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THE STRUCTURE OF CINNAMOLIDE, CINNAMOSMOLIDE AND CINNAMODIAL, SESQUITERPENES WITH DRIMANE SKELETON FROM CINNAMOSMA FRAGRANS BAILLON.

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From an acetone extract of the bark of Cinnamosma fragrans Baillon (Canellaceae), a tree growing in Madagascar, we have obtained, after chromatography on silica gel, three compounds: cinnamolide (1), $C_{15}H_{22}O_2$, m. 125-6°, $[\alpha]_D^{20}$ -29.4° (c = 1), cinnamosmolide (2), $C_{17}H_{24}O_5$, m. 204°, $[\alpha]_D^{20}$ -332.4° (c = 1) and cinnamodial (3), $C_{17}H_{24}O_5$, m. 141-3°, $[\alpha]_D^{20}$ -421.5 (c = 1).

The first compound, cinnamolide, showed in infrared region absorption bands at 1750, 1688 cm^{-1} and absorbed in UV at 224 mμ (lg ε = 3.94) thus indicating the presence of an α,β- unsaturated γ-lactone in its structure. The p.m.r. spectrum exhibited signals of the following groups: $\geq C-CH_3$ (0.81, s, 3H), $(CH_3)_2C<$ (0.93, s, 6H), $-\underset{|}{C}H-C\underline{H}_2-O-$ (AB part of an ABX system: 4.04, q, 1H; 4.40, q, 1H) $-CH_2-C\underline{H}=C<$ (6.86, q, 1H; J_1= 3 c/s and J_2= 8 c/s). Except of the α,β- unsaturated lactone, cinnamolide did not contain any other functional group. On dehydrogenation with selenium at 280-300° 1 gave 1,2,5-trimethylnaphtalene (4); on hydrogenation over PtO_2 (Adams) in acetic acid yielded dihydrocinnamolide (5), $C_{15}H_{24}O_2$, m. 134-5°, $[\alpha]_D^{20}$ -4.69° (c = 1) showing in infrared spectrum a band at 1772 cm^{-1} (saturated γ-lactone) and no absorption in UV. The lactone (5) on treatment with 5% KOH in methanol epimerized to give 6, $C_{15}H_{24}O_2$, m. 119-20°, $[\alpha]_D^{20}$ -7.35° (c = 1), showing an infrared absorption at 1772 cm^{-1} (saturated γ-lactone). We could conclude from the above data that cinnamolide could be identical with a product of an internal Cannizzaro reaction of polygodial described by Barnes and Loder[1].

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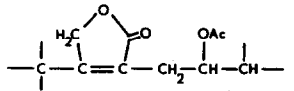
Actually, the compounds 5 and 6 were identical (mixed melting points and comparison of the infrared spectra) with dihydroconfertifoline and isodihydroconfertifoline[2], respectively, thus proving unequivocally the structures and absolute configurations of cinnamolide and its derivatives as 1, 5 and 6[2].

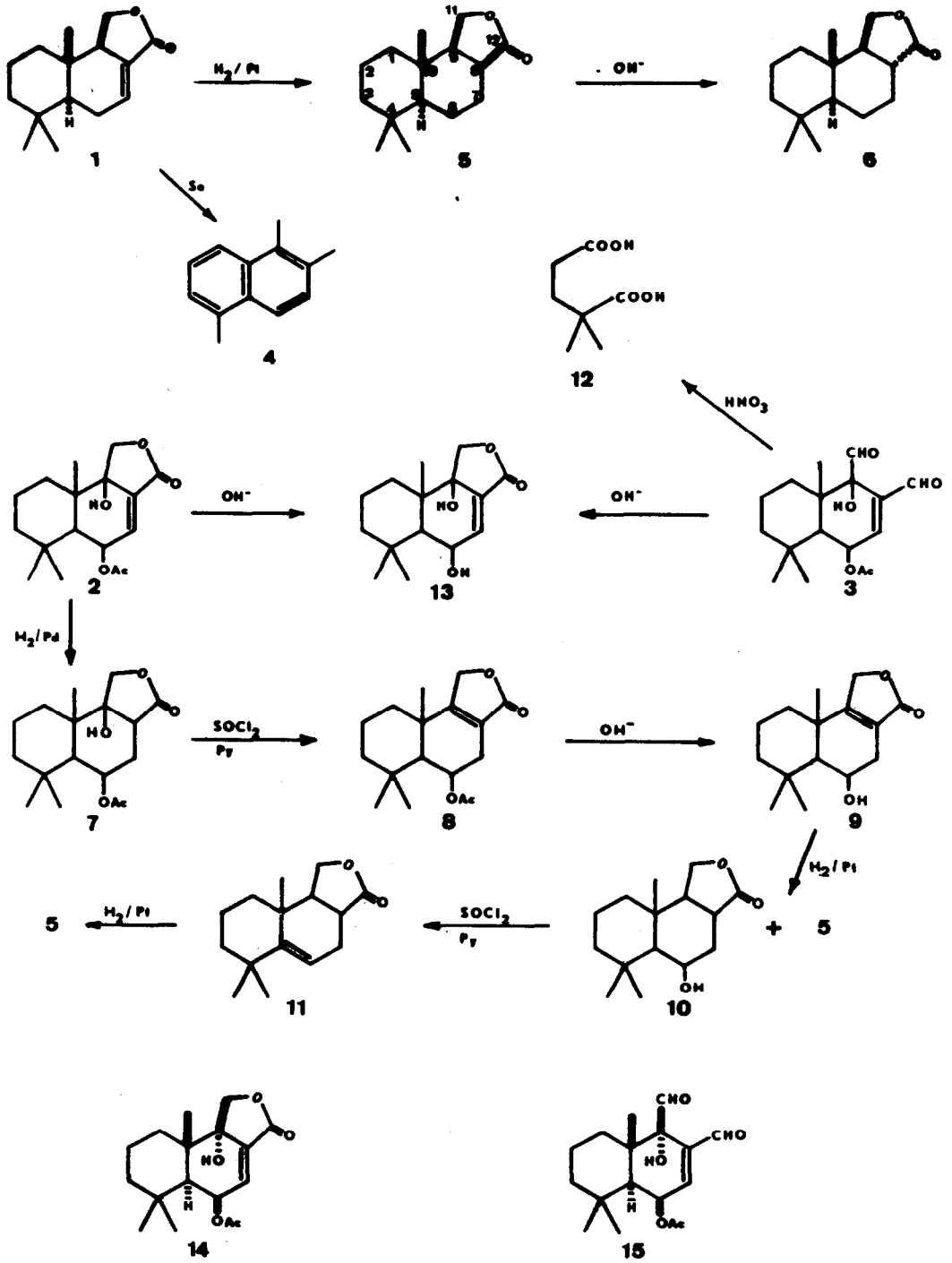
The other lactone, cinnamosmolide (2), exhibited an UV absorption at 211 mμ (isooctane) and in infrared region showed the absorption bands at 3573, 3432 cm^{-1} (-OH), 1735, 1240 cm^{-1} (CH_3-COO-) and 1763, 1703 and 832 cm^{-1} (α,β- unsaturated γ-lactone). According to a p.m.r. spectrum, cinnamosmolide contained three quarternary methyl groups (1.03, 1.13, 1.17, s); further the p.m.r. spectrum confirmed the presence of the CH_3-COO- group (2.08, s, 3H), the tertiary -OH group (3.63, s, 1H), of a grouping $-CH_2-O-$ (4.40, q, 2H; AB system), of a grouping $\geq$CH-CHOAc (2.15, d, 1H; J = 4.3 c/s), of a grouping $\geq$CH-CHOAc-CH= (5.80, t, 1H; $J_1 = J_2 = 4.3$ c/s) and a vinylic proton =CH-CHOAc (6.78, d, 1H; J = 4.3 c/s). The additional two unsaturations in empirical formula of 2 were ascribed to the presence of two carbocyclic rings.

On hydrogenation over Pd/C in ethyl acetate, 2 yielded dihydrocinnamosmolide (7), $C_{17}H_{26}O_5$, m. 150°, $[\alpha]_D^{20}$ -44.2° (c = 1), which did not show any UV absorption more; according to the IR spectrum the γ-lactone (1784 cm^{-1}), the acetoxy group (1734, 1240 cm^{-1}) and hydroxyl group (3477, 3590 cm^{-1}) remained in the molecule. Its p.m.r. spectrum exhibited signals of the following groups: CH_3-C$\leq$ (1.0, s, 6H and 1.32, s, 3H), CH_3-COO- (2.02, s, 3H), $-CH_2-O-$ (3.92, d, 1H and 4.48, d, 1H), AcO-CH$<$ (5.35, m, 1H) and HC-C=O (2.8, q, 1H).

On treatment with $SOCl_2$ in pyridine solution at room temperature, 7 dehydrated yielding an unsaturated lactone (8), $C_{17}H_{24}O_4$, m. 146°, $[\alpha]_D^{20}$ -13.7° (c = 1), showing an UV absorption at 216 mμ (lg ε = 4.15) and exhibiting in its p.m.r. spectrum signals of the same groupings as in 7 and no new signals indicating the presence of vinylic hydrogens appeared in the spectrum (of course, the quartet at 2.8 of the spectrum of 7 disappeared). The spin-spin decoupling experiments showed that because of the presence of homoallylic couplings, a system

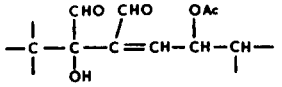


had to be present in the molecule, which enabled us to locate the acetylated hydroxy group in position γ- to the lactonic carbonyl. On saponification with 5% KOH in methanol 8 gave 9 (the latter could be reacetylated back to 8), $C_{15}H_{22}O_3$, m. 190-1°, $[\alpha]_D^{20}$ +39.2° (c = 1), showing an UV absorption at 218 mμ (lg ε = 4.05). The last mentioned compound was hydrogenated over PtO_2 (Adams) in acetic acid solution, giving hydroxylactone 10, $C_{15}H_{24}O_3$, m. 192-3°, $[\alpha]_D^{20}$ -15.6 (c = 1), as


1
H_2 / Pt
5
. OH⁻
6
Se
4
COOH
COOH
12
HNO_3
CHO
CHO
HO
OAc
3
OH⁻
OH⁻
HO
OH
13
2
OAc
H_2/Pd
HO
OAc
7
$SOCl_2$
Py
OAc
8
OH⁻
OH
9
H_2/Pt
5
H_2/Pt
11
$SOCl_2$
Py
10
+ 5
HO
OAc
14
CHO
CHO
HO
OAc
15

main product which did not absorb in ultraviolet region and exhibited infrared absorption bands at 3604, 3491 cm^{-1} (-OH) and 1771 cm^{-1} (γ-lactone). On treatment with $SOCl_2$ in pyridine 10 yielded mainly an unsaturated non-conjugated lactone 11, $C_{15}H_{22}O_2$, m. 81-2°, $[\alpha]_D^{20}$ -76.9° (c = 1)(IR absorption 1770 and 1645 cm^{-1}), whose p.m.r. spectrum exhibited the presence of one vinylic hydrogen atom only (at 5.68), thus locating the double bond in the position 5,6. 11 was hydrogenated over PtO_2 (Adams) in acetic acid giving dihydroconfertifoline (5), m. 134-5°, $[\alpha]_D^{20}$ -4.9 (c = 0.5). On the basis of above data we could ascribe the formula 2 to cinnamosmolide. Moreover, the formation of dihydroconfertifoline proved that the absolute configuration of the carbon 10 of cinnamosmolide was identical with that of the former (absolute configuration of 5 is known[2]).

Cinnamodial (3), UV max. 219 mμ (lg ε = 4.07; isooctane) possessed according to the infrared spectrum an acetoxy group (1740, 1240 cm^{-1}), two aldehyde groups, one of them being unsaturated (2870, 2720, 1726, 1690, 1655 cm^{-1}) and a hydroxy group (3470 cm^{-1}). The p.m.r. spectrum exhibited signals of three CH_3-C≤ (1.03, 1.17, 1.35, s) and of the groups CH_3-COO- (2.13, s, 3H), -OH (4.1, d, 1H; J = 1.4 c/s), =C(CHO)-CH=O (9.5, s, 1H), HO-C(CHO)-CH=O (9.78, d, 1H; J = 1.4 c/s; after exchange with D_2O a singlet), ≻CH-CH(CHO)Ac (2.03, d, 1H; J = 4.8 c/s), ≻CH-CHOAc-CH= (5.89, t, 1H; J_1= J_2= 4.8 c/s) and =CH-CH(CHO)Ac (7.0, d, 1H; J = 4.8 c/s). The relative positions of the functional groups



were confirmed by means of spin-spin decoupling experiments. Further, cinnamodial on oxidation with nitric acid furnished as a main product α,α-dimethylglutaric acid (12) identified by g.v.c. retention time and mass spectrum[3] of its dimethylester. Therefore we could conclude that also this compound could belong to the drimane sesquiterpenes where all the oxygen containing functional groups were concentrated in one of the two alicyclic rings, i.e. the ring A should be free of such functions.

3 treated with hot aqueous 2N NaOH underwent an internal Cannizzaro reaction (together with saponification of the acetoxy group) yielding a dihydroxy α,β-unsaturated lactone (13), $C_{15}H_{22}O_4$, m. 178-9°, $[\alpha]_D^{20}$ -237,5° (c = 0.5), identical with the product of the same treatment of cinnamosmolide (2). This fact proves the identity of skeletons of 2 and 3 and shows that the functional groups in both compounds in question possess the same configuration (together with absolute configuration of the carbon 10 - see formulas 1, 5 and 6).

The stereochemistry of the ring juncture of 2 and 3 follows from the fact

that as a by-product of the hydrogenation of 9 also dihydroconfertifoline (5) was formed besides the main product 10. The formation of 5 was due to double bond migration from the position 8,9 to the stable one (7,8) followed by the hydrogenolysis of so formed allylic alcohol. Therefore, the configuration of C_5 must be identical with that one in confertifoline, i.e. the hydrogen has to be oriented α.

According to the observed coupling constants between H_6 and H_5 (J = 1.5 c/s) and H_6 and H_7 ($J_1=J_2=$ 3.5 c/s), resulted from spin-spin decoupling experiments for 8 and 9, the axial orientation of the acetoxy group in cinnamosmolide is much more probable than the equatorial one. This fact therefore defines its configuration as β.

Comparing 2 and 3 with other drimane sesquiterpenes found in nature and taking into consideration biogenetic reasons, we concluded that probable configurational assignment of C_9 of both new compounds in question had to be identical with that found previously[2] (e.g. the same as in case of 1) which defines the absolute stereostructure of cinnamosmolide as 14 and cinnamodial as 15.

The final proof of the absolute stereochemistry of the above compounds, however, is still under investigation.

IR spectra were measured with a Perkin-Elmer mod 21 instrument in $CHCl_3$ solution; UV spectra with a Perkin-Elmer mod 137 instrument in CH_3OH solution; optical rotation on a Perkin-Elmer mod 141 polarimeter in $CHCl_3$ solution; mass spectra on a LKB gas chromatograph-mass spectrometer; p.m.r. spectra on a Perkin-Elmer mod R10 instrument and on a Varian HA 100 in $CDCl_3$ solution (TMS as internal standard; values are in δ=ppm; s=singlet, d=doublet, t=triplet, m=multiplet)

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REFERENCES

(1) S.C.Barnes and J.W.Loder, Austr.J.Chem., 15, 322 (1962)

(2) H.H.Appel, J.D.Connolly, K.H.Overton and R.P.M.Bond, J.Chem.Soc., 4685 (1960)

(3) L.Canonica, G.Jommi, P.Manitto, U.M.Pagnoni and F.Pelizzoni, Gazz.Chim.Ital., 96, 662 (1966)