 (s, 1H), 4.76 (d, *J*=3.24, 1H), 5.71 (q, *J*=7.0, 1H), 7.05–7.78 (m, 15H).

(R,R)-3e (60% de)

Colorless solid; mp 182–183 °C; ^{1}H NMR ($CDCl_3$) δ 1.33 (d, *J*=7.3, 2.4H, *RR*-isomer), 1.39 (d, *J*=7.3, 0.6H, *SS*-isomer), 3.08 (d, *J*=8.9, 1H), 3.29 (dd, *J*=2.7, 8.9, 1H), 4.38 (d, *J*=2.2, 0.2H, SS-isomer), 4.45 (d, *J*=2.2, 0.8H, *RR*-isomer), 4.67 (d, *J*=3.5, 0.8H, *RR*-isomer), 4.72 (d, *J*=3.5, 0.2H, *SS*-isomer), 5.04 (q, *J*=6.8, 1H), 6.88–7.74 (m, 12H); ^{13}C NMR ($CDCl_3$) δ 15.7, 44.4, 47.1, 49.0, 50.2, 120.7, 121.0, 123.4, 124.5, 126.7, 126.8, 127.0, 127.2, 127.8, 127.9, 136.6, 139.0, 141.0, 142.5, 145.3, 147.1, 175.7, 177.3; IR (nujol) 3459, 1767, 1693, 1516, 1377; Anal. Calcd for $C_{26}H_{20}N_2O_5$: C, 70.90; H, 4.58; N, 6.36; Found: C, 71.00; H, 4.46; N, 6.40.

(10S)-10-[2,5-dioxo-1-((S)-1-phenylethyl)-3-pyrrolidinyl]-9(10H)-anthracenone (S)-4

A solution of *(R,R)*-**3c** (395 mg, 1.0 mmol, 80% de) and 4-dimethylaminopyridine (DMAP, 122 mg, 1.0 mmol) in toluene (10 mL) was refluxed for 24 h. After evaporation, 0.5 M HCl (6 mL) was added to the residue. The mixture was extracted with CH_2Cl_2 (15 mL×3). The combined extracts were washed with sat. NaCl, dried (Na_2SO_4), and evaporated. The residue was purified by silica gel flash chromatography (20% EtOAc in hexane) to give *(S)*-**4** (290 mg, 58% yield). Recrystallization (MeOH/EtOAc) afforded *(S)*-**4** of 100% de as single crystals; colorless prism; mp 132–134 °C; $[\alpha]_D^{20}$ −200.0 (c 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 1.70 (d, *J*=7.6, 3H), 1.81 (dd, *J*=5.1, 18.4, 1H), 2.17 (dd, *J*=9.2, 18.4, 1H), 3.33–3.42 (m, 1H), 5.09 (d, *J*=3.0, 1H), 5.33 (q, *J*=7.6, 1H), 7.02–7.70 (m, 11H), 8.23–8.30 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 16.0, 28.7, 41.4, 49.3, 50.3, 127.6, 127.7, 127.8, 127.9, 128.2, 128.3, 132.3, 133.2, 133.3, 133.6, 138.1, 138.9, 142.6, 174.7, 177.7, 183.7; IR (nujol) 1775, 1699, 1658; Anal. Calcd for $C_{26}H_{21}NO_3$: C, 78.97; H, 5.35; N, 3.54; Found: C, 79.19; H, 5.29; N, 3.52.

Single-crystal X-ray structure analysis of (S)-4

A colorless prismatic crystal having approximate dimensions of 0.10×0.60×0.30 mm was mounted on a glass fiber. Intensity measurements were performed on a Rigaku AFC7R diffractometer using Ni-filtered Cu-Kα radiation from a rotating anode X-ray generator run at 40 kV–300 mA. Cell constants obtained by a least-squares refinement using the setting angles of 25 carefully centered reflections in the range $44.09° < 2\theta < 57.88°$, corresponded to a monoclinic cell with dimensions: a=11.2810(6) Å, b=8.048(2) Å, c=12.3381(7) Å, β=114.561(4)° and V=1018.3(3) Å^3. For Z=2 and M=395.46, the calculated density is 1.29 g/cm^3. Based on the systematic absence of 0k0: k≠2n, packing considerations and a statistical analysis of intensity distribution, the space group was determined to be $P2_1$ (#4). The diffraction data were collected at a temperature of 20±1 °C using ω−2θ scan technique to a maximum 2θ value of 120.2°. Omega scan width of (1.57+0.30 tanθ)° was scanned for each reflection at an ω-speed of 8.0°/min. Of the 1732 reflections which were collected, 1642 were unique. The structure was partially solved by direct methods (SIR88)[12] and expanded using Fourier techniques (DIRDIF92).[13] The non-hydrogen atoms were refined anisotropically. Hydrogen atoms were refined isotropically. The final cycle of full-matrix least-squares refinement was carried out 1298 observed reflections ($I > 3.00\sigma(I)$) and 353 variable parameters, and converged to R=0.037 and R_w=0.039. All calculations were performed using the teXsan[14] crystallographic software package.

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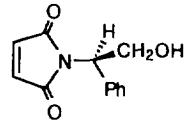
8. Hydroxymethyl derivative was also synthesized and subjected to the single and double asymmetric syntheses. Comparable degree of asymmetric induction with that in Tables 1 and 2 was observed in both the cases.



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11. The ratio of the product diastereomers can be calculated as follows.

$$\left(\frac{RR}{SS}\right)_{\text{double}} = \left(\frac{RR}{SS}\right)_{\text{cat}} \times \left(\frac{RR}{SS}\right)_{\text{maleimide}} \quad \text{in the matched pair}$$

$$\left(\frac{RR}{SS}\right)_{\text{double}} = \left(\frac{RR}{SS}\right)_{\text{cat}} \Big/ \left(\frac{RR}{SS}\right)_{\text{maleimide}} \quad \text{in the mismatched pair}$$

Next equation transforms the diastereomer ratio to ee or de.

$$\text{ee(de)} = (RR/SS - 1)/(RR/SS + 1)$$

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