*Journal of Natural Products*
*Vol. 47, No. 6, pp. 924-933, Nov-Dec 1984*

# $^{13}$C-NMR STUDY OF CEDROL, 6-ISOCEDROL, AND α-CEDRENE

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ABSTRACT.—The $^{13}$C-nmr spectral assignment of the structurally complex cedrol molecule (**1**) was corroborated using double quantum coherence measurements at 90.8 MHz combined with measurement of long-range heteronuclear $^{13}$C, $^{1}$H spin-spin coupling constants. Moreover, the assignments for the $^{13}$C-chemical shifts of all methyl groups of cedrol (**1**) were confirmed using 6-isocedrol (**11a** and α-cedrene (**13**), closely related molecules in which deuterium labeling is easy. In the case of α-cedrene, the $^{13}$C- and $^{1}$H-spectra were assigned using heteronuclear chemical shift correlation measurements. According to the $^{13}$C-nmr chemical shifts of the methyl groups *gem* to the tertiary alcohol, the conformational analysis of the six-membered ring of cedrol suggests a preferential boat conformation, while in 6-isocedrol a chair conformation is preferred.

Since the report of the isolation of cedrol (**1**) by Walter in 1841 (1), this tricyclic sesquiterpene has been the object of numerous studies (2-5), including several attempts to assign its $^{13}$C-nmr spectrum (6-8). Although the complete assignment of the $^{13}$C-nmr spectrum of cedrol has been reported (9), the fact that three of the methyl signals appear within a narrow chemical shift range of 3.5 ppm makes it desirable to gain independent evidence for the assignment. In this respect, the use of two-dimensional nmr techniques can make considerable contributions to the spectral interpretation of structurally complex natural products.

For the ascription of the methyl signals, it was necessary to resort to 6-isocedrol (**11a**) and α-cedrene (**13**), closely related molecules in which deuterium labeling is easier, thus allowing unambiguous assignments. The sequence employed for the preparation of the deuterated samples **9, 11b, 17,** and **18** is summarized in Figure 1.

A sample of α-cedrene-12-*d* (**9**) was obtained from cedrol (**1**) via transannular lead tetraacetate oxidation (10) to give 6,12-oxycedrane (**2**). Cleavage of the tetrahydrofuran ring was achieved (11) with $BF_3$-etherate/$Ac_2O$ to yield α-cedren-12-ol acetate (**3**). Hydrolysis of the acetate **3** with MeOH-NaOH afforded α-cedren-12-ol (**4**), as verified by the absence of the acetate signal in the $^{1}$H-nmr spectrum and the upfield shift of the C-12 methylene group. The alcohol **4** was transformed into the derived tosylate. However, removal of the ester tosylate with $LiAlD_4$ did not prove successful probably because of its neopentylic nature. An alternative procedure, involving oxidation of the alcohol **4** with $Na_2Cr_2O_7$/ $H_2SO_4$ yielded α-cedren-12-al (**5**). This aldehyde (**5**) was reduced by means of $LiAlD_4$ to α-cedren-12-ol-12-*d* (**6**), identical with the unlabeled molecule except for the integrated peak area corresponding to the C-12 primary alcohol in the $^{1}$H-nmr spectrum.

The deuterated alcohol **6** was reoxidized to α-cedren-12-al-12-d (**7**) as previously described and transformed into the derived ethylenedithioketal (**8**) by treatment with 1,2-ethanedithiol and *p*-toluenesulfonic acid. Raney nickel desulfurization of the ethylenedithioketal **8** afforded the desired α-cedrene-12-d (**9**).

Reaction of labeled α-cedrene-12-*d* (**9**) with *m*-chloroperbenzoic acid (12) gave *exo*-5,6-epoxycedrane-12-*d* (**10**) (12). Its reduction with $LiAlH_4$ afforded 6-isocedrol-12-*d* (**11b**) as shown by $^{1}$H-nmr analysis.

On the other hand, 6-isocedrol-11-*d* (**17**) was obtained by treatment of 6-isocedrol (**11a**) with $Ac_2O$ to yield the derived acetate (**12**) and a mixture of α- (**13**) and β-cedrene (**14**). The acetate **12** was separated by chromatography on a silica gel column. The mixture of α-(**13**) and β-cedrene (**14**) was reacted with *m*-chloroperbenzoic acid to

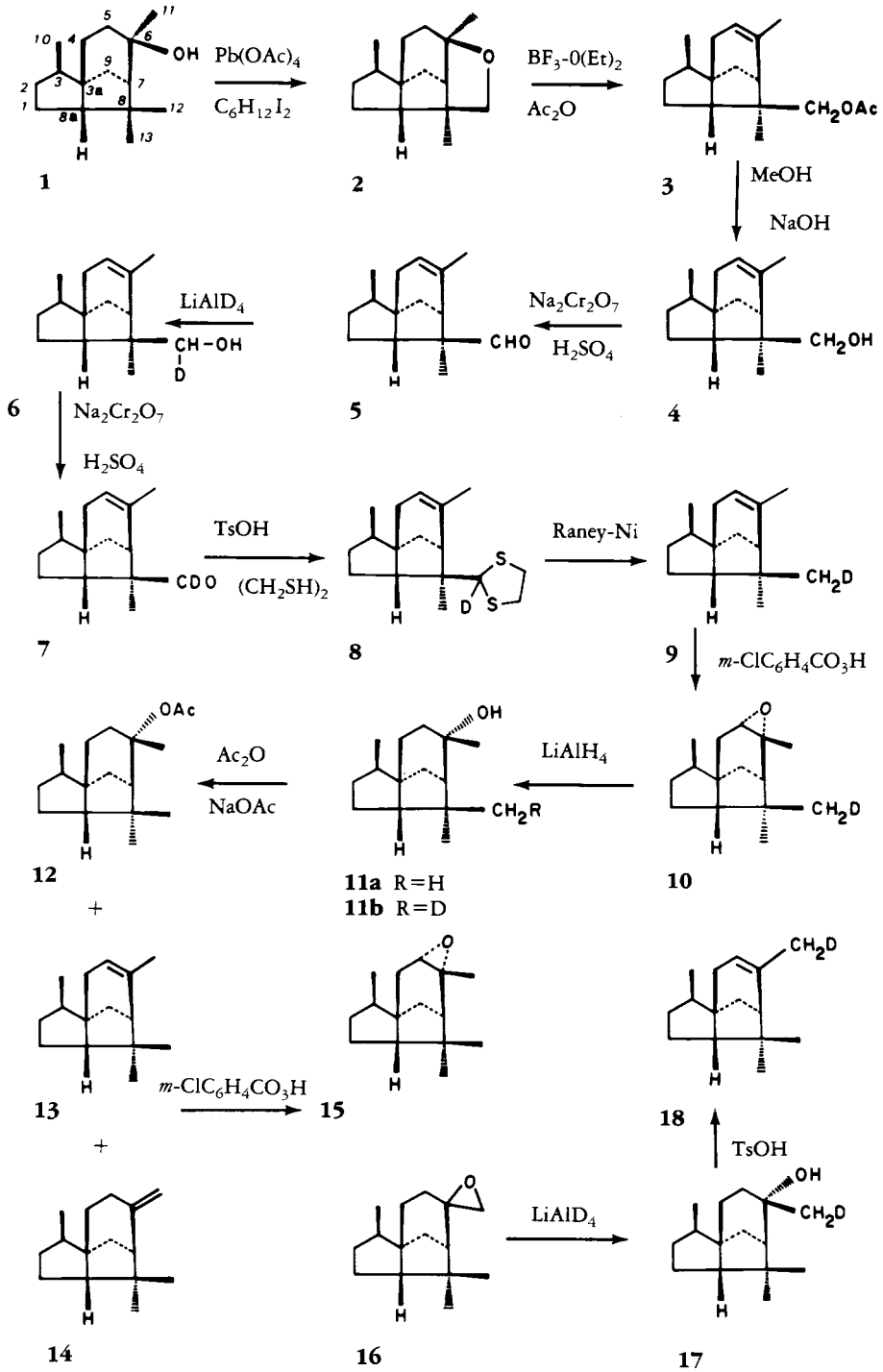



FIGURE 1. Synthetic route for the preparation of α-cedrene-12-*d* (**9**), 6-isocedrol-12-*d* (**11b**), 6-isocedrol-11-*d* (**17**), and α-cedrene-11-*d* (**18**).

yield a mixture of *exo*-5,6-epoxycedrane (**15**) and *exo*-6,11-epoxycedrane (**16**). The two epoxycedranes were easily separated by chromatography on a silica gel column.

*Exo*-6,11-epoxycedrane (**16**) was transformed into 6-isocedrol-11-*d* (**17**) by treatment with $LiAlD_4$. Dehydration of the tertiary alcohol of **17** with *p*-toluenesulfonic

acid further gave the also desired α-cedrene-11-*d* (**18**). Both compounds show $^1$H-nmr spectra identical to the unlabeled compounds except for the integrated peak areas of the methyl groups at which deuterium had been introduced.

In the case of cedrol (**1**) unambiguous $^{13}$C-nmr signal assignment for all carbons, except for the distinction of the individual *gem*-dimethyl peaks, and establishment of C-C bonds was obtained from a carbon-carbon connectivity plot (13, 14) obtained at 90.8 MHz after two-dimensional double quantum coherence measurements. This technique is based on the identification of the satellite signals owing to molecules having two directly attached $^{13}$C-atoms, while suppressing the strong signals from the normal $^1$C-nmr spectrum. Identification of directly bonded carbons is made possible by the fact that they generate the same double quantum coherence frequencies, thus allowing establishment of the carbon skeleton. Therefore, there is no need to resort to specific isotopic enrichment, a technique that is not always practical.

The main problem in using the double quantum coherence method lies in selecting the appropriate weak satellite signals that appear together with spinning side bands and traces of impurities. In the case of strongly coupled AB systems (15), the method is not recommended, because distorted intensities arise. Finally, sensitivity for materials with natural isotopic abundance is low. Thus, from the two-dimensional methods currently available double quantum coherence measurements represent the most difficult method not only due to the sensitivity problem but also because of the need for proper setting of other experimental parameters such as pulse delays, relaxation delay, and spectral width. However, the advantage of the technique is that it allows unambiguous assignments, making it a powerful method that, in certain cases, provides complete structural determination.

The complete C-C linking for cedrol (**1**) is depicted in Figure 2. In this respect it is worth mentioning that even in the case where several carbon atoms possess quite similar double quantum coherence frequencies, the linkage of pairs of atoms can be recognized since the diagonal line included in Figure 2 passes through the center of the connectivity lines. This is particularly evident for the pairs of signals labeled as a-k and b-e on Figure 2.

In the case of α-cedrene (**13**) the $^{13}$C-nmr spectrum was assigned by comparison with the data afforded by the carbon-carbon connectivity plot of cedrol (**1**) combined with the two-dimensional heteronuclear $^{13}$C-$^1$H-chemical shift correlation measurements obtained at 90.8/361.1 MHz (Figure 3) and long-range heteronuclear spin-spin coupling constants.

The two quaternary $sp^3$ carbons 3a and 8 were easily assigned from unidimensional measurements by comparison with the chemical shifts for the same carbons in **1**, while the low field $sp^2$ signals are trivial to assign from a coupled spectrum.

The assignment of the methine carbons 3, 7, 8a was achieved using the two-dimensional nmr spectrum. The signal at 41.6 ppm in the $^{13}$C-domain was ascribed to C-3 by comparison with cedrol (**1**). Furthermore, on the $^1$H-slice of the chemical shift correlation diagram, the multiplicity of the signal at 1.73 ppm shows that it corresponds to the most coupled proton, a situation in agreement with H-3 which is coupled to the secondary methyl protons and to the hydrogens at C-2. In contrast both H-7 and H-8a are only vicinal to a single methylene group.

In order to assign the remaining methine carbons C-7 and C-8a it was also necessary to resort to the $^1$H-domain of the bidimensional spectrum. The signal at 55.0 ppm in the $^{13}$C-spectrum generates a doublet at 1.79 ppm being the X nucleus of an ABX $^1$H-$^1$H system. The AB portion of that system belongs to the signal at 40.7 ppm in the $^{13}$C-spectrum. Careful observation of the structure of α-cedrene (**13**) reveals that this ABX

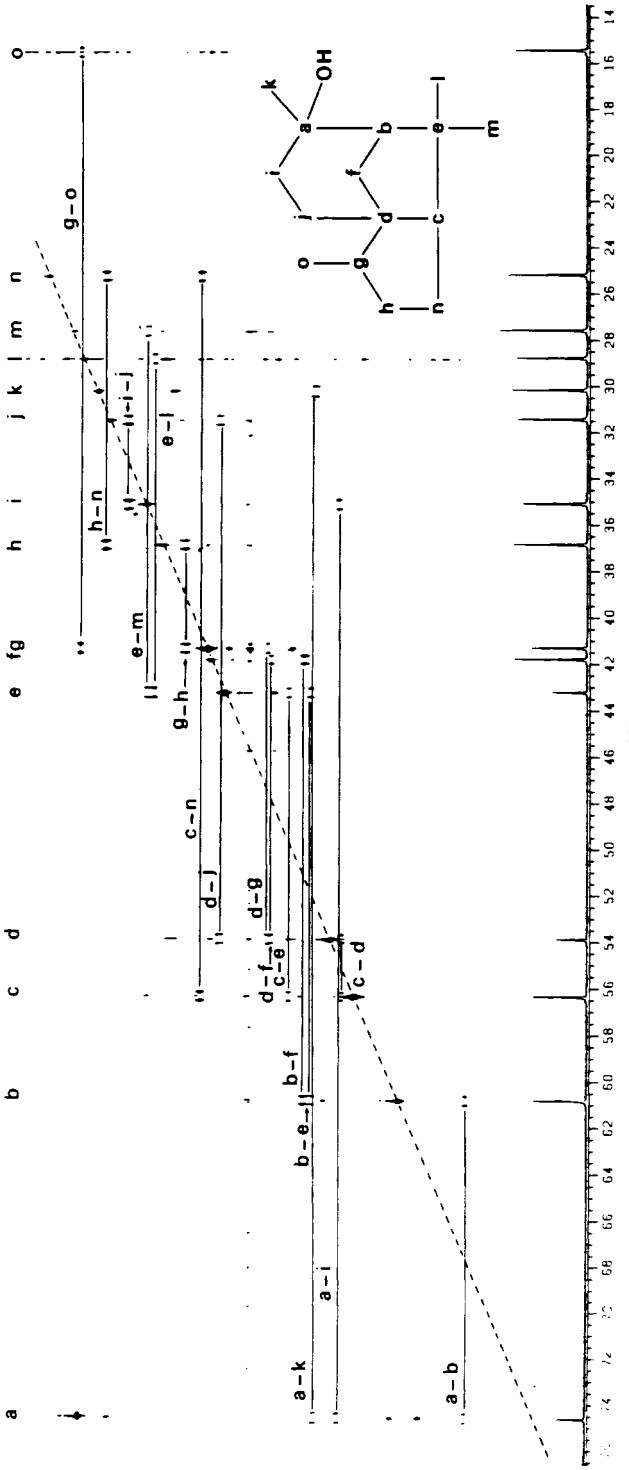



FIGURE 2. Carbon-carbon connectivity plot (90.8 MHz) of cedrol (**1**).

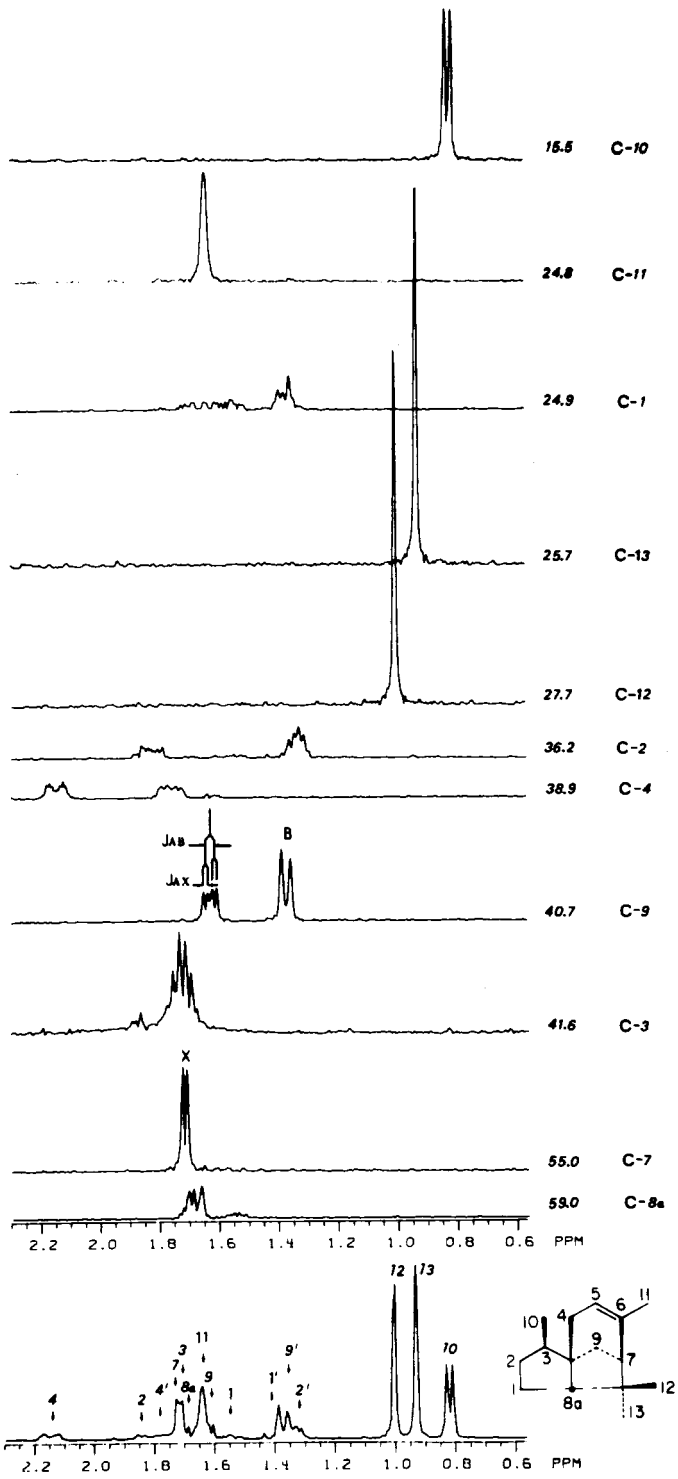



FIGURE 3. Two-dimensional heteronuclear $^{13}C$-$^{1}H$-chemical shift correlation spectrum (90.8/361.1 MHz) of α-cedrene (**13**).

system can only arise from interactions of the two protons (1.43 and 1.70 ppm) at C-9 with the proton at C-7 (1.79 ppm). Therefore, the carbon at 59.0 ppm in the $^{13}$C-domain and the proton at 1.75 ppm in the $^{1}$H-spectrum belong to position C-8a.

The methylene carbons 1 and 2 of **13** were ascribed by comparison with cedrol (**1**) since they are almost invariant. The chemical shifts for the corresponding protons are shown in Table 1. Assignment of the $^{13}$C-chemical shift of C-9 (see above) allows direct correlation with the signals at 1.70 and 1.43 ppm in the $^{1}$H-domain. The remaining methylene at 38.9 ppm in the $^{13}$C-spectrum belongs to C-4.

TABLE 1. Nmr Parameters of the Cedranolides[a]

| Assignment | Cedrol (**1**) $^{13}$C | 6-Isocedrol (**11a**) $^{13}$C | α-Cedrene (**13**) | |
|---|---|---|---|---|
| | | | $^{13}$C | $^{1}$H |
| 1 | 25.4 | 25.3 | 24.9 | 1.45 and 1.63 |
| 2 | 37.0 | 36.9 | 36.2 | 1.40 and 1.89 |
| 3 | 41.5 | 41.7 | 41.6 | 1.73 |
| 3a | 54.1 | 53.3 | 53.8 | — |
| 4 | 31.6 | 30.5 | 38.9 | 1.83 and 2.22 |
| 5 | 35.3 | 34.3 | 119.0 | 5.26 |
| 6 | 75.0 | 73.1 | 140.1 | — |
| 7 | 61.0 | 61.4 | 55.0 | 1.79 |
| 8 | 43.4 | 41.8 | 48.0 | — |
| 8a | 56.6 | 56.2 | 59.0 | 1.75 |
| 9 | 42.0 | 39.9 | 40.7 | 1.43 and 1.70 |
| 10 | 15.6 | 15.4 | 15.5 | 0.89 |
| 11 | 30.2 | 30.6[b] | 24.8[b] | 1.71[b] |
| 12 | 27.7 | 28.1[b] | 27.7[b] | 1.07[b] |
| 13 | 28.9 | 29.0 | 25.7 | 1.00 |

[a]in ppm from internal TMS.
[b]carbon labeled with deuterium.

This experiment also confirmed the secondary methyl group to the signal at 15.5 ppm in the $^{13}$C-spectrum. The $^{1}$H- and $^{13}$C-chemical shifts of α-cedrene (**13**) are summarized in Table 1.

For 6-isocedrol (**11a**) the $^{13}$C-spectrum assignment, excepting the distinction of the *gem*-dimethyl group signals, was attained by comparison with the chemical shifts of cedrol (**1**) (Table 1).

The $^{13}$C-nmr analysis of the deuterated analogues of cedrene (**13**) and 6-isocedrol (**11a**) allowed definite ascription of the C-11 and C-12 resonances. Because the chemical shift of the secondary methyl signal is essentially invariant in the three sesquiterpenes, its assignment to the higher-field signal is also secured; thus, the remaining methyl peak in **11a** and **13** is that owing to C-13. Chemical shift analogies on going from either **11a** or **13** to **1**, permitted completion of the assignment of the methyl groups in cedrol (**1**).

Independent evidence from coupled spectra obtained under gated decoupling, reveals that the long-range couplings of C-12 and C-13 are invariant in compounds **1, 11a,** and **13**. The apparent long-range multiplicity of C-12 corresponds to a quintet, while that of C-13 appears as a sextet. This is in agreement with the pertinent Karplus relationship (16) that follows from dihedral angles of a Dreiding model, inasmuch as C-12 is almost 90° with respect to H-7. Thus, C-12 shows long-range couplings to the C-13 protons and to H-8a, while C-13 is further coupled to H-7. This procedure is similar to the one developed for the distinction of the *gem*-dimethyl group of cyperene (17).

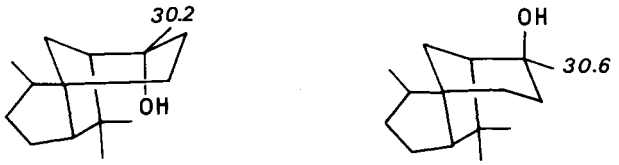
The $^{13}$C-data for cedrol (**1**) afforded by the two-dimensional plot are in agreement with earlier (9) assignments for this molecule. However, in the case of α-cedrene (**13**), the same workers based differentiation of the methyl groups at C-12 and C-13 on the hypothesis that C-13 is least affected by the transformation of cedrol (**1**) into cedrene (**13**), an assumption that unfortunately does not hold, as shown by deuterium labeling of C-12. These authors (9) also report that the most difficult task in the assignment of cedrol is the differentiation between C-4 and C-9, which was established using several off-resonance decoupling experiments. The C-C connectivity plot for **1** reveals that in the case of cedrol (**1**) these assignments are indeed correct. However, for α-cedrene (**13**) careful observation of the two dimensional correlation spectra shows that they were not correctly assigned previously.

Once the C-11 methyl signal has been ascribed unambiguously in **1**, **11a**, and **13**, it is possible to perform a conformational analysis for the six-membered ring of cedrol (**1**).

As far as configurational assignments are concerned, the utility of $^{13}$C-nmr spectroscopy for tertiary alcohols containing a *gem*-methyl group has been demonstrated in a few natural products such as methyl *ent*-labdan-8β-ol-15-oate (18) and cheilanthatriol (19). It is evident that in such alcohols the common $^{1}$H-nmr procedure, which consists of observation of coupling constants and subsequent estimation of dihedral angles from Karplus-type relationships, cannot be applied. Therefore, configurational assignments are based on the chemical shifts of the methyl carbon in *cis*- and *trans*-1-methyl-4-tertbutylcyclohexanol, as well as other 4-substituted derivatives (20). It has been noted that such methyl chemical shifts show definite ranges according to their geometric environment, the equatorials being in the 30.3 to 32.9 ppm region and the axials in the 22.5 to 26.1 ppm region.

An alternative procedure involves the use of nOe to obtain information on both configuration and conformation (21). In cedrol (**1**) the fact that the absolute configuration is known (5) and the C-11 methyl group has been unambiguously ascribed allows us to perform a conformational analysis of the six-membered ring of (**1**) based on $^{13}$C-chemical shifts.

The data in Table 1 show that the C-11 methyl group, although being α in **1** and β in **11a**, shows chemical shifts of 30.2 and 30.6, respectively. Therefore, by comparison with 1-methyl-4-tertbutylcyclohexanol, they both must be equatorial. It follows that the six-membered ring of 6-isocedrol (**11a**) has a preferred chair conformation, while for cedrol, in contrast, (**1**) the boat conformation, which results in relief of 1,3-diaxial interactions, is preferred.




**1** **11a**

FIGURE 4. Conformation of the six-membered ring of cedrol (**1**) and 6-isocedrol (**11a**).

## EXPERIMENTAL

SPECTRA.—The nmr spectra were measured in $CDCl_3$ solutions containing TMS as the internal reference. For $^{1}$H-measurements a Varian Associates EM-390 spectrometer was used, while one-dimensional

$^{13}$C-spectra were obtained on a Varian Associates XL-100A-FT-16K system. The two-dimensional spectra were recorded using a NT-360 system operated with standard Nicolet software. Ir spectra were obtained on a Nicolet MX-1 spectrometer. Melting points were determined on a Fisher-Johns apparatus and are uncorrected.

α-CEDROL (**1**).—This compound was recrystallized from methanolic solutions: it gave mp 86-88°, lit: 85.5° (22); ir ν max (KBr) 3382, 2975, 2957, 1464, 1127 cm$^{-1}$; $^1$H-nmr ($CDCl_3$, 90 MHz) δ 0.83 (3H, d, $J$=6.5 Hz, $CH_3$-10) 1.02 (3H, s, $CH_3$-13), 1.28 (3H, s, $CH_3$-12), 1.32 (3H, s, $CH_3$-11) ppm.

6,12-OXYCEDRANE (**2**).—Lead tetraacetate (3 g) and $CaCO_3$ (300 mg) were heated under reflux in cyclohexane (80 ml) for 30 min (10). Iodine (300 mg) and cedrol (1 g) were added and the mixture was refluxed 4 h. After cooling, the precipitate was filtered off and washed with $Et_2O$. The combined organic solutions were washed consecutively with 5% aqueous $Na_2S_2O_3$ and $H_2O$. The organic phase was dried ($Na_2SO_4$) and the solvent evaporated. The residue was adsorbed from light petroleum ether on to a silica gel column. The combined petroleum ether fractions followed by distillation yielded 600 mg of **2**; bp 59°/0.25 mm, lit: (bath temp.) 100°/0.10 mm (10); ir ν max (neat) 2955, 1461, 1377, 1167, 1130 cm$^{-1}$; $^1$H-nmr ($CDCl_3$, 90 MHz) δ 0.83 (3H, d, $J$=6.5 Hz, $CH_3$-10), 1.00 (3H, s, $CH_3$-13), 1.10 (3H, s, $CH_3$-11), 3.36, 3.46 (2H, $AB_q$, $J$=7.5 Hz, $H_2$-12) ppm.

α-CEDREN-12-OL ACETATE (**3**).—$BF_3$ etherate (0.5 ml) was added dropwise at room temperature to 6,12-oxycedrane (**2**) (500 mg) in $Ac_2O$ (20 ml) (11). After stirring for 30 min, the mixture was poured onto ice and extracted with $Et_2O$. The organic phase was washed with aqueous $NaHCO_3$, with $H_2O$, and then dried ($Na_2SO_4$). Removal of the $Et_2O$ afforded 350 mg of an oil bp 57°/0.25 mm; lit: (bath temp) 90-95°/0.1 mm (11); ir ν max (neat) 1735, 1240, 1045 cm$^{-1}$; $^1$H-nmr ($CDCl_3$, 90 MHz) δ 0.85 (3H, d, $J$=6.5 Hz, $CH_3$-10) 1.00 (3H, s, $CH_3$-13), 1.67 (3H, q, $J$=1.3 Hz, $CH_3$-11), 1.97 (3H, s, $COCH_3$), 3.81, 3.92 (2H, $J$=11.5 Hz, $H_2$-12), 5.20 (1H, m, H-5) ppm.

α-CEDREN-12-OL (**4**).—α-Cedren-12-ol acetate (**3**) (3.0 g) was dissolved in 30 ml of MeOH, treated with 800 mg of NaOH in 2 ml of $H_2O$ and refluxed for 2 h (11). After cooling, the solvent was evaporated to a small volume, diluted with $H_2O$ and extracted with EtOAc. The organic layer was washed several times with $H_2O$, dried ($Na_2SO_4$), and evaporated to dryness. The residue was chromatographed on a silica gel column yielding 2.5 g of an oil; lit: mp 50-51° (11); ir ν max (neat) 3407, 2953, 2935, 1453, 1376, 1032 cm$^{-1}$; $^1$H-nmr ($CDCl_3$, 90 MHz) δ 0.83 (3H, d, $J$=7 Hz, $CH_3$-10), 1.03 (3H, s, $CH_3$-13), 1.70 (3H, s, $CH_3$-11), 3.47, 3.56 (2H, $AB_q$, $J_{AB}$=7 Hz, $H_2$-12), 5.26 (1H, m, H-5) ppm.

α-CEDREN-12-AL (**5**).—To a vigorously stirred solution of 1 g of α-cedren-12-ol (**4**) in 20 ml of $Me_2CO$ maintained at 0° was added slowly 5 ml of a solution (0°) prepared from 1 g of sodium dichromate, 0.75 ml of $H_2SO_4$, and sufficient $H_2O$ to make 5 ml of solution (11). After stirring the solution for 15 min, ice $H_2O$ was added, the product was extracted with EtOAc, washed with $H_2O$ and $NaHCO_3$ solution, dried ($Na_2SO_4$), and concentrated. The residue was chromatographed on a silica gel column with petroleum ether as eluant giving 400 mg of α-cedren-12-al (oil); ir ν max (neat) 2952, 2946, 1719, 1470, 1446, 907 cm$^{-1}$; $^1$H-nmr ($CDCl_3$, 90 MHz) δ 0.88 (3H, d, $J$=6.5 Hz, $CH_3$-10) 1.00 (3H, s, $CH_3$-13), 1.58 (3H, q, $J$=1.3 Hz, $CH_3$-11), 5.26 (1H, m, H-5), 9.51 (1H, s, CHO) ppm.

α-CEDREN-12-OL-12-D (**6**).—Lithium aluminum deuteride (300 mg) was slowly added at room temperature to a solution of 1 g of α-cedren-12-al (**7**) in 15 ml of dioxane and the mixture was refluxed 12 h. Excess deuteride was destroyed by cautiously adding a few drops of EtOAc followed by $H_2O$. The reaction mixture was filtered, dried ($Na_2SO_4$), and concentrated. The residue was purified by chromatography on a silica gel column with petroleum ether as eluant to give 900 mg of **6**. The title compound exhibited an identical $^1$H-nmr spectrum to that of α-cedren-12-ol (**4**), except for the integrated peak area corresponding to the primary alcohol methylene signal.

α-CEDRENE-12-AL-12-D (**7**).—This compound was prepared from α-cedren-12-ol-12-*d* (**6**) using the procedure described for the preparation of **5**. The title compound exhibited identical $^1$H-nmr spectrum to the unlabeled compound (**5**), except for the integrated peak area corresponding to the aldehyde signal.

α-CEDREN-12-ETHYLENEDITHIOKETAL-12-D (**8**).—A solution containing 1 g of α-cedren-12-al-12-*d*, 0.8 ml of 1,2-ethanedithiol, and 80 mg of *p*-toluenesulfonic acid in $C_6H_6$ was refluxed during 2 h. The reaction mixture was poured into an excess of cold 10% NaOH solution and extracted with EtOAc. The organic layer was washed several times with $H_2O$, dried over $Na_2SO_4$, and concentrated. The residue was chromatographed on a silica gel column with petroleum ether to give 1 g of **8** (oil); ir ν max (neat) 2954, 2948, 2940, 1472, 1446, 1434, 1375 cm$^{-1}$; $^1$H-nmr ($CDCl_3$, 90 MHz) δ 0.82 (3H, d, $J$=6.5 Hz, $CH_3$-10), 1.15 (3H, s, $CH_3$-13), 1.81 (3H, q, $J$=1.3 Hz, $CH_3$-11), 3.30-3.00 (4H, m, $(-CH_2S)_2$), 5.32 (1H, m, H-5) ppm.

α-CEDREN-12-D (**9**).—Reduction was accomplished by refluxing 1 g of α-cedren-12-ethylenethioketal-12-*d* (**8**) with 5 g of Raney-nickel in dioxane for 48 h. Evaporation of the solvent followed by chromatography on a silica gel column with petroleum ether as eluant afforded 600 mg of (oil) bp lit: 100°/4 mm (12) ir ν max (neat) 3020, 2980, 1660, 825 $cm^{-1}$; $^1$H-nmr ($CDCl_3$, 90 MHz) δ 0.85 (3H, d, $J$=6.5 Hz, $CH_3$-10), 0.95 (3H, s, $CH_3$-13), 1.02 (2H, s, $CH_2D$-12), 1.68 (3H, q, $J$=1.3 Hz, $CH_3$-11), 5.20 (1H, m, H-5) ppm.

EXO-5,6-EPOXYCEDRANE-12-D (**10**).—α-Cedrene (500 mg) was dissolved in 10 ml of $CHCl_3$ and cooled to 0° (12). To the vigorously stirred solution, 500 mg of *m*-chloroperbenzoic acid in $CHCl_3$ was added and the mixture was allowed to react for 30 min at 10°. After filtration, the $CHCl_3$ solution was washed, dried ($Na_2SO_4$), and evaporated. The residue was chromatographed on a silica gel column with petroleum ether to yield 450 mg of **10** (oil) bp lit: 120/2 mm (12); $^1$H-nmr ($CDCl_3$, 90 MHz) δ 0.83 (3H, d, $J$=6.5 Hz, $CH_3$-10), 1.00 (3H, s, $CH_3$-13), 1.19 (2H, s, $CH_2D$-12), 1.45 (3H, s, $CH_3$-11), 3.03 (1H, d, $J$=4 Hz, H-5β) ppm.

6-ISOCEDROL-12-D (**11**).—Lithium aluminum hydride (350 mg) was slowly added at room temperature to a solution of 500 mg of exo-5, 6-epoxycedrane-12-*d* (**10**) (12). The mixture was kept at room temperature overnight with stirring. After workup in the usual manner, the residue was chromatographed on a silica gel column to yield 400 mg of **11** (oil); lit: bp 118-120°/1.4 mm (12), ir ν max (neat), 3390, 3384, 2952, 2937, 1459, 1376, 1150 $cm^{-1}$; $^1$H-nmr ($CDCl_3$, 90 MHz) δ 0.85 (3H, d, $J$=6.5 Hz, $CH_3$-10), 1.02 (3H, s, $CH_3$-13), 1.14 (2H, s, $CH_2D$-12), 1.32 (3H, s, $CH_3$-11) ppm.

EXO-6,11-EPOXYCEDRANE (**16**).—A solution of 500 mg of 6-isocedrol (**11a**) in 3 ml of $Ac_2O$ containing 500 mg of sodium acetate was refluxed during 2 h. Water was added followed by extraction with EtOAc. The organic layer was washed with $NaHCO_3$ solution, dried ($Na_2SO_4$), and concentrated. The mixture was partially separated by chromatography on a silica gel column. The petroleum ether fractions afforded a mixture of α-(**13**) and β-cedrenes (**14**) (227 mg) while 6-isocedrol acetate (**12**) was eluted using a 94:6 petroleum ether-$CHCl_3$ mixture. The latter shows the following characteristics mp 40-41°; ir (KBr) ν max, 2975, 2964, 1726, 1375, 1264 $cm^{-1}$; $^1$H-nmr ($CDCl_3$, 90 MHz) δ 0.83 (3H, d, $J$=6.5 Hz, $CH_3$-10), 0.98 (3H, s, $CH_3$-13), 1.17 (3H, s, $CH_3$-12), 1.55 (3H, s, $CH_3$-11), 1.91 (3H, s, $COCH_3$).

The mixture of α-(**13**) and β-cedrenes (**14**) (227 mg) was dissolved in 5 ml of $CHCl_3$ and cooled to 0°. To the vigorously stirred solution, 231 mg of *m*-chloroperbenzoic acid in $CHCl_3$ was added and the mixture was allowed to react for 30 min at 10°. After filtration, the $CHCl_3$ solution was washed twice with a 10% $NaHCO_3$ solution, dried ($Na_2SO_4$), and evaporated. The residue was chromatographed on a silica gel column with petroleum ether giving 98 mg of *exo*-6,11-epoxycedrane (**16**) followed by 113 mg of exo-5,6-epoxycedrane (**15**). *Exo*-6,11-epoxycedrane (**16**) showed a $^1$H-nmr spectrum ($CDCl_3$, 90 MHz) 0.87 (3H, d, $J$=6.5 Hz, $CH_3$-10), 0.95 (3H, s, $CH_3$-13), 1.1 (3H, s, $CH_3$-12), 2.45 (2H, s, $CH_2$-11).

6-ISOCEDROL-11-D (**17**).—Lithium aluminum deuteride 700 mg was added to a solution containing 98 mg of *exo*-6,11-epoxycedrane (**16**) in 5 ml of THF (12). The reaction mixture was kept at room temperature for 12 h with vigorous stirring. Excess deuteride was destroyed as previously described. The residue obtained after work up was purified by chromatography on a silica gel column with petroleum ether to give 91 mg of 6-isocedrol-11-d (**17**). The title compound exhibited an identical $^1$H-nmr spectrum to that of compound **11**, except for the integrated area of the methyl signal at which deuterium was introduced.

α-CEDRENE-11-D (**18**).—To a solution of 91 mg of 6-isocedrol-11-d (**17**) in 3 ml of toluene, 8 mg of *p*-toluenesulfonic acid was added and the mixture was refluxed for 1.5 h. After the reaction was completed, EtOAc was added and the organic solution was washed with $NaHCO_3$ solution and then with $H_2O$. The organic layer was concentrated and purified by chromatography on a silica gel column eluting with petroleum ether to give 80 mg of α-cedrene-11-*d* (**18**). The title compound exhibited an identical $^1$H-nmr spectrum, except for the integrated peak area of the methyl group at which deuterium was introduced.

## ACKNOWLEDGMENTS

We are indebted to Dr. L.F. Johnson (Nicolet Magnetics) and to Dr. O. Castañeda (Nicolet-México) for the bidimensional nmr measurements.

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*Received 26 January 1984*