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Enantioface-Differentiating Epoxidation of Alkylidenemalononitriles with Molecular Oxygen, catalyzed by Chiral Tertiary Amines

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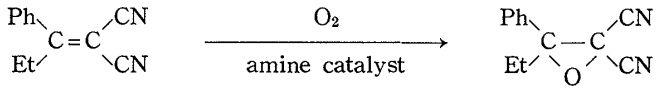
The present paper describes the enantioface-differentiating epoxidation of alkylidenemalononitriles with molecular oxygen, catalyzed by chiral tertiary amines. In the light of the by-product formation, the reaction path was concluded to involve intermolecular nucleophilic attack of a hydroperoxide intermediate catalyzed by a chiral tertiary amine. A similar epoxidation was demonstrated with cumylhydroperoxide in the presence of nicotine.

Keywords——enantioface-differentiation; epoxidation with molecular oxygen; alkylidenemalononitriles; 2,2-dicyanooxiranes; hydroperoxide; chiral tertiary amine; asymmetric synthesis

Methods now available for catalytic enantioface-differentiating epoxidation of olefins include hydrogen peroxide or hydroperoxide oxidation catalyzed by quaternary ammonium salts derived from alkaloids under phase-transfer conditions,[1] and by molybdenum[2] or vanadium[3] complexes possessing chiral ligands.

The preceding communication[4] reported our finding that (1-phenylalkylidene)malononitriles can be asymmetrically oxidized with molecular oxygen to yield optically active oxiranes in the presence of chiral tertiary amines. We now wish to describe this reaction in detail.

After our first finding of enantioface-differentiating epoxidation of (1-phenylpropylidene)-malononitrile (Ia) with oxygen, catalyzed by nicotine, we examined the effects of solvent, temperature and amine catalyst on the chemical yield.



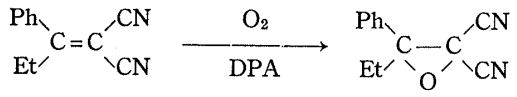
Ia IIa

The reactions of Ia in the presence of N,N-dimethyl-α-phenylethylamine (DPA) were carried out with various solvents and at various temperatures; the results are shown in Table I. The yield of 2,2-dicyano-3-ethyl-3-phenyloxirane (IIa) was best in dimethylformamide (DMF) and diethylene glycol diethyl ether (diglye) at temperatures of 20° and 30°, respectively. Particularly in DMF, the reaction proceeded at lower temperature within a shorter period.

Table II shows the effects of several base catalysts on the reaction of Ia in DMF at 20°. No epoxidation occurred without a base catalyst. Better yields of IIa were obtained in the runs with aliphatic tertiary amines such as nicotine, DPA and N-methylpiperidine. On the other hand, a weaker base such as pyridine required a prolonged reaction time, and stronger bases, such as 1,8-diazabicyclo[5,4,0]-7-undecene (DBU) and trimethylbenzylammonium hydroxide (Triton B), did not give IIa but unidentified resinous materials.

Extensive epoxidation of a number of alkylidenemalononitriles was examined in DMF in the presence of nicotine. The oxirane products, IIb—g, were purified by silica gel column chromatography in order to avoid thermal isomerization. The results are summarized in Table III. It appears that a reactive substrate should possess a methylene or methine moiety at C_2 of alkylidenemalononitrile, *i.e.*, R^1 or R^2=RCH_2 or R_2CH in the structure, $R^1R^2C{=}C(CN)_2$. The substrate Ib where R^1=Ph and R^2=Me, suffered a base-catalyzed polymerization similar

TABLE I. Temperature and Solvent Effects[a] in the Epoxidation[b] of Ia with Molecular Oxygen



Ia IIa

Solvent	React. temp (°C) 1.5	10	20	30	40
DMF	16.9 (19)	19.4 (10.5)	21.1 (9)	19.8 (8)	0
Diglye			20.4 (36)	21.6 (27)	16.5 (18)
Anisole		Not react.		8.7 (51)	
Toluene		Not react.		14.1 (24)	
Nitrobenzene		Not react.		9.8 (23)	

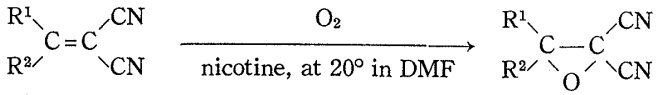
Conditions: Ia, 0.02 mol; DPA, 0.02 mol; solvent, 20 ml; O_2, 9.2 ml/min.
a) Yields, from which the effects were calculated, are based on the product, IIa, actually isolated. Values in parentheses indicate reaction times (hr).
b) In every run, IIIa was obtained as a by-product.

TABLE II. Effect of Base Catalyst on the Epoxidation of Ia with Molecular Oxygen

Base	Reaction time (hr)	Yield[a] of IIa
Pyridine	120	10.3
N-Methylpiperidine	7	14.8
DPA	9	21.1
Nicotine	12	18.5

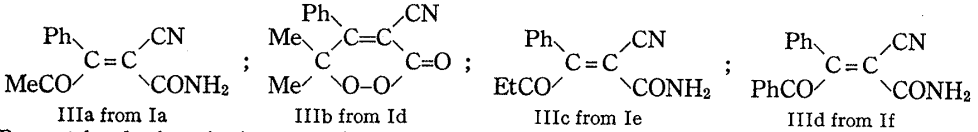
Conditions: Ia, 0.02 mol; solvent (DMF), 20 ml; base, 0.02 mol; O_2, 9.2 ml/min; reaction temperature, 20°.
a) Based on the product, IIa, isolated. IIIa was obtained in every run as a by-product.

TABLE III. Epoxidation of Alkylidenemalononitriles with Molecular Oxygen



Substrate	R^1	R^2	Reaction time (hr)	Yield (%) of Oxirane		By-product[a]	
Ic	Ph	H	46.5		0		—
Ib	Ph	Me	8.5		0[b]		—
Ia	Ph	Et	12.0	IIa	18.5	IIIa	2.3
Id	Ph	iso-Pr	45.0	IIb	6.0	IIIb	4.4
Ie	Ph	*n*-Pr	104.5	IIc	23.4	IIIc	13.2
If	Ph	$PhCH_2$	92.5	IId	12.5	IIId	27.5
Ig	Ph	Ph	309.0		0		—
Ih	Et	*n*-Bu	65.0	IIe	33.5		—
Ii	Et	Et	22.0	IIf	17.2		—
Ij	$-CH_2(CH_2)_3CH_2-$		27.0	IIg	22.3		—

Conditions: substrate, 0.02 mol; nicotine, 0.02 mol; DMF, 20 ml; O_2, 9.2 ml/min.
a) The following by-products were obtained.



IIIa from Ia IIIb from Id IIIc from Ie IIId from If

b) Base-catalyzed polymerization occurred.

to that reported previously.[5] Substrate in which one of the cyano groups of Ib is replaced by hydrogen did not undergo epoxidation. In the runs with Ia, Id, Ie and If, by-products, β-acetyl-α-cyanocinnamamide (IIIa), 6,6-dimethyl-3-oxo-5-phenyl-3,6-dihydro-1,2-dioxin-4-carbonitrile (IIIb), α-cyano-β-propionylcinnamamide (IIIc) and its β-benzoyl analog (IIId), respectively, were obtained.

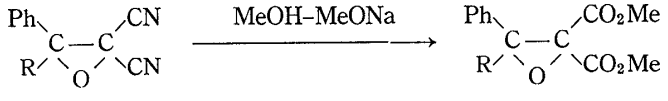
Table IV shows the results of epoxidation of Ia, Id, Ie, If and Ih with nicotine, (+)-D-DPA and (−)-L-DPA as chiral base catalysts. In the cases of the oxirane products IIa, IIb and IIc, obtained from Ia, Id and Ie, respectively, appreciable specific rotation was observed, and those of the former two products were reversed when the opposite enantiomer of DPA was used.

Table IV. Enantioface-differentiating Epoxidation with Molecular Oxygen

Subst. No.	Optically active *tert*-amine	Reaction time (hr)	Yield of product (%)		$[\alpha]_D^{26}$
Ia	Nicotine	12.0	IIa	18.5	+1.93° (*c*=12.70, EtOH)
	(+)-D-DPA	7.0	IIa	21.5	−0.82° (*c*=34.15, EtOH)
	(−)-L-DPA	7.0	IIa	19.8	+0.64° (*c*=33.04, EtOH)
Id	Nicotine	45.0	IIb	6.0	−3.27° (*c*=15.00, EtOH)
	(+)-D-DPA	48.0	IIb	14.7	+0.49° (*c*=22.22, EtOH)
	(−)-L-DPA	48.0	IIb	11.3	−0.59° (*c*=21.94, EtOH)
Ie	Nicotine	104.0	IIc	23.4	+1.55° (*c*=18.67, EtOH)
If	Nicotine	92.5	IId	12.5	+0.08° (*c*=18.41, C_6H_6)
Ih	Nicotine	65.0	IIe	33.5	+0.04° (neat)

Conditions: substrate, 0.02 mol; optically active *tert*-amine, 0.02 mol; DMF, 20 ml; O_2, 9.2 ml/min; temperature, 20°.

The enantiomeric excesses of IIa and IIc were then determined by the use of the optically active nuclear magnetic resonance (NMR) shift reagent, tris(trifluoromethylhydroxymethylene-*d*-camphorato)praseodymium (III) [Pr(tfc)$_3$]. Although no differences appeared in the proton resonances of enantiomers of IIa, its 2,2-bis(methoxycarbonyl) derivative, IVa, to which IIa was easily converted by treatment with methanolic sodium methoxide, exhibited distinct differences between the methyl proton (–$COOCH_3$) resonances of the enantiomers. By calculation from the peak ratio, the enantiomeric excess of IVa ($[\alpha]_D^{26}$ +2.00°) was determined to be 6.0%, which corresponds to that of IIa ($[\alpha]_D^{26}$ +1.93°). The product, IIc, was also converted to its 2,2-bis(methoxycarbonyl) derivative, IVb, and in the same way, the enantiomeric excess of IIc ($[\alpha]_D^{26}$ +1.55°) was determined to be 5.5%.



IIa, c IVa, b

R= Et : 6.0 e.e.% (IIa, $[\alpha]_D^{26}$ +1.93°; IVa, $[\alpha]_D^{26}$ +2.00°)
R=*n*-Pr: 5.5 e.e.% (IIc, $[\alpha]_D^{26}$ +1.55°; IVb, $[\alpha]_D^{26}$ +1.40°)

The effect of several solvents and of variation of the reaction temperature on the optical yields under the selected standard reaction conditions were compared in the case of Ia, and the results are shown in Tables V and VI. Table V shows that at 30°, the best optical yields were obtained in anisole and nitrobenzene as solvents. Table VI shows that a decrease of the temperature tended to raise the optical yield, with DMF as a solvent.

While it is possible that the epoxidation is induced by molecular oxygen, we sought to elucidate its mechanistic function, paying particular attention to the by-products, IIIa—d, which were described above (see Table III); their identities are summarized in Table VIII.

It is very likely that formation of these by-products is initiated by base-catalyzed hydroperoxidation at the C_2-methylene or methine of alkylidenemalononitriles, as shown in Chart 1.

Table V. Solvent Effect on the Enantioface-differentiating Epoxidation of Ia

Solvent	Reaction time (hr)	Yield of IIa (%)	$[\alpha]_D^{26}$ (c in EtOH)	Optical yield (e.e. %)
DMF	18.0	18.3	+1.87 (20.09)	5.8
Diglye	75.5	18.2	+2.42 (20.04)	7.5
Anisole	47.0	8.5	+2.70 (20.34)	8.4
Toluene	139.0	13.3	+2.29 (21.55)	7.1
Nitrobenzene	66.5	15.2	+2.70 (20.40)	8.4

Conditions: Ia, 0.01 mol; nicotine, 0.01 mol; solvent, 20 ml; O_2, 9.2 ml/min; reaction temperature, 30°.

Table VI. Temperature Effect on the Enantioface-differentiating Epoxidation of Ia

Reaction temp. (°C)	Reaction time (hr)	Yield of IIa (%)	$[\alpha]_D^{26}$ (c in EtOH)	Optical yield (e.e.%)
0	17.0	12.7	+2.46 (20.33)	7.6
10	18.0	17.3	+2.16 (20.86)	6.7
20	19.5	19.0	+1.97 (20.55)	6.1
30	18.0	18.3	+1.87 (20.09)	5.8

Conditions: Ia, 0.01 mol; nicotine, 0.01 mol; DMF, 20 ml; O_2, 9.2 ml/min.

The by-products IIIa, IIIc and IIId, produced from Ia, Ie and If, respectively, are probably formed from a peroxide anion, **2**, by intramolecular nucleophilic attack at the nitrile carbon followed by β-elimination in a way similar to the well-known alkaline amidation by hydroperoxide.[6] Since lack of hydrogen at C_2 in **2** makes β-elimination impossible, the run with Id should give a cyclic peroxide, **6**, from which IIIb is formed by hydrolysis.

The by-product formations thus confirm the intermediacy of hydroperoxidation at C_2 of the substrates. The epoxidation, therefore, is considered to proceed by intermolecular attack of the hydroperoxide initially formed from the substrate, as shown in Chart 2. Presumably in the asymmetric epoxidation, a chiral environment may be provided by interaction between the hydroperoxide and the chiral base catalyst.

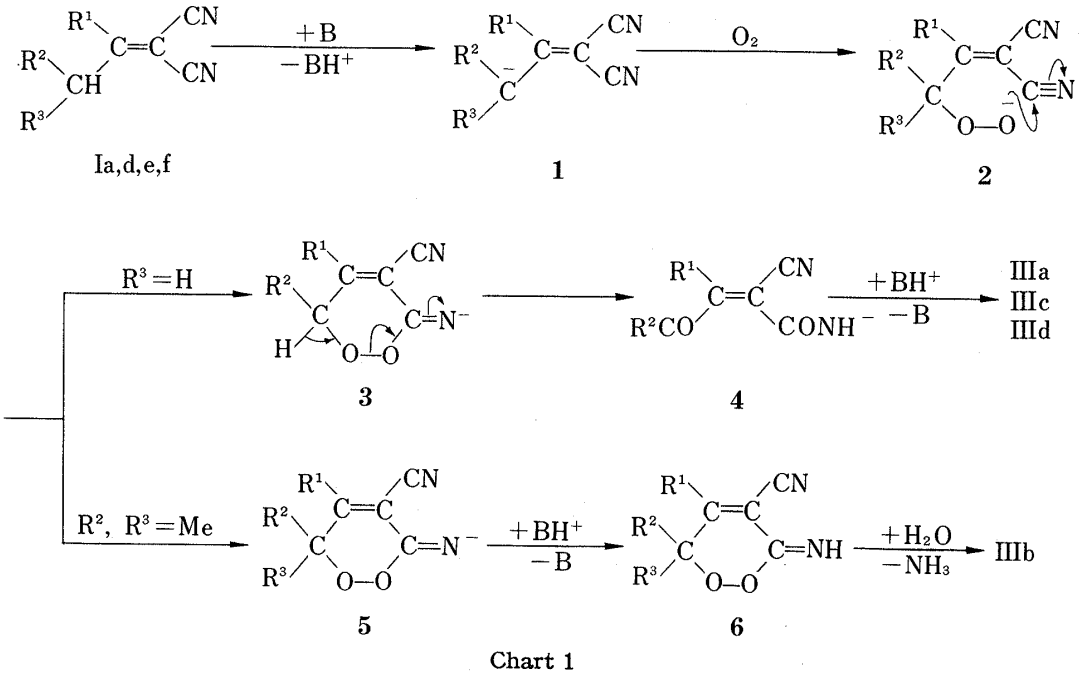
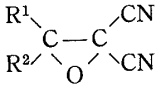


Chart 1

Based on the above assumption, attempts were made to carry out asymmetrical epoxidation of Ia with a number of available hydroperoxides, such as cumylhydroperoxide (Va), *tert*-butylhydroperoxide (Vb) and tritylhydroperoxide (Vc) under the following conditions: 20° in DMF under a stream of N_2 and with a molar proportion of hydroperoxide and nicotine to Ia of 2:2:1. Vc was virtually inert, presumably owing to its thermal stability, whereas Va and Vb gave the oxirane IIa in 25.3 and 76.3% yields, respectively. The specific rotation of

TABLE VII. Physical and Analytical Data for IIa—g,



Compd. No.	R^1	R^2	Appearance (recryst. solv.)	mp (°C) or bp (°C/Torr)	Formula	Analysis (%) Calcd (Found) C	H	N
IIa	Ph	Et	Colorless oil	—	$C_{12}H_{10}N_2O$	72.71 (73.27	5.09 5.07	14.13 14.27)
IIb	Ph	iso-Pr	Colorless needles (*n*-hexane)	64.5—66.0	$C_{13}H_{12}N_2O$	73.56 (73.60	5.70 5.77	13.20 13.08)
IIc	Ph	*n*-Pr	Colorless oil	—	$C_{13}H_{12}N_2O$	73.56 (73.88	5.70 5.83	13.20 12.93)
IId	Ph	$PhCH_2$	Colorless prisms (*n*-hexane)	94.0—96.0	$C_{17}H_{12}N_2O$	78.44 (78.32	4.65 4.60	10.76 10.74)
IIe	Et	*n*-Bu	Colorless oil	63 (0.4)	$C_{10}H_{14}N_2O$	67.38 (67.16	7.92 7.98	15.72 15.62)
IIf	Et	Et	Colorless oil	43 (0.25)	$C_8H_{10}N_2O$	63.98 (63.13	6.71 6.59	18.65 18.37)
IIg	$-CH_2(CH_2)_3CH_2-$		Colorless oil	75—76 (3)	$C_9H_{10}N_2O$	66.65 (66.80	6.22 6.25	17.27 17.37)

Compd. No.	IR ν_{max} cm^{-1} (CN)	NMR δ (ppm in $CDCl_3$) (J=Hz)
IIa	2240	0.97 (3H, t, J=7, $C\underline{H}_3CH_2$), 1.62—2.82 (2H, m, $CH_3C\underline{H}_2$), 7.37 (5H, s, C_6H_5)
IIb	2240	1.04 (3H, d, J=7.0, CH_3), 1.26 (3H, d, J=7.0, CH_3), 1.80—2.36 (1H, sx, J=7.0, $Me_2C\underline{H}$), 7.44 (5H, s, C_6H_5)
IIc	2240	0.90 (3H, t, J=8.0, CH_3), 1.16—2.80 (4H, m, $-CH_2CH_2-$) 7.43 (5H, s, C_6H_5)
IId	2230	3.28 (1H, d, J=14.0, $PhC\underline{H}_AH_B-$), 3.72 (1H, d, J=14.0, $PhCH_A\underline{H}_B-$), 7.14 (5H, s, C_6H_5), 7.27 (5H, s, C_6H_5)
IIe	2240	1.00—1.95 (14H, m, alkyl protons)
IIf	2240	1.11 (6H, t, J=8.0, $C\underline{H}_3CH_2$) 1.57—2.11 (4H, m, $CH_3C\underline{H}_2$)
IIg	2240	1.50—1.98 (10H, m, cyclohexyl protons)

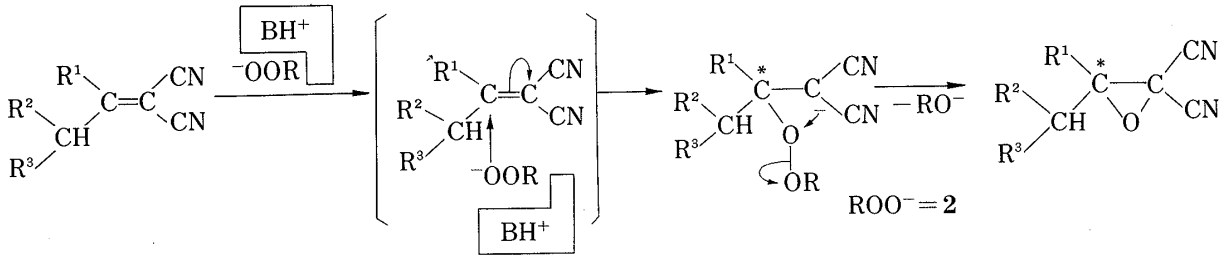


Chart 2

the product in the former case was $[\alpha]_D^{26}$ −0.630° (c=24.07, EtOH), whereas that in the latter case was almost negligible. These observations and the assembled data shown in Table IV suggest that the asymmetric epoxidation is attributable to the hydroperoxide structure, which is suitable for providing a chiral environment with the chiral base catalyst.

Experimental[7]

Materials——Alkylidenemalononitriles, Ia—j, were prepared by condensation of the corresponding aldehydes or ketones with malononitrile by the use of ammonium acetate–acetic acid as a catalyst. Ia: Colorless prisms (EtOH), mp 68—69° (lit.[8] mp 69—70°). Ib: Colorless prisms (MeOH), mp 93—95° (lit.[8] mp 93—94°). Ic: Colorless needles (MeOH), mp 82—84° (lit.[9] mp 83.5—84°). Id: Colorless needles (EtOH), mp 57—58.5° (lit.[8] mp 60—62°). Ie: Colorless needles (EtOH), mp 56.5—57.5°. *Anal.* Calcd for $C_{13}H_{12}N_2$: C, 79.56; H, 6.16; N, 14.28. Found: C, 79.42; H, 6.15; N, 14.32. If: Colorless needles (EtOH), mp 80—81° (lit.[10] mp 80—81°). Ig: Colorless needles (EtOH), mp 137—138° (lit.[8] mp 140—141°). Ih: Colorless liquid, bp 129—130° (15 Torr) [lit.[11] bp 109—110° (4 Torr)]. Ii: Colorless liquid, bp 110—111° (0.4 Torr) [lit.[12] bp 150° (19 Torr)]. Ij: Colorless liquid, bp 113° (4 Torr) [lit.[13] bp 137—138° (10 Torr)].

(+)-D-DPA and (−)-L-DPA were prepared by N,N-dimethylation of D- and L-α-phenylethylamine with HCO_2H–HCHO, respectively. (+)-D-DPA: bp 187—189°, $[\alpha]_D^{26}$ +67.4° (neat); (−)-L-DPA: bp 187—189°, $[\alpha]_D^{26}$ −67.8° (neat).

Va,[14] Vb[15] and Vc[16] were prepared according to the methods reported previously.

Epoxidation of Alkylidenemalononitriles with Molecular Oxygen General Procedure——A constant stream of oxygen (9.2 ml/min) was bubbled into a solution of one of Ia—j (0.02 mol) and 0.02 mol of base [nicotine, DPA, (+)-D-DPA, (−)-L-DPA, N-methylpiperidine, pyridine, DBU or Triton B] in 20 ml of an appropriate solvent (DMF, anisole, diglye, nitrobenzene or toluene) in a cylindrical flask equipped with a

Table VIII. Physical and Analytical Data for IIIa—d

Compd. No.	Appearance (recryst. solvt.)	mp (°C)	Formula	Analysis (%) Calcd (Found) C	H	N
IIIa	Pale yellow prisms (EtOH)	188—189	$C_{12}H_{10}N_2O_2$	67.28 (67.13	4.71 4.98	13.08 12.97)
IIIb	Pale yellow needles (EtOH)	205—207.5	$C_{13}H_{12}N_2O_2$	68.41 (68.80	5.30 5.32	12.27 12.37)
IIIc	Colorless needles (EtOH)	151—153	$C_{13}H_{11}NO_3$	68.11 (68.35	4.84 4.87	6.11 6.29)
IIId	Pale yellow prisms (EtOH–H_2O)	162—164 (dec.)	$C_{17}H_{12}N_2O_2 \cdot 1/2H_2O$	71.57 (71.77	4.59 4.70	9.82 9.60)

Compd. No.	IR ν_{max}^{KBr} (cm^{-1})	NMR δ (ppm)[a] (J=Hz)
IIIa	3360, 3175 (NH_2) 2210 (CN) 1720 ($COCH_3$) 1663 ($CONH_2$)	1.52 (3H, s, CH_3CO), 6.84 (1H, s, $-N\underline{H}_A H_B$), 9.21 (1H, s, $-NH_A\underline{H}_B$), 7.51—7.73, 7.94—8.20 (5H, m, C_6H_5)
IIIb	3250 (broad, NH_2) 2200 (CN) 1700 (COC_2H_5) 1650 ($CONH_2$)	0.67 (3H, t, J=8, $C\underline{H}_3CH_2$), 1.57—2.08 (2H, m, $CH_3C\underline{H}_2$), 6.92 (1H, s, $-N\underline{H}_A H_B$), 9.17 (1H, s, $-NH_A\underline{H}_B$), 7.57—7.77, 7.97—8.18 (5H, m, C_6H_5)
IIIc	2250 (CN) 1760 (CO)	1.47 (3H, s, CH_3), 1.58 (3H, s, CH_3), 7.60 (5H, s, C_6H_5)
IIId	3470, 3440, 3370 3270 (NH_2, OH) 2230 (CN) 1700 (COC_6H_5) 1645 ($CONH_2$)	6.60 (1H, bs, $-N\underline{H}_A H_B$) 9.50 (1H, s, $-NH_A\underline{H}_B$) 7.12—7.98 (10H, m, C_6H_5)

a) IIIa, IIIb and IIId were measured in DMSO-d_6 and IIIc in $CDCl_3$.

thermometer and a gas inlet tube fitted with a fused porous bottom of sintered ground glass. Bubbling was continued until the starting material was no longer detectable on TLC. The solvent was evaporated off under reduced pressure and the resulting residue was dissolved in 50 ml of benzene. The benzene solution was washed twice with 20 ml portions of 1 N HCl, then with 5% $NaHCO_3$ and dried over anhyd. $MgSO_4$. After the benzene had been evaporated off under reduced pressure, the resulting residual oily material was subjected to chromatography on a silica gel column (eluent, benzene–hexane) to give pure oxirane as an oily material or as crystals.

The runs with Ia, Id, Ie and If were slightly different. In the runs with Ia, Ie and If, crystals of IIa, IIIc and IIId, respectively, were deposited in the reaction solution and were collected by suction. Recrystallization from EtOH or EtOH–H_2O gave pure crystals. Treatment of the filtrate in the manner described above gave the oxiranes IIa, IIc and IId, respectively. In the run with Id, IIIb was precipitated from the oily residue obtained by concentration of the reaction solution and collected by suction. Recrystallization from EtOH gave colorless needles of IIIb. The oily filtrate obtained above was chromatographed on silica gel to give IIb.

Physical properties and the results of microanalyses of the oxiranes, IIa—g, are listed in Table VII.

Preparation of IVa—b——A MeONa solution prepared from 0.46 g (0.02 mol) of Na metal and 10 ml of MeOH was added dropwise at 0—10° to a stirred solution of 0.01 mol of IIa ($[\alpha]_D^{26}$ +1.93°) or IIc ($[\alpha]_D^{26}$ +1.55°) in 20 ml of MeOH, and stirring was continued for 1—1.5 hr. Then, 20 ml of 2 N HCl was added to the reaction solution at ice-bath temperature and stirring was continued for a further 0.5—1 hr. The reaction mixture was concentrated in a rotary evaporator under reduced pressure and the resulting oily material was dissolved in benzene. The benzene solution was washed with water and dried over $MgSO_4$. Removal of the benzene by evaporation and purification of the resulting residue through a silica gel column (eluent, benzene: hexane = 1: 1) gave IVa or IVb.

IVa: Yield, 79.4%. mp 74.5—75.5°. *Anal.* Calcd for $C_{14}H_{16}O_5$: C, 63.62; H, 6.10. Found: C, 64.07; H, 6.16. IR ν_{max}^{KBr} cm^{-1}: 1750 (CO). NMR δ (in $CDCl_3$): 0.87 (3H, t, J = 7.0 Hz, $C\underline{H}_3CH_2$), 1.42—2.40 (2H, m, $CH_3C\underline{H}_2$), 3.30 (3H, s, CH_3CO_2), 3.80 (3H, s, CH_3CO_2), 7.24 (5H, s, C_6H_5). $[\alpha]_D^{26}$ = +2.00° (c = 15.41, EtOH).

IVb: Yield, 90.4%. Colorless oil. *Anal.* Calcd for $C_{15}H_{18}O_5$: C, 64.73; H, 6.52. Found: C, 64.92; H, 6.52. IR $\nu_{max}^{liq.}$ cm^{-1}: 1755 (CO). NMR δ (in $CDCl_3$): 0.85 (3H, t, J = 6.0 Hz, $C\underline{H}_3CH_2CH_2$), 1.05—2.44 (4H, m, $CH_3C\underline{H}_2C\underline{H}_2$), 3.37 (3H, s, CH_3CO_2), 3.89 (3H, s, CH_3CO_2), 7.29 (5H, s, C_6H_5). $[\alpha]_D^{26}$ +1.40° (c = 13.53, EtOH).

Determination of Enantiomeric Excess——A solution of 30 mg of IVa—b and 15 mg of $Pr(tfc)_3$ in 6 ml of C_6D_6 was subjected to NMR measurements (JEOL FT-100 machine, at 100 MHz). Enantiomeric excess was determined from the peak ratio of methyl proton signals of the methoxycarbonyl grouping at lower magnetic field. IVa with $[\alpha]_D^{26}$ +2.00°, which had been derived from IIa with $[\alpha]_D^{26}$ +1.93°, showed D/L = 0.886, which corresponds to 6.0 e.e.%. IVb with $[\alpha]_D^{26}$ +1.40°, which had been obtained from IIc with $[\alpha]_D^{26}$ +1.55°, showed D/L = 0.896, which corresponds to 5.5 e.e.%.

Reaction of Ia with Va—c in the Presence of Nicotine——A solution of one of Va—c (0.02 mol) in 5 ml of DMF was added to a 20 ml DMF solution of Ia (1.82 g, 0.01 mol) and nicotine (1.62 g, 0.02 mol) under a stream of N_2 at 20°. When Ia was no longer detectable on TLC, the reaction solution was concentrated under reduced pressure and the resulting residue was dissolved in benzene. The benzene solution was washed twice with 20 ml portions of 2 N HCl followed by 5% $NaHCO_3$ and dried over anhyd. $MgSO_4$. The benzene was evaporated off under reduced pressure and the resulting residue was subjected to silica gel column chromatography with benzene–hexane (1: 1) as an eluent. IIa was obtained in the runs with Va (25.3%) and Vb (76.3%) in the yields shown in parentheses, but in the run with Vc, no IIa was isolated. The former product (from Va) showed $[\alpha]_D^{26}$ −0.63° (c = 24.07, EtOH), but the latter (from Vb) showed no optical rotation.

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(at 100 MHz) spectrophotometers. Chemical shift values are given in δ (ppm) relative to tetramethylsilane as an internal standard. The following abbreviations are used: s, singlet; d, doublet; t, triplet; q, quartet; sx, sextet; m, multiplet; b, broad. The optical rotations were measured with a Perkin Elmer 241 polarimeter.

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