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# An X-Ray Crystallographic Study on *cis-trans* Configurational Assignment to "*cis-*" and "*trans-*1,8-Terpins"[1)] and a Proposal of New Designation for Discriminating between the Configurational Isomers

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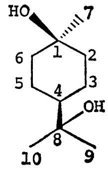
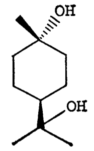
The crystal structures of "*cis*-terpin" (terpin hydrate) and "*trans*-terpin" were elucidated by X-ray crystallography. This crystal structure elucidation showed that the hydroxyl group at C-1 and the 1-hydroxy-1-methylethyl group at C-4 are in *cis* and *trans* relationships in the "*cis*-" and "*trans*-1,8-terpin" molecules, respectively, similarly to the structures in solutions. A new designation for discriminating between the configurational isomers is proposed on the ground of the IUPAC Rule for Nomenclature.

It has been documented[2–5)] that "*cis*-1,8-terpin" and "*trans*-1,8-terpin" are configurational isomers represented by structures (**1**) and (**2**), respectively and that the spatial arrangement of the hydroxyl group at C-1 and the 1-hydroxy-1-methylethyl group at C-4 of **1** was deduced to be *cis* on the basis of the preferential formation of 1,8-cineol (**3**) from **1** on reaction with aqueous sulfuric acid. The stereochemistry of these 1,8-terpins had been deduced by the ease of ring closure to the cineol. However, a controversy as to the stereochemical structure of these terpins was raised on the ground of observation that 1,8-cineol (**3**) had also been produced from "*trans*-1,8-terpin" (**2**) under the same acidic conditions.[6)] Reexamination of the *cis-trans* configurational assignment of these terpins by the $^1$H NMR method[6,7)] dispelled the ambiguity, bearing out the earlier assigned structures. All the studies hitherto done have dealt with the configuration of 1,8-terpins in solutions. In order to clarify unambiguously the configurational isomer of "*cis*-" and "*trans*-1,8-terpins," the determination of the molecular structures of the "1,8-terpins" was made by X-ray crystallographic analyses. On the other hand, there have been various designations and no consistency among the nomenclatures[3,8,9)] of the "1,8-terpins." A new designation for discriminating between these 1,8-terpins is, therefore, required to standardize their nomenclature.

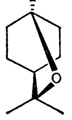
In this paper, we will deal with the configurational assignment of "*cis*-" and "*trans*-1,8-terpins" in the crystals and propose a new designation for discriminating between the configurational isomers of the "1,8-terpins."



**1**



**2**



**3**

## Results and Discussion

*Molecular and Crystal Structures of **1** and **2**.* Crystallographic analyses of "*cis*-1,8-terpin" (**1**) and "*trans*-1,8-terpin" (**2**) were performed by the direct method

Table 1. Final atomic coordinates (×10$^4$) and thermal parameters of **1**, with standard deviations in parentheses

(1) The non-hydrogen atoms.

| Atom | $x$ | $y$ | $z$ | $B_{eq}$$^{a)}$/Å$^2$ |
|---|---|---|---|---|
| C (1) | 10261 (3) | 1481 (2) | 381 (2) | 3.0 |
| C (2) | 10079 (4) | 1492 (2) | −281 (2) | 3.9 |
| C (3) | 9962 (4) | 2250 (2) | −531 (2) | 3.5 |
| C (4) | 11055 (3) | 2735 (2) | −361 (1) | 2.8 |
| C (5) | 11212 (3) | 2736 (2) | 308 (1) | 3.1 |
| C (6) | 11332 (3) | 1971 (2) | 544 (2) | 3.3 |
| C (7) | 10439 (5) | 713 (2) | 612 (2) | 4.7 |
| C (8) | 10977 (3) | 3500 (2) | −631 (2) | 3.2 |
| C (9) | 9838 (4) | 3924 (2) | −447 (2) | 4.6 |
| C (10) | 11081 (4) | 3479 (2) | −1299 (2) | 4.4 |
| O (1) | 9149 (2) | 1773 (1) | 626 (1) | 3.4 |
| O (2) | 11990 (2) | 3930 (1) | −410 (1) | 3.2 |
| O (3) | 9495 (4) | 2095 (2) | 1779 (1) | 5.3 |

a) $B_{eq}=8\pi^2(U_1+U_2+U_3)/3$, where $U_1$, $U_2$, and $U_3$ are the principal components of $U$ matrix.

(2) The hydrogen atoms.

| Atom | $x$ | $y$ | $z$ | $B$/Å$^2$ |
|---|---|---|---|---|
| H[C(2)] | 1847 (36) | 1348 (19) | 2138 (16) | 4.2 |
| H[C(2)] | 3260 (33) | 1251 (18) | 2030 (14) | 3.6 |
| H[C(3)] | 2449 (38) | 270 (20) | 1495 (16) | 5.0 |
| H[C(3)] | 4212 (33) | 2528 (19) | 362 (15) | 4.0 |
| H[C(4)] | 6742 (28) | 2487 (15) | 516 (12) | 1.8 |
| H[C(5)] | 9412 (29) | 490 (14) | 2112 (12) | 1.9 |
| H[C(5)] | 8000 (38) | 470 (21) | 2003 (16) | 4.3 |
| H[C(6)] | 1422 (35) | 2012 (18) | 1032 (15) | 4.3 |
| H[C(6)] | 1958 (33) | 1772 (17) | 410 (14) | 2.9 |
| H[C(7)] | 9803 (43) | 374 (21) | 481 (18) | 6.7 |
| H[C(7)] | 498 (40) | 681 (20) | 1062 (16) | 5.4 |
| H[C(7)] | 1138 (34) | 450 (18) | 466 (14) | 3.7 |
| H[C(9)] | 5414 (39) | 1802 (21) | 1450 (16) | 5.3 |
| H[C(9)] | 6097 (34) | 1000 (18) | 1443 (14) | 3.4 |
| H[C(9)] | 6787 (37) | 1740 (19) | 1400 (15) | 4.1 |
| H[C(10)] | 4909 (42) | 582 (21) | 645 (18) | 7.0 |
| H[C(10)] | 4210 (39) | 1261 (20) | 573 (17) | 4.3 |
| H[C(10)] | 4763 (38) | 1009 (20) | 9 (17) | 6.2 |
| H(1) | 9210 (46) | 1798 (23) | 990 (19) | 7.0 |
| H(2) | 7532 (37) | 1226 (20) | 512 (15) | 4.0 |
| H(3) | 9559 (53) | 1930 (27) | 2189 (22) | 10.9 |
| H(4) | 9908 (31) | 2146 (16) | 1782 (13) | 2.9 |

Table 2. Bond lengths and angles of **1**, with standard deviations in parentheses

| Bond length($l$/Å) | | Bond angle($\phi$/°) | |
|---|---|---|---|
| C(1)-C(2) | 1.520(5) | C(2)-C(1)-C(6) | 109.3(3) |
| C(1)-C(6) | 1.524(5) | C(2)-C(1)-C(7) | 111.8(3) |
| C(1)-C(7) | 1.523(5) | C(2)-C(1)-O(1) | 105.6(3) |
| C(1)-O(1) | 1.442(4) | C(6)-C(1)-C(7) | 111.6(3) |
| C(2)-C(3) | 1.514(5) | C(6)-C(1)-O(1) | 109.4(3) |
| C(3)-C(4) | 1.541(5) | C(7)-C(1)-O(1) | 108.6(3) |
| C(4)-C(5) | 1.534(5) | C(1)-C(2)-C(3) | 113.3(3) |
| C(4)-C(8) | 1.541(5) | C(2)-C(3)-C(4) | 112.0(3) |
| C(5)-C(6) | 1.514(5) | C(3)-C(4)-C(5) | 109.7(3) |
| C(8)-C(9) | 1.529(6) | C(3)-C(4)-C(8) | 112.7(3) |
| C(8)-C(10) | 1.528(5) | C(5)-C(4)-C(8) | 113.7(3) |
| C(8)-O(2) | 1.452(4) | C(4)-C(5)-C(6) | 111.1(3) |
| | | C(5)-C(6)-C(1) | 113.5(3) |
| | | C(4)-C(8)-C(9) | 113.8(3) |
| | | C(4)-C(8)-C(10) | 111.8(3) |
| | | C(4)-C(8)-O(2) | 108.6(3) |
| | | C(9)-C(8)-C(10) | 110.3(3) |
| | | C(9)-C(8)-O(2) | 104.3(3) |
| | | C(10)-C(8)-O(2) | 107.6(3) |

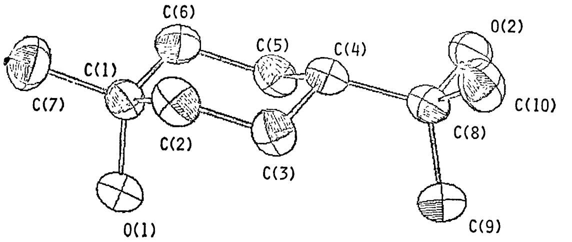


Fig. 1. ORTEP drawing of the molecular structure of "*cis*-1,8-terpin" (**1**).

Table 3. Final atomic coordinates (×10⁴) and thermal parameters of **2**, with standard deviations in parentheses

(1) The non-hydrogen atoms.

| Atom | $x$ | $y$ | $z$ | $B_{eq}$[a)]/Å² |
|---|---|---|---|---|
| C (1) | 1200(2) | 1324(6) | 1428(2) | 2.3 |
| C (2) | 1807(2) | 3108(5) | 1425(2) | 2.5 |
| C (3) | 2548(2) | 2400(5) | 1137(2) | 2.7 |
| C (4) | 2931(2) | 462(5) | 1540(2) | 2.0 |
| C (5) | 2330(2) | −1357(5) | 1509(2) | 2.4 |
| C (6) | 1593(2) | −637(6) | 1804(2) | 2.5 |
| C (7) | 784(2) | 793(7) | 689(2) | 3.4 |
| C (8) | 3718(2) | −236(6) | 1313(2) | 2.7 |
| C (9) | 4318(2) | 1568(8) | 1429(3) | 5.0 |
| C (10) | 3614(2) | −1030(8) | 553(2) | 4.5 |
| O (1) | 582(1) | 2072(4) | 1795(1) | 3.2 |
| O (2) | 3988(1) | −2027(4) | 1758(1) | 3.3 |

a) $B_{eq}=8\pi^2(U_1+U_2+U_3)/3$, where $U_1$, $U_2$, and $U_3$ are the principal components of $U$ matrix.

(2) The hydrogen atoms.

| Atom | $x$ | $y$ | $z$ | $B$/Å² |
|---|---|---|---|---|
| H[C(2)] | 1558(20) | 4295(62) | 1127(18) | 3.1 |
| H[C(2)] | 1974(17) | 3590(51) | 1944(15) | 2.0 |
| H[C(3)] | 2898(18) | 3673(54) | 1167(16) | 3.5 |
| H[C(3)] | 2420(20) | 2119(63) | 598(18) | 3.2 |
| H[C(4)] | 3097(20) | 939(61) | 2092(18) | 1.8 |
| H[C(5)] | 2594(20) | −2617(62) | 1823(18) | 2.6 |
| H[C(5)] | 2189(20) | 1866(61) | 991(18) | 3.0 |
| H[C(6)] | 1231(20) | −1751(60) | 1816(18) | 3.7 |
| H[C(6)] | 1777(20) | −237(62) | 2363(18) | 2.4 |
| H[C(7)] | 1130(18) | 258(56) | 373(17) | 3.9 |
| H[C(7)] | 379(19) | −328(60) | 676(17) | 4.9 |
| H[C(7)] | 536(20) | 2272(63) | 463(19) | 7.1 |
| H[C(9)] | 4742(20) | 1111(61) | 1368(18) | 3.9 |
| H[C(9)] | 4132(20) | 3054(63) | 1041(19) | 8.8 |
| H[C(9)] | 4384(21) | 2093(66) | 1984(19) | 6.8 |
| H[C(10)] | 3419(21) | 77(64) | 213(19) | 7.3 |
| H[C(10)] | 3244(22) | −2215(69) | 440(20) | 7.1 |
| H[C(10)] | 4109(20) | −1366(61) | 419(18) | 4.6 |
| H(1) | 789(19) | 2460(64) | 2235(18) | 5.5 |
| H(2) | 4425(21) | −2300(64) | 1737(18) | 5.5 |

using MULTAN.[10)] Final atomic coordinates, bond lengths, and bond angles are given in Tables 1 and 2 for **1**, and Tables 3 and 4 for **2**. The perspective view (Fig. 1) of the "*cis*-terpin" molecule showed that the hydroxyl group at C-1 is *cis* to the 1-hydroxy-1-methylethyl group at C-4. This corroborates the previously assigned configurational isomer[3–9)] of "*cis*-1,8-terpin." Furthermore, it was found that the hydroxyl group at C-1 and the 1-hydroxy-1-methylethyl group at C-4 are axial and equatorial, respectively and also the C-8 hydroxyl group is gauche to the hydrogen atom at C-4. Each hydroxyl group at C-1 and C-8 is linked by intermolecular hydrogen bonding to water of crystallization, as shown in Fig. 2. On the other hand, H(2) is linked to O(1)′ by intermolecular hydrogen bonding. The molecules of the "1,8-terpin" are packed along the a axis and the crystal structure is stabilized by the network of hydrogen bondings (Fig. 2).

On the other hand, the perspective view (Fig. 3) of a molecule of "*trans*-terpin" indicated that the hydroxyl group at C-1 is *trans* to the 1-hydroxy-1-methylethyl group at C-4. Both the hydroxyl group at C-1 and the 1-hydroxyl-1-methylethyl group at C-4 are equatorially oriented, and the C-8 hydroxyl group is gauche to the C-4 hydrogen atom similarly to the case of **1**. As shown in Fig. 4, the "*trans*-1,8-terpin" molecules form an infinite chain along the a axis by intermolecular hydrogen bonding. The chain is coupled with the next chain by other intermolecular hydrogen bonding to form pairs of the chain. These pairs build up the layered structure by the van der Waals force among the hydrophobic groups.

*A Proposal of New Designation for Discriminating between* "cis-" *and* "trans-*1,8-Terpins.*" 1,8-Terpins have two different substituents, such as the methyl and the hydroxyl groups, at the 1-position. For designating the steric relationship of these terpins, an arbitrary selection of these two substituents as the reference substituent has thrown the nomenclature of the terpins in confusion. The IUPAC Rule for Nomenclature (E. 2.3.4.)[11)] has recommended that,

Table 4. Bond lengths and angles of **2**, with standard deviations in parentheses

| Bond length($l$/Å) | | Bond angle($\phi$/°) | |
|---|---|---|---|
| C(1)-C(2) | 1.524(5) | C(2)-C(1)-C(6) | 109.5(3) |
| C(1)-C(6) | 1.525(5) | C(2)-C(1)-C(7) | 112.0(3) |
| C(1)-C(7) | 1.530(5) | C(2)-C(1)-O(1) | 108.7(3) |
| C(1)-O(1) | 1.442(4) | C(6)-C(1)-C(7) | 112.3(3) |
| C(2)-C(3) | 1.531(4) | C(6)-C(1)-O(1) | 109.3(3) |
| C(3)-C(4) | 1.531(5) | C(7)-C(1)-O(1) | 104.9(3) |
| C(4)-C(5) | 1.528(4) | C(1)-C(2)-C(3) | 113.5(3) |
| C(4)-C(8) | 1.546(4) | C(2)-C(3)-C(4) | 111.0(3) |
| C(5)-C(6) | 1.534(4) | C(3)-C(4)-C(5) | 109.3(3) |
| C(8)-C(9) | 1.517(5) | C(3)-C(4)-C(8) | 113.8(3) |
| C(8)-C(10) | 1.534(5) | C(5)-C(4)-C(8) | 113.2(3) |
| C(8)-O(2) | 1.442(4) | C(4)-C(5)-C(6) | 111.1(3) |
| | | C(5)-C(6)-C(1) | 112.8(3) |
| | | C(4)-C(8)-C(9) | 110.6(3) |
| | | C(4)-C(8)-C(10) | 112.7(3) |
| | | C(4)-C(8)-O(2) | 105.3(3) |
| | | C(9)-C(8)-C(10) | 110.9(3) |
| | | C(9)-C(8)-O(2) | 109.7(3) |
| | | C(10)-C(8)-O(2) | 107.5(3) |

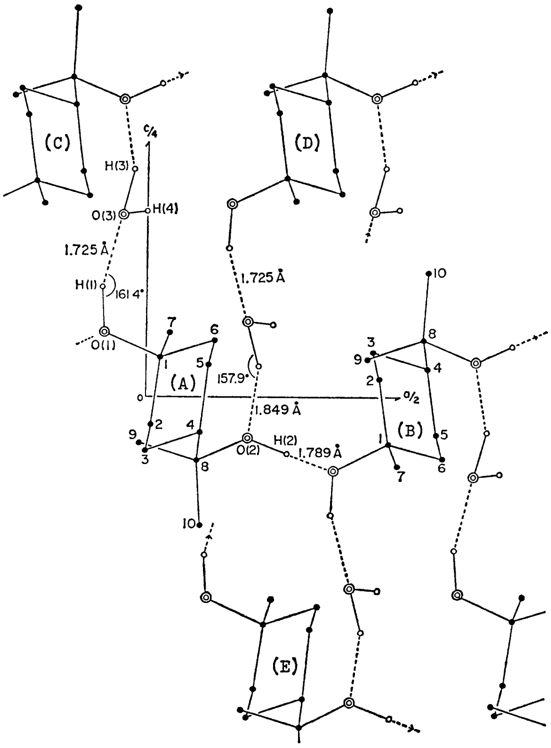


Fig. 2. Projection of **1** viewed along the b axis. The atoms indicated with ●, ◎, and ○ denote carbon, oxygen, and hydrogen atoms, respectively. The transformations of the atomic coordinates are (A) $x$, $y$, $z$; (B) $1/2+x$, $1/2-y$, $-z$; (C) $-1/4+x$, $-1/4+y$, $1/4-z$; (D) $1/4+x$, $1/4+y$, $1/4-z$; (E) $1/4+x$, $3/4-y$, $-1/4+z$.

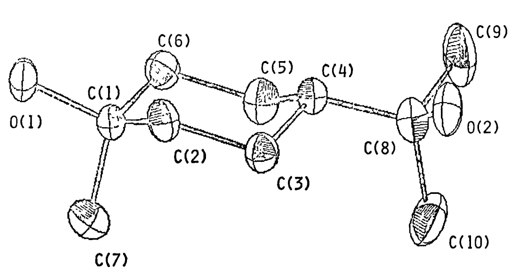


Fig. 3. ORTEP drawing of the molecular structure of "*trans*-1,8-terpin" (**2**).

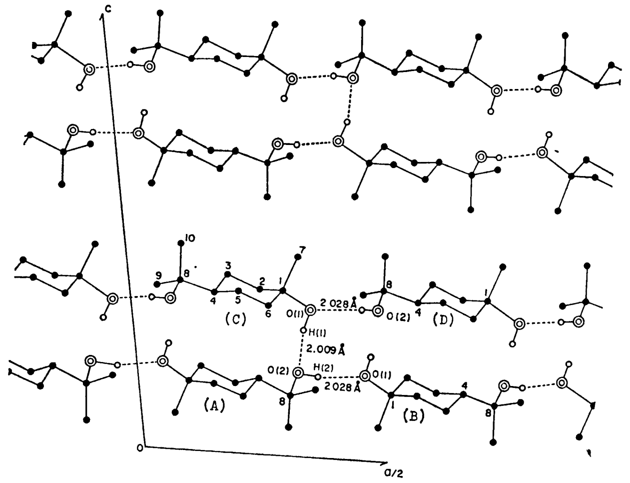


Fig. 4. Projection of **2** viewed along the b axis. The atoms indicated with ●, ◎, and ○ denote carbon, oxygen, and hydrogen atoms, respectively. The transformations of the atomic coordinates are (A) $x$, $y$, $z$; (B) $1/2+x$, $-1/2+y$, $z$; (C) $1/2-x$, $1/2+y$, $1/2-z$; (D) $1-x$, $1+y$, $1/2-y$.

when two different substituents locate at the same position of a monocycle, a characteristic group or a predominant substituent in the sequence rule is expressed by adding *r* as the reference substituent and a substituent being in the *cis* or *trans* relationship to this reference substituent is expressed by *c* or *t*, instead of *cis* or *trans*, respectively. According to the IUPAC Rule, therefore, "*cis*-terpin" (**1**) should be represented as *c*-4-(1-hydroxy-1-methylethyl)-1-methyl-*r*-1-cyclohexanol and "*trans*-terpin" (**2**) as *t*-4-(1-hydroxy-1-methylethyl)-1-methyl-*r*-1-cyclohexanol. In the case of using *p*-menthane as a conventional name, **1** and **2** are called *c*-4-*p*-menthane-*r*-1,8-diol and *t*-4-*p*-menthane-*r*-1,8-diol, respectively. However, it is hard to exclude the designation of "terpin" for the reason that this designation has been most widely used for a long time among chemists in the field of terpenoids. For the nomenclature of compounds **1** and **2** by using the appellation of "terpin," we will propose that "*cis*-1,8-terpin" (**1**) is expressed as *c*-1,8-terpin and "*trans*-1,8-terpin" (**2**) as *t*-1,8-terpin, hereafter.

## Experimental

*Material.* "*cis*-1,8-Terpin" (**1**), mp 105—106 °C (lit,[6]) 104—105 °C), used for X-ray analysis was obtained by repeated recrystallization of the commercial terpin hydrate (Yoneyama Kogyo Yakuhin Co. Ltd.). "*trans*-1,8-Terpin" (**2**), mp 157—158 °C (lit,[12]) 158—159 °C), was prepared from 1,8-cineol (**3**) according to the literature method[12]) and purified by repeated recrystallization. A single crystal of **1** and **2** for X-ray studies was prepared by crystallization from hot water. Spectroscopic data (IR and $^1$H NMR) of each compound were identical with the data[6,7] reported for the corresponding terpins.

*Crystallographic Measurements.* The crystallographic analyses were performed on a Syntex R3 diffractometer using graphite-monochromated Mo $K\alpha$ radiation. Cell dimensions were derived by the least-squares method from setting angles of 18 well-centered diffraction peaks for **1** and 15 peaks for **2**. Intensity data were collected by $\omega$-scan ($\theta_{max}=58.0°$), and $I_0>1.96\sigma(I_0)$ were used as observed reflections; 1091 reflections for **1** and 1261 reflections for **2**.

*Crystal Data of **1**.* $C_{10}H_{20}O_2 \cdot H_2O$, $M=190.28$. Crystal dimensions 0.20 mm × 0.25 mm × 0.23 mm. Orthorhombic, $a=10.930(2)$, $b=18.425(5)$, $c=22.791(6)$ Å, $U=4589.8$ Å$^3$, $D_c=1.03$ g cm$^{-3}$, $Z=16$, $D_m=1.08$ g cm$^{-3}$, $\mu$(Mo $K\alpha$)$=$ 0.8 cm$^{-1}$. Space group Fdd2.

*Crystal Data of **2**.* $C_{10}H_{20}O_2$, $M=172.26$. Crystal dimensions 0.47 mm × 0.50 mm × 0.30 mm. Monoclinic, $a=17.167(2)$, $b=6.233(2)$, $c=19.325(6)$ Å, $\beta=98.910(2)°$, $U=2043.1$ Å$^3$, $D_c=1.12$ g cm$^{-3}$, $Z=8$, $D_m=1.16$ g cm$^{-3}$, $\mu$(Mo $K\alpha$)$=0.8$ cm$^{-1}$. Space group C2/c.

*Structure Analyses and Refinements.* The phases of 106 reflections with $|E|>1.65$ for **1** and 172 reflections with $|E|>1.80$ for **2** were determined by MULTAN.[10] An $E$ map for the best solution yielded positions for all atoms except hydrogens. These atomic parameters were anisotropically refined, followed by a difference map to find the positions of all hydrogen atoms. Anisotropic refinement for carbon and oxygen atoms and isotropic refinement for hydrogen atom by full-matrix least-squares calculation reduced the R index finally to 0.044 for **1** and 0.049 for **2**.

The complete $F_o-F_c$ data and the tables of anisotropic thermal parameters for **1** and **2** are deposited as Document No. 8208 at the Office of the Editor of the Bulletin of the Chemical Society of Japan.

## References

1) The double quotation marks denote the long-standing trivial names used for 1,8-terpins.

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