

HETEROCYCLES IX.¹ ASYMMETRIC EPOXIDATION OF A QUINONE AND
SYNTHESES OF CHIRAL LACTONES²

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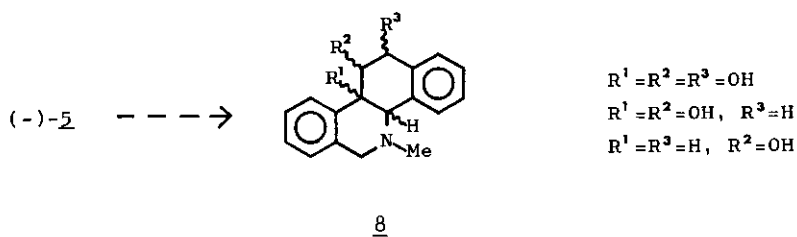
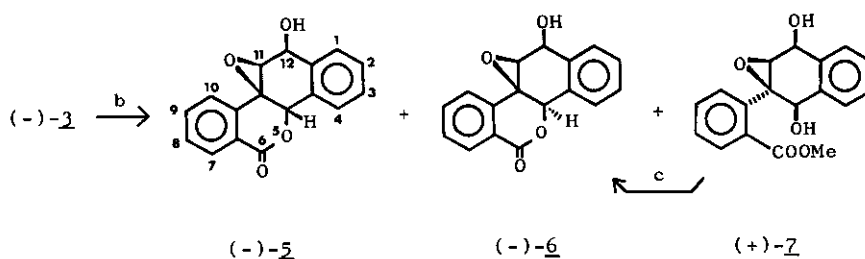
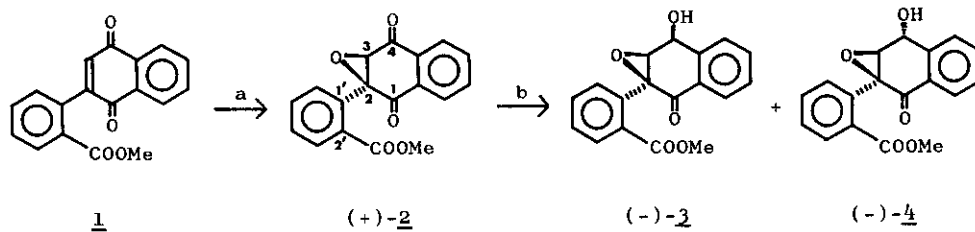
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Abstract --- The epoxy diketone (2) is obtained in optically active form by the phase-transfer chiral epoxidation of the quinone (1). The transformation of 2 to the lactones (5) and (6) is carried out without the loss of optical activity.

The asymmetric epoxidation of enones under phase-transfer conditions in the presence of chiral onium salts as catalysts has been reported.³ In connection with the syntheses of benzo/c/phenanthridines,⁴ we have investigated the asymmetric epoxidation of the quinone (1)⁵ to the chiral epoxy diketone (2), and the syntheses of the chiral lactones (5) and (6) from 2.

tert-Butyl hydroperoxide (75%, 0.4 ml) was added to a stirred mixture of 1 (101 mg), 1-benzylquininium chloride (BQC)⁶ (2.6 mg) and powdered sodium hydroxide (27 mg) in toluene (10 ml) with cooling. The mixture was vigorously stirred at 0°C for 30 min and then at room temperature for 1 h. Work-up of the reaction mixture and preparative thin-layer chromatography (silica gel; benzene/ethyl acetate=20/1, v/v) gave the crude⁷ (+)-2 (101 mg, 95%, 78% ee)⁸ as light yellow crystals of mp 135-137° with $\alpha_{589}^{23}+9.2^\circ$, $\alpha_{577}^{22}+12.5^\circ$, $\alpha_{546}^{22}+20.0^\circ$ and $\alpha_{435}^{22}+175.1^\circ$ (c=1.0, dioxane). Its recrystallization from ethanol furnished (+)-2 (66 mg, 100% ee) as colorless prisms of mp 140-141.5° with $\alpha_{589}^{24}+10.5^\circ$, $\alpha_{577}^{24}+13.3^\circ$, $\alpha_{546}^{24}+22.0^\circ$ and $\alpha_{435}^{24}+200.3^\circ$ (c=1.3, dioxane).

Reduction of (+)-2 with sodium borohydride at -50°C for 1 h afforded the (-)-epoxy ketones (3) (76%), $\alpha_{589}^{22}-52.0^\circ$ (c=0.1, chloroform) and (4) (23%), $\alpha_{589}^{25}-136.3^\circ$ (c=0.3, chloroform). The ir spectra showed intramolecular hydrogen-bondings at 3520 (OH--O) and 3587 cm^{-1} (OH-- π) for (-)-3 and (-)-4, respectively.⁹ The configurations of the 4-hydroxyl groups in (-)-3 and (-)-4 are established to be cis and trans with respect to the oxirane rings, respectively, on the basis of these ir data.



- a) $\text{tert-BuOOH/NaOH/BQC/toluene}$
 b) $\text{NaBH}_4/\text{MeOH}$
 c) $\text{Al}_2\text{O}_3/\text{MeOH-CHCl}_3$

Chart 1

Further reduction of (-)-3 with sodium borohydride gave the cis-(-)-lactone (5) (44%), $[\alpha]_{589}^{23} -217.8^\circ$ (c=0.2, chloroform), trans-(-)-lactone (6) (1%), $[\alpha]_{589}^{20} -104.0^\circ$ (c=0.1, chloroform) and cis-(+)-diol (7) (38%), $[\alpha]_{589}^{23} +161.4^\circ$ (c=0.3, chloroform). From this result, it can be seen that the 12-hydroxyl groups in (-)-5 and (-)-6, and the 4-hydroxyl group in (+)-7 have the same configuration as that of the 4-hydroxyl group in (-)-3. The cis steroidal conformation of the B/C ring fusion in (-)-5 is determined on the basis of the presence of a W-path coupling between the 4b-proton (δ 5.76, d, J 1 Hz) and 11-proton (δ 3.58, dd, J 3 and 1 Hz) in the nmr spectrum.

Alumina-induced lactonization of (+)-7 afforded (-)-6 (74%) which showed a characteristic signal for the 4-proton at δ 7.91 (dd, J 8 and 2 Hz) (5: δ 7.36) in the nmr spectrum owing to interaction of the 4b-O(5) bond. The optical purities (100%) of (-)-5 and (-)-6 were confirmed by the nmr spectra using tris-/3-(heptafluoropropylhydroxymethylene)-d-camphorato/europium(III).

The syntheses of chiral benzo/c/phenanthridines (8) are now in progress.

REFERENCES AND NOTES

1. For part VIII, see Y. Harigaya, S. Takamatsu, H. Yamaguchi, T. Kusano, and M. Onda, Chem. Pharm. Bull., 1980, 28, accepted for publication.
2. The structures of all compounds obtained were supported by the ir, nmr and mass spectra.
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4. Y. Harigaya, K. Yotsumoto, and M. Onda, Abstracts of Papers, 100th Annual Meeting of Pharmaceutical Society of Japan, Tokyo, April, 1980, p. 63.
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7. The word "crude" means a mixture of enantiomers in unequal amounts.
8. The enantiomeric excess (ee) was determined by the nmr spectrum using $\text{Eu}(\text{hfc})_3$. Distinct difference was observed for the Me signal of the 2'-COOMe group in 2.
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