A SIMULTANEOUS DETERMINATION OF ENANTIOMERIC PURITY AND CHIRALITY OF A CERTAIN CYCLIC ENONE RELATING TO THE GIBBANE FRAMEWORK

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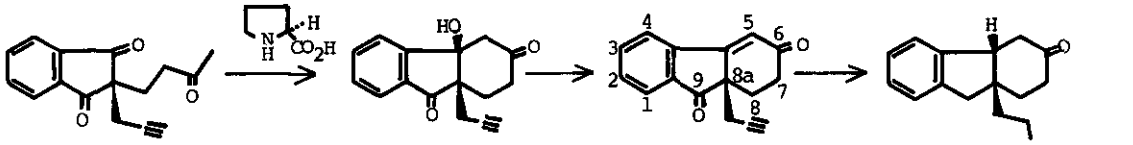
Abstract——A simultaneous determination of enantiomeric purity and chirality of a certain cyclic enone relating to the gibbane framework has been achieved using ^{1}H-nmr spectroscopy.

Recently we have developed an enantioselective synthesis of the gibbane framework starting from a symmetric triketone(1) employing asymmetric aldolization catalyzed by L-proline[1,2]. Absolute configuration of the cyclization products could be deduced unambiguously by correlating the tricyclic ketone(4) derived from the key intermediate(3) to the corresponding methoxy analogue[2](9) synthesized from L-glutamic acid via (6),(7), and (8) (Scheme 1). However, their enantiomeric purities could not be determined since they did not show any anisochromisms in their ^{1}H-nmr spectra using $Eu(tfc)_3$ or $Pr(tfc)_3$ as chiral shift reagents. We now report here a ^{1}H-nmr spectroscopic method for the simultaneous determination of enantiomeric purity and chirality of the enone(3) in relation to the above mentioned asymmetric aldolization promoted by proline[1].

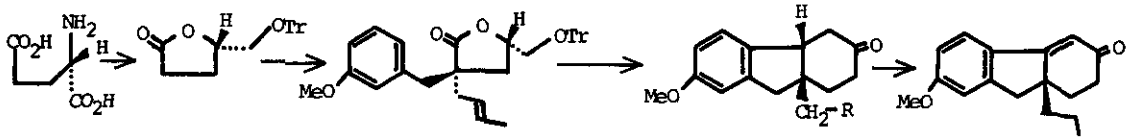
The method consists in chemo- and stereoselective reductive amination at the C-6 center of the enone(3) with chiral 1-phenethylamine perchlorate[3] and simple measurement of ^{1}H-nmr spectrum of the resulted amine. Since both (+)- and (-)-enones, ((+)-3)[1] and ((-)-3)[4], upon chemo- and stereoselective reductive amination with each of (R)-(+)- and (S)-(-)-1-phenethylamines, should afford two diastereomeric sets of aminoalcohols[5], (11)((+):(R))(or(11')((-):(S)) and (12)((+):(R))(or(12')((-):(S)), enantiomeric purity can be simply deduced by measuring relative intensity of particular signal(s) of the two diastereomers contained in the product, For this purpose, a signal of the C-5 olefinic proton proved to be the best reference which appeared at δ5.83 ppm(doublet, J=3.1 Hz) for (11)(or(11'))and at δ6.11 ppm(doublet, J=2.7 Hz)

for (12)(or(12'))[6]. As appeared in the table enantiomeric purities obtained by this method are well paralleled to the values simply calculated from the observed optical rotations.

At the same time, chirality of the enantiomeric enones, ((+)-3) and ((-)-3), could be simply deduced by comparing chemical shift of the C-5 proton of the amino-alcohols. Since the difference of chemical shift between two sets of the amines clearly reflects their stereochemistries, we could easily recognize the isomer showing higher value to be (11)(or(11')), while the other showing lower value to be (12)(or(12')) by taking account of the anisotropic effect of the phenyl group which shields the C-5 proton of the former amine more effectively (Scheme 2). Result deduced from the chemical shift comparison also well corresponds to the conclusion derermined by the chemical correlation to L-glutamic acid: the enone(10), on the reaction with (R)-(+)-1-phenethylamine, formed the amine(11(9-OH=H)) with more shielded C-5 proton(5.59, doublet, J=2.8 Hz), while (10), on the reaction with the (S)-(-)-isomer gave the amine(12(9-OH=H)) with less shielded C-5 proton(5.86, doublet, J=2.8 Hz).



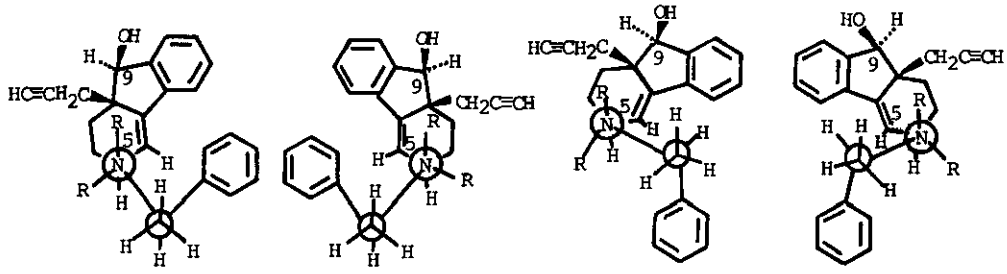
(1) (2) (3) (4)



(5) (6) (7) (8) R=CH=CHMe (10)

Tr=trityl (9) R=CH_2CH_2Me

SCHEME I



(11):(+)/(R)(+) (11'):(-)/(S)(-) (12):(+)/(S)(-) (12'):(-)/(R)(+)

R=H or lone pair

SCHEME 2

TABLE

1-phenetylamine / enone	(R)-(+) 11(11'):12(12')[a]	% e.e.	(S)-(-) 11(11'):12(12')[a]	% e.e.	$\left[\frac{[\alpha]_D}{186.5}\right]\times 100$	Chirality of 8a of the enone
(+)-(3) ($[\alpha]_D$+186.5°)	100 : 0	100.0	0 : 100	100.0	100.0	R
(+)-(3) ($[\alpha]_D$+168.3°)	92.5 : 6.5	86.0	9.1 : 90.9	81.8	90.2	R
(-)-(3) ($[\alpha]_D$-148.7°)	14 : 86	72.0	88 : 12	76.0	79.2	S
(±)-(3)	52.2 : 47.8	4.4	48.4 : 51.6	3.2	0	
(+)-10	11 (9-OH=H) : 12 (9-OH=H)[b]		11 (9-OH=H) : 12 (9-OH=H)[b]			
	100 : 0	100.0	0 : 100	100.0		R

a) relative intensity of protons at δ5.83 and 6.11 ppm.

b) relative intensity of protons at δ5.59 and 5.86 ppm.

PROCEDURE

A mixture of the enone(3)(1.0 equimol) and 1-phenethylamine perchlorate (1.2 equimol) in benzene was refluxed azeotropically for 36 h and the solvent was removed in vacuo. The residue was dissolved in methanol and the mixture was reduced with sodium borohydride(1.1 equimol) with stirring at -20∿26 °C. After stirring for 10 min, the solvent was removed in vacuo and the residue was extracted with methylene chloride. The extract was washed throughly with brine and dried over sodium sulfate. Evaporation of the solvent in vacuo left the crude amine which was directly measured in deuteriochloroform without further purification.

REFERENCES AND NOTES

1. S. Takano, C. Kasahara, and K. Ogasawara, J. Chem. Soc., Chem. Commun., in press.
2. S. Takano, C. Kasahara, and K. Ogasawara, J. Chem. Soc., Chem. Commun., in press.
3. The amine perchlorate was obtained as a hygroscopic crystalline mass by mixing the amine with 70% perchloric acid(0.95 equimol), followed by azeotropical removal of water using benzene, and was used without further purification.
4. The (-)-enone((-)-3), mp 147∿148 °C, was prepared from (1) in 68% overall yield using D-proline as a catalyst[1]. Similarly, the racemic enone((±)-3), mp 184∿185 °C, was prepared in 78% yield from (1) using DL-proline as a catalyst.
5. The carbonyl group at the C-9 center was also reduced stereoselectively under the reaction conditions.
6. ^{1}H-nmr spectra were measured with a JEOL PS-100 instrument in deuteriochloroform with tetramethylsilane as internal standard.

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