

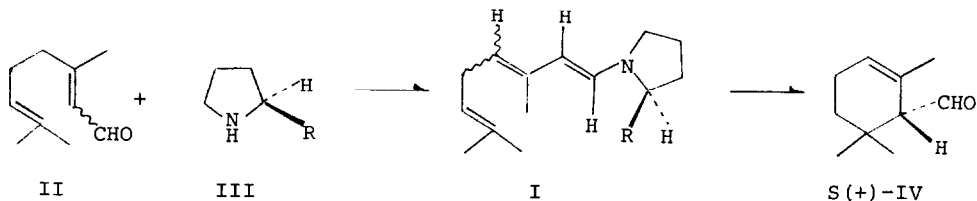
A BIOGENETIC-TYPE ASYMMETRIC CYCLIZATION SYNTHESSES OF
OPTICALLY ACTIVE α -CYCLOCITRAL AND TRANS- α -DAMASCONE

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(Received in Japan 9 December 1972; received in UK for publication 2 January 1973)

In vivo, acyclic terpenes having no asymmetric center are generally converted to cyclic terpenes carrying several asymmetric carbons by the so-called enzymic cyclization reaction. Aiming to achieve the same kinds of transformation as those observed in vivo by chemical means,¹⁾ we applied the acid-catalyzed biogenetic-type cyclization of the citral-pyrrolidine enamine (I_a) developed previously in our laboratory²⁾, to the optically active enamines (I_{b-f}) prepared from citral (a mixture of cis- and trans-isomers) (II)³⁾ and several kinds of optically active pyrrolidines (III_{b-f})^{4,5)} easily prepared from commercially available L-proline.

This communication concerns with the preliminary results of the above-mentioned biogenetic-type asymmetric synthesis and the subsequent conversion of



a: R=H; b: R=Me; c: R=i-Pr; d: R=CON ; e: R=CONEt₂; f: R=COOEt

optically active α -cyclocitral(S(+)-IV)⁶⁾ thus obtained to optically active trans- α -damascone(S(+)-V), a famous perfume which recently synthesized from optically active α -ionone.⁷⁾

Table. Asymmetric Cyclizations of Citral(II) to S(+)- α -Cyclocitral(S(+)-IV) via Enamines(I_{b-f})

Run	Enamine(I _{b-f}) Formations		Asymmetric Cyclizations		
	Optically Active Pyrrolidines(III) Used.	Molar Ratio of III/II	Isolated Yield ^a	Formed S(+)- α -Cyclocitral [α] _D ²⁰ (c, EtOH)	Optical Yield ^b
1	III _b	1.2	26	+72.3°(0.678)	12
2	III _c	1.2	26	+158.6°(0.710)	27
3	III _d	1.0	8	+131.1°(0.810)	22
4	III _e	1.0	4	+198.1°(0.284)	33
5	III _f	1.0	9	1.8°(1.108)	0.3

a) Based on II

b) Calculated based on the assumption that S(+)-IV showing [α]_D²⁰+594.5°(EtOH) was 100% optically pure.⁸⁾

Results of the asymmetric cyclization were summarized in the Table.

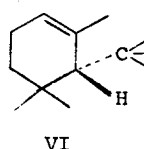
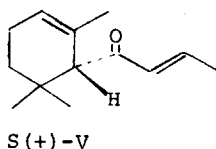
Reaction conditions for the formations of I_{b-f} from II and III_{b-f} were identical with those previously reported,²⁾ except for the molar ratio of III_{b-f} and II¹⁰⁾ which are shown in the Table. All the cyclization reactions were carried out using the best condition (0° in conc. sulfuric acid-water(ratio by vol. 10:1) for 3 hr), which had afforded dl-IV in the highest yield.²⁾ Work-up procedure was also identical with that described before.²⁾ In every case, formation of the trace amount of β -cyclocitral was definitely observed in the crude reaction product.²⁾

That S(+)-IV was isolated in very low yield in runs 3,4 and 5, is conceivably due to the competition of the decomposition of I_{d,e,f} in conc. sulfuric acid

with the acid-catalyzed cyclization. Since the enamine(I_c) afforded 27% optically active S(+)-IV in 26% yield, further studies using optically active pyrrolidines which have an acid-stable alkyl or aryl substituent at α-position, would let us to find out more suitable III for the asymmetric cyclization than those examined here.

It is reasonably expected that S(+)-IV produced by this novel asymmetric cyclization will be one of the best key intermediates for the total syntheses of several kinds of optically active terpenes, for example, (+)-α-ionone and (+)-α-carotene, having the partial structure(VI).

We also visualized the above-mentioned expectation by converting S(+)-IV obtained by the asymmetric reaction to S(+)-V in two steps. That is, treatment



of S(+)-IV showing $[\alpha]_D^{20} + 172.4^\circ$ ($c=0.282$, EtOH), 29% optically pure, with 1-propenyl lithium (a mixture of cis- and trans-isomers) in ether at 20° for 19 hr, followed by the oxidation with chromium trioxide-pyridine and the subsequent geometrical isomerization of the olefinic double bond in the reaction medium, afforded S(+)-V, $[\alpha]_D^{20} + 89.2^\circ$ ($c=1.058$, CHCl₃), 28% optically pure, in 66% yield based on S(+)-IV. S(+)-V thus prepared was confirmed by comparing its spectral data with those reported.⁷⁾

Improvement of the asymmetric synthesis and total syntheses of other optically active terpenes carrying partial structure(VI) are under progress.

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8. Reduction of S(+)-IV, $[\alpha]_D^{20} + 131.1^\circ$ (c=0.810, EtOH) with sodium borohydride gave S(+)- α -cyclogeraniol, $[\alpha]_D^{20} + 26.9^\circ$ (c=0.610, EtOH). On the other hand, reduction of R(-)- α -cyclogeranic acid, $[\alpha]_{546}^{20} - 334.3^\circ$ (c=1.096, EtOH), 84.4% optically pure,⁹⁾ prepared by the resolution of dl- α -cyclogeranic acid,⁹⁾ with lithium aluminium hydride, afforded R(-)- α -cyclogeraniol, $[\alpha]_D^{20} - 103.1^\circ$ (c=0.686, EtOH). Calculations based on the above transformations, clearly disclosed that optically pure S(+)-IV should have $[\alpha]_D^{20} + 594.5^\circ$ (EtOH).
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10. We chose these molar ratios by considering the volatility of III_{b-f}.