

ASYMMETRIC INDUCTION IN THE DIELS-ALDER REACTIONS OF  
 $\alpha$ -HYDROXYACYLNITROSO COMPOUNDS

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**Summary:** Transient, chiral  $\alpha$ -hydroxyacylnitroso compounds (2), able to form intramolecular hydrogen bonds, react stereoselectively with cyclopentadiene and cyclohexa-1,3-diene; the cycloadduct (6) of the latter diene and the nitroso derivative of (*S*)-mandelic acid has been converted into the known (-)-oxazine derivative (9).

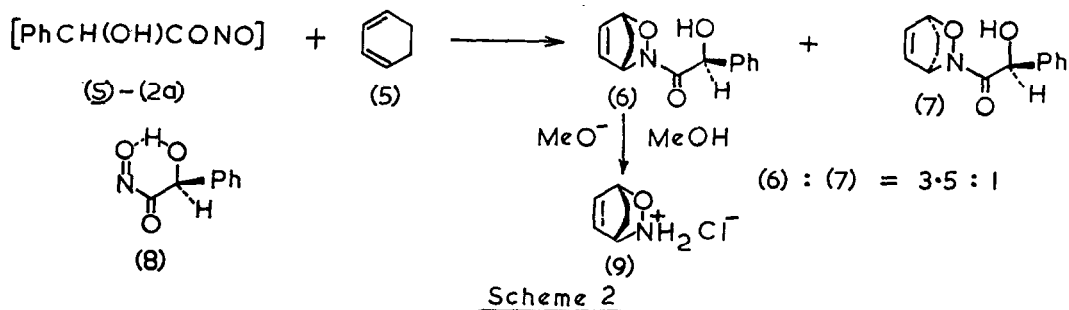
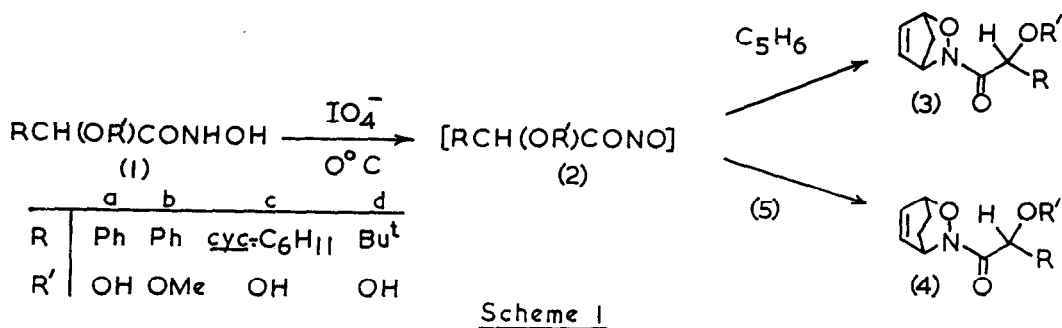
Acylnitroso compounds, XCONO (X = R, RO, or RR'N), can serve as transient dienophiles for the synthesis of dihydro-oxazines and the derived amino alcohols (e.g. Scheme 1).<sup>1</sup> We suggested<sup>2</sup> that intramolecular hydrogen bonding in chiral  $\alpha$ -amino or  $\alpha$ -hydroxy derivatives [e.g. (8)] might enhance asymmetric induction in reactions with achiral dienes. We report here cycloaddition reactions of the chiral *C*-nitrosocarbonyl compounds (2) with cyclopentadiene and cyclohexa-1,3-diene.

The racemic hydroxamic acids (1)<sup>3</sup> were added to well-stirred, two-phase mixtures of either cyclopentadiene or cyclohexadiene in ethyl acetate, and sodium periodate in aqueous sodium acetate (adjusted to pH 6), at 0 °C. The cycloadducts (3) or (4) were isolated<sup>2</sup> as oily mixtures of diastereoisomers. The ratios<sup>4</sup> of diastereoisomers, measured by <sup>1</sup>H n.m.r. spectroscopy, are recorded in the Table. Moderate<sup>4</sup> asymmetric induction was observed for the  $\alpha$ -hydroxy derivatives (a, c, and d), the highest ratio of diastereoisomers (ca. 5:1) being observed for the mandelic derivatives of cyclopentadiene (3a) and the *t*-butylglycolic derivatives of cyclohexadiene (4d). The ratios for the *O*-methylmandelic derivatives (3b) and (4b) were smaller than those for the corresponding hydroxy derivatives (3a) and (4a). This may be a consequence of hydrogen bonding [see (8)], although the greater size of the methoxy group, compared with the hydroxy group, might cause a similar effect.

The relative configurations of the diastereoisomeric cycloadducts (4a) were determined as follows. A mixture of the cycloadducts (6) and (7) was prepared as before from the hydroxamic acid, m.p. 137-138 °C,  $[\alpha]_D -164^\circ$  (c 2.5 in H<sub>2</sub>O), derived from (*S*)-mandelic acid (Scheme 2). The mixture was treated with acetic anhydride in pyridine and the resulting, oily *O*-acetates were separated by t.l.c. (SiO<sub>2</sub> plates). The major, less polar, acetate (6; OH = OAc),  $[\alpha]_D +36^\circ$  (c 0.65 in MeOH), was cleaved with methanolic sodium methoxide at room temperature to give the corresponding oxazine, isolated as the known,<sup>5</sup> crystalline hydrochloride (9),  $[\alpha]_D -24^\circ$  (c 1.0 in MeOH) (lit.  $-24^\circ$ ). Preferential formation of the cycloadduct (6) is consistent with *endo* addition of a hydrogen-bonded<sup>6</sup> nitroso compounds (8) from the face *anti* to the phenyl group.

Table.

		a	b	c	d
Ratios of the diastereoisomers of the	(3)	5.1	2.6	3.6	3.4
cycloadducts (3) and (4)(Scheme 1)	(4)	3.5	2.1	2.5	4.6



Kresze *et al.* achieved high asymmetric induction ( $> 95\%$  e.e.) in the synthesis of the oxazine (9) using  $\alpha$ -chloronitroso compounds,  $\text{RR}'\text{C(Cl)NO}$ , derived from epiandrosterone<sup>5</sup> or mannose.<sup>7</sup> In these examples, the nitroso group is attached directly to a chiral centre whereas for acylnitroso compounds interposition of a carbonyl group is obligatory. Recently, Defoin *et al.* reported<sup>8</sup> a 6:4 mixture of diastereoisomers for the cycloaddition of the *O*-methylmandelic derivative (2b) and an azacyclohexadiene; the corresponding hydroxy derivative (2a) was not studied. The influence of intramolecular hydrogen-bonding on the cycloaddition reactions of chiral 1-hydroxybut-3-en-2-ones has been explored by Choy *et al.*<sup>9</sup>

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#### References and Notes

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- The hydroxamic acids (1) were prepared by treatment of the methyl esters of the corresponding, known carboxylic acids with methanolic hydroxylamine.
- Higher ratios were achieved at lower temperatures but comparison of data was then less discriminating; e.g. (1d) and (5) with  $\text{Et}_4\text{NIO}_4$  in  $\text{CH}_2\text{Cl}_2$ -MeOH at ca.  $-70^\circ\text{C}$  gave (4d), ratio ca. 10:1.
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- Hydrogen-bonding between the hydroxy and carbonyl groups is possible,<sup>9</sup> but preferential *exo*, *anti* addition would then be required to produce an excess of the diastereoisomer (6).
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