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SYNTHESIS OF THE OPTICALLY ACTIVE DEHYDROVOMIFOLIOL. A SYNTHETIC PROOF OF THE ABSOLUTE CONFIGURATION OF (+)-ABSCISIC ACID

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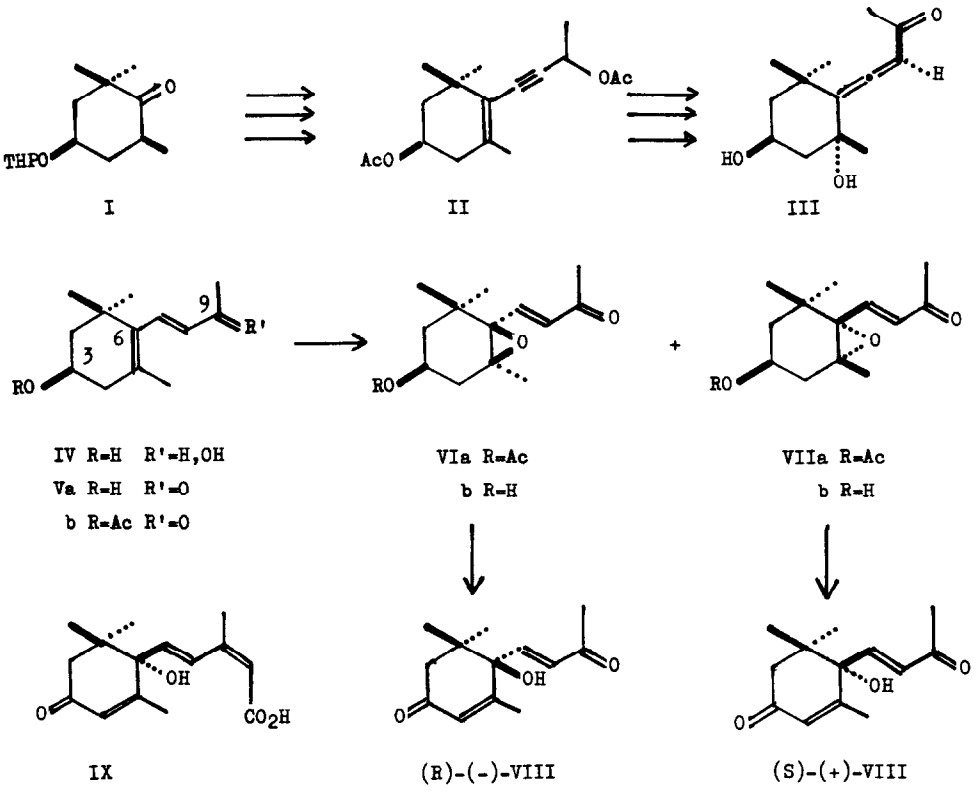
The elucidation of the absolute configuration of (+)-abscisic acid (IX) was of considerable recent research interest (1-7). In continuation of our previous work on the synthesis of the optically active grasshopper ketone (III) starting from an optically active ketone (I)(8), we have now accomplished the synthesis of the optically active dehydrovomifoliol [(S)-(+)-VIII] (9). This added another evidence favoring the absolute stereochemistry IX assigned for (+)-abscisic acid.

The optically active ketone (I), $[\alpha]_D^{19}$ +36.6° (c=1.6, $CHCl_3$); CD(c=0.22, MeOH)$[\theta]_{300}$ + 1,530, was converted to the enyne diacetate (II) as previously described (8). This was treated with $LiAlH_4$ in THF to give 3β-hydroxy-β-ionol (IV), which in turn was oxidized with 2,3-dichloro-5,6-dicyano-p-benzoquinone (DDQ) in dioxane. The product was chromatographed (Al_2O_3) to give 3β-hydroxy-β-ionone (Va), $[\alpha]_D^{22}$ -76.8° (c=1.08, $CHCl_3$), in 44% yield (10,11). Acetylation of the ketol (Va) with Ac_2O in C_5H_5N gave in quantitative yield the acetate (Vb).

Subsequent epoxidation with m-chloroperbenzoic acid in $CHCl_3$ yielded two crystalline epoxides after chromatographic (SiO_2) purification. The steric course of this type of reaction is known to give a cis-epoxide as a major and less strongly adsorbed product



(8,12,13). The structure VIa was therefore assigned to the major product obtained in 20% yield after several recrystallizations, mp 110-111°; δ (100 MHz, CCl_4) 0.97 (3H, s), 1.15 (3H, s), 1.27 (3H, s), 1.92 (3H, s), 2.17 (3H, s), 4.75 (1H, m), 6.15 (1H, d, J=16Hz), 6.79 (1H, d, J=16Hz); $[\alpha]_D^{22}$ + 3.7° (c=0.6, $CHCl_3$); CD (c=0.026, MeOH) $[\theta]_{231}$ + 22,500. The minor and less easily eluted product VIIa was obtained in 6.4% yield, mp 125-126°; δ (100MHz, CCl_4) 0.96 (3H, s), 1.15 (3H, s), 1.18 (3H, s), 1.92 (3H, s), 2.17 (3H, s), 4.75 (1H, m), 6.18 (1H, d, J=16Hz) 6.85 (1H, d, J=16Hz); $[\alpha]_D^{22}$ -90.2° (c=0.41, $CHCl_3$) ; CD (c=0.039, MeOH) $[\theta]_{232}$ - 34,300. The latter trans-epoxide (VIIa) was entirely identical with the degradation product of violaxanthin (mp. 124-125°)(14) kindly supplied by Dr. R.S. Burden on the basis of mmp (124-125°), IR, NMR and CD (c=0.031, MeOH) $[\theta]_{232}$ -34,700. The NMR spectrum of our VIIa was also in good accord with that of Dr. S. Isoe's photooxidation product (reported values : mp 126-127°; $[\alpha]_D^{15}$ -77.5°) of zeaxanthin (3).

Conversion of the trans-epoxide (VIIa) into (S)-(+)-dehydrovomifoliol (VIII) was effected by hydrolysis (5% KOH/MeOH) to a ketol (VIIb), mp 58°, followed by its oxidation (CrO_3/C_5H_5N) in an overall yield of 80%. During the Sarett oxidation, base-catalyzed opening of a β,γ-epoxy ketone took place. This reaction is known to result in the retention of the configuration of the C-O bond (15). The resulting hydroxy diketone, (S)-(+)-VIII, was an oil, δ (100 MHz, $CDCl_3$) 1.02 (3H, s), 1.10 (3H, s), 1.87 (3H, d, J=1.5 Hz), 2.26 (1H, d, J=17Hz), 2.50 (1H, d, J=17Hz), 2.60 (1H, br. s), 5.92 (1H, s), 6.42 (1H, d, J=16Hz), 6.82 (1H, d, J=16Hz); $[\alpha]_D^{21}$ + 266.3° (c=0.3, $CHCl_3$); CD (c=0.006, MeOH) $[\theta]_{320}$ -7,400; $[\theta]_{243}$ + 150,000; $[\theta]_{209}$ -110,000. The IR and NMR spectra of this material was superimposable on those of an authentic racemate (VIII) and the chiroptical data were in good accord with those reported for the natural dehydrovomifoliol (9). In the same manner the cis-epoxide (VIa) gave the antipodal hydroxy diketone, (R)-(-)-VIII, as an oil, $[\alpha]_D^{21}$ -229.3° (c=0.3, $CHCl_3$); CD (c=0.007, MeOH) $[\theta]_{320}$ + 7,900; $[\theta]_{243}$ - 120,000; $[\theta]_{209}$ + 79,000. The conversion of (S)-(+)-dehydrovomifoliol (VIII) into (S)-(+)-abscisic acid (IX) is well-documented (6,9).

This and the previous synthesis starting from the common intermediate (I) thus provided a link between grasshopper ketone (III) and (+)-abscisic acid (IX). In view of the established stereochemistry of the former by X-ray analysis (16), the present work confirmed the revised (S)-stereochemistry (IX) of the latter as well as the accepted stereochemistries of zeaxanthin and violaxanthin (13).

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