

ORGANIC REACTIONS AT HIGH PRESSURE ASYMMETRIC INDUCTION IN THE DIELS-ALDER
REACTION OF *p*-BENZOQUINONE WITH CHIRAL 2,4-PENTADIENOIC ACID DERIVATIVES¹

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Abstract: Asymmetric induction in the high pressure (15 kbar, 1.5 GPa) Diels-Alder reaction of *p*-benzoquinone with chiral 2,4-pentadienoic acid derivatives is evaluated. The reactions afford 4a,5,8,8a-tetrahydro-1,4-naphthalenediones in up to 50% enantiomeric excess.

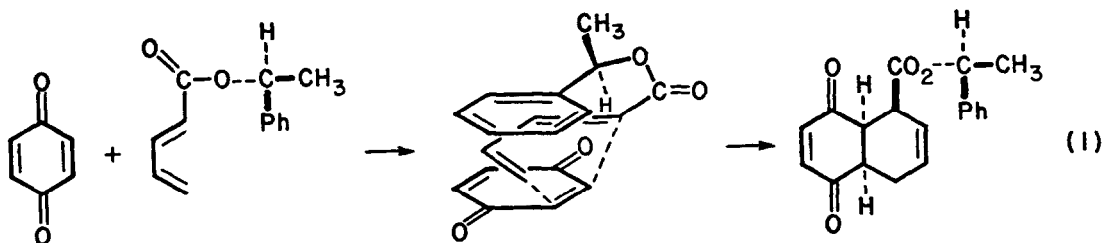
Earlier work in our laboratories³ has demonstrated the utility of high pressure in the Diels-Alder synthesis of heat-sensitive adducts related to aklavinone.^{3,4} Due to the chiral properties of this naturally occurring antibiotic, a strategy for synthesizing this material in high optical purity was an attractive goal. In light of Trost's recently postulated π -stacking model⁵ accounting for asymmetric induction in Lewis acid promoted cycloadditions, the present study was undertaken to evaluate chiral induction in the high pressure Diels-Alder reaction of *p*-benzoquinone with a series of chiral 2,4-pentadienoic acid derivatives.

The results of our survey of chiral ester and amide groups are summarized in Table I. The reactions were performed⁶ in sealed Teflon[®] tubes containing equimolar amounts of *p*-benzoquinone and chiral diene in methylene chloride (solutions 0.5 M in each reactant). The tubes were pressurized at 15 kbar (1.5 GPa) hydrostatic pressure at 18°C-20°C for the indicated time. The reactions were depressurized and each reaction mixture concentrated *in vacuo* at 20°C to afford good to excellent yields of adducts as mixtures of diastereomers.

Chiral induction in the adducts was assayed by comparison of carbon-13 NMR peak intensities. These were found to agree well with the integrated proton ratios of doubled resonances for entries 1, 2, 5, 6 and 8. The extent of induction in the 4a,5,8,8a-tetrahydro-1,4-naphthalenedione products ranged from 2% to 50% with the (-)-8-phenylmenthyl⁷ ester giving the best results. Interestingly, this chiral ester grouping has also produced high optical yields in Lewis acid catalyzed cycloaddition studies when incorporated into a dienophilic acrylate ester.⁸ From

our results, it is seen that the bulkier menthyl esters generally afford the highest optical yields. When the (-)-8-biphenylmenthyl ester is employed, however, charge-transfer complex formation between *p*-quinone and the biphenyl moiety inhibits cycloaddition. Within the menthyl series, the unsubstituted (-)-menthyl ester proved the most convenient owing to the availability of the chiral alcohol and the higher yield obtained in preparing the starting dienoic ester. The more readily crystallized product also permitted kinetic resolution of the product giving a 25% yield of cycloadduct exhibiting 90% enantiomeric excess (ee) following two recrystallizations.

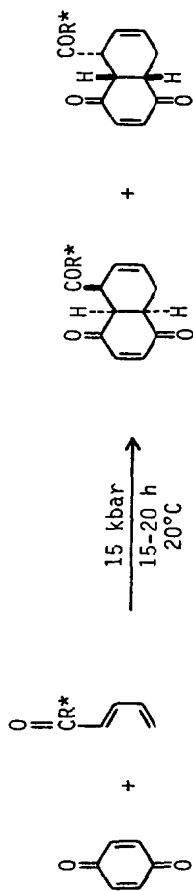
The (-)-1-phenylethyl 2,4-pentadienoate (see equation 1) provides the closest topological analogy to the 1-(*S*)-0-methylmandeloxyl-1,3-butadiene employed in the Trost study⁵ differing only in the polarity of the diene.⁹ Although, intuitively, elevated pressures should favor the rigid molecular orientation required in stacking three π systems, the charge transfer interaction^{5,10} between *p*-benzoquinone and the electron poor dienoic esters is expected to be relatively weak. High pressure reaction of *p*-benzoquinone with the (-)-1-phenylethyl dienoic



ester proceeded smoothly to afford a 98% isolated yield of crystalline adduct but only 6% ee was realized. Applying Trost's conditions (1.6 eq. $B(OAc)_3$, 0°C, $CHCl_3$) gave no reaction after 3 days while Lewis acid plus pressure (1.6 eq. $B(OAc)_3$, 15 kbar, 18°C, 24 h, CH_2Cl_2) gave the adduct quantitatively with 18% ee. Product of 18% optical purity was also obtained when the reaction of the same chiral ester was run in (-)-1-phenylethanol as the solvent.¹¹ Thus the polarity of the diene (important to the charge transfer nature of the transition state) and the ability of the reactants to chelate to a Lewis acid appear to be critical factors in attaining the optimum alignment required for total asymmetric induction.

In conclusion, a series of optically active electron poor dienes has been added to *p*-benzoquinone to afford good to excellent yields of pure 4a,5,8,8a-tetrahydro-1,4-naphthalenedione-5-carboxylic acid derivatives in moderate optical yields. Such adducts could not be

TABLE I. Asymmetric Induction in High Pressure Diels-Alder Reactions



Expt	R	t(h)	Yield ^a	% ee	Expt	R	t(h)	Yield ^a	% ee
1		23	98	2	6		22	58 (25) ^b	36 (90) ^b
2		21	98	6	7 ^c		24	60	46
3		19	94	14	8 ^c		23	62	50
4		17	92	15	9 ^c		20	<10 ^d	—
5		20	88	22					

^aSatisfactory spectral and analytical data were obtained. The yields are isolated. ^bYield and % enantiomeric excess following two recrystallizations. ^cPrepared by procedure in Ref. 7 and found to be >99% pure by ¹⁹F NMR of the ester with (-)- α -methoxy- α -trifluoromethylphenylacetic acid. ^dCharge transfer complex formed, starting materials recovered.

produced under typical conditions involving high temperatures or Lewis acids required at ambient pressure. Although our results do not approach the excellent induction seen in a number of studies of Lewis acid promoted cycloadditions they represent the highest optical yields attained to date under high pressure.¹²

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References and Notes

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