

Isotopic Multiplets in the Carbon-13 NMR Spectra of Polyols with Partially Deuterated Hydroxyls. 5. β -Diols

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Abstract: Deuterium isotope effects on carbon-13 chemical shifts result in characteristic multiplets in the ^{13}C NMR spectra of β -diols and related polyols with partially deuterated hydroxyls. The phenomenon is observable under conditions of slow chemical exchange, e.g., in Me_2SO solutions. The multiplet patterns are analogous to those due to spin-spin couplings. The magnitude of the three-bond effect (the γ -effect) decreases linearly with increasing degree of substitution of the carbon atom. This suggests that the main mechanism for these effects is isotopic perturbation of the thermal distribution of molecules over excited vibrational states. Long-range effects extending over four and five bonds are interpreted in terms of isotopic perturbation of chemical equilibria. In the cases of 2,2,4-trimethyl-1,3-pentanediol and 2,2,6,6-tetramethylcyclohexanol, these equilibria involve intramolecular hydrogen bonding. For *trans*-1,3-cyclohexanediol, a preference for the equatorial orientation of deuterated hydroxyl groups is indicated.

Carbon atoms in the vicinity of partially deuterated hydroxyl groups exhibit multiplet structure in the proton-decoupled carbon-13 NMR spectrum.¹⁻⁴ These multiplets result from small upfield deuterium isotope effects on the carbon-13 chemical shifts and are observable under conditions of slow (relative to the magnitude of the isotope effect) chemical exchange between the protio and deuterio forms. Early work demonstrated doublet structure for hydroxyl-bearing carbon atoms of alcohols, phenols,² and carbohydrates.¹ In the case of alcohols and phenols, doublet structure was also observed for carbon atoms vicinal to the hydroxyl bearing one.² Downfield isotope shifts extending across four bonds to the para carbon of phenols have also been reported.² More recently, work conducted at higher resonance frequencies has shown that, in the spectra of carbohydrates, higher multiplets, e.g., octets, can also be observed.^{3,4} Each line in such multiplets is due to one or more isotopomers. The multiplicity depends on the details of the hydroxylic environment: whether or not the carbon atom is bonded to a hydroxyl and how many hydroxyls there are on vicinal carbons. Long-range isotope effects observed with some carbohydrates are thought to be transmitted through hydrogen bonds⁴ or to be due to isotopic perturbation of chemical equilibria involving hydrogen bonds.⁵

Structural trends in the magnitude of the isotope effects suggest the possible use of the phenomenon in the elucidation of molecular structure, as well as for spectral assignments.³⁻⁷ Toward this end, a more systematic investigation was undertaken of isotopic multiplets in the ^{13}C NMR spectra of aliphatic β -diols and related mono- and polyhydric alcohols. In addition to the effects transmitted across two and three bonds, long-range effects extending over four and five single bonds were also observed. Presented here are the results of this investigation, including descriptions of multiplet patterns, structural trends in the magnitude of the isotope effects, and interpretations of the long-range effects.

Experimental Section

Diols and related alcohols were obtained from commercial sources except for 2,4-dimethyl-2,4-pentanediol and 2,2,6,6-tetramethylcyclohexanol, which were from the Hercules Research Center collection. The

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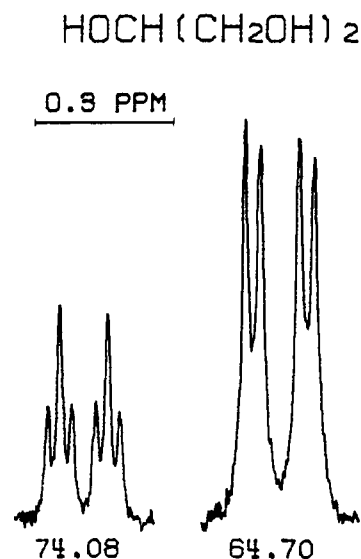


Figure 1. Isotopic multiplets in the ^{13}C NMR spectrum of glycerol (17) with partially deuterated hydroxyls.

materials were dissolved in $\text{Me}_2\text{SO}-d_6$ to a concentration of ca. 0.2 M. Partial deuteration was achieved by the addition of a calculated amount of D_2O followed by treatment with CaSO_4 (nonindicating Drierite) and filtering.² Carbon-13 NMR spectra were recorded at ambient temperature ($24 \pm 1^\circ\text{C}$) at 90.56 MHz on a Nicolet 360WB spectrometer operating in the pulsed Fourier transform mode. Low-power broad-band proton decoupling was achieved by using the MLEV-64 sequence.⁸ When necessary, spectral resolution was enhanced with use of apodization routines supplied by the instrument manufacturer. The central component of the solvent resonance was used as an internal reference with a chemical shift of 41,105 ppm relative to TSP. A few experiments in acetone- d_6 were carried out in a similar fashion with the solvent peak at a chemical shift of 29.8 ppm.

Results and Discussion

Multiplet Patterns. Several multiplet types can be observed in the ^{13}C NMR spectra of polyols with partially deuterated hydroxyls. The multiplet pattern reflects details of the hydroxylic environment of the carbon atom. For an isolated hydroxyl group there are two possible isotopic species: COH and COD. The β -isotope effect is an upfield chemical shift, Δ_β , of ca. 100 ppb of the COD species relative to COH. Thus, under conditions of

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Table I. Carbon-13 Chemical Shifts^a and Deuterium Isotope Effects^b

	C1	C2	C3	C4	other
alcohols					
methanol (1)	50.1				
	130				
ethanol (2)	57.6	29.1			
	123	61			
2,2-dimethylpropanol (neopentanol) (3)	72.9	34.0	27.8		
	127	22			
2,3-dimethyl-2-butanol (4)	28.0	72.5	39.7	19.2	
	57	110	36		
diols					
1,4-butanediol (5)	62.3	30.8			
	123	52			
2,3-dimethyl-2,3-butanediol (pinacol) (6)	26.5	75.1			
	51	119, 10			
2,2-dimethyl-1,3-propanediol (neopentane glycol) (7)	69.0	38.6			23.0
	126	21, 21			
2,2,4-trimethyl-1,3-pentanediol (8)	71.1	41.3	79.7	30.1	25.1; 23.4
	134, -14	24, 14	114	22	22.2; 18.6
(2 <i>R</i> ,4 <i>R</i>)-2,4-pentanediol (9)	25.9	64.7	50.1		
	52	115	52, 52		
(2 <i>R</i> ,4 <i>S</i>)-2,4-pentanediol (10)	25.5	66.2	49.7		
	61	113	56, 56		
2-methyl-2,4-pentanediol (11)	32.2; 30.6	71.1	52.2	65.5	26.5
	57; 48	118	47, 47	121	65
2,4-dimethyl-2,4-pentanediol (12)	33.2	71.8	54.8		
	52	123	34, 34		
2,2,4,4-tetramethyl- <i>cis</i> -1,3-cyclobutanediol (13)	78.5	43.8			31.0; 17.7
	123	33, 33			
2,2,4,4-tetramethyl- <i>trans</i> -1,3-cyclobutanediol (14)	79.9	41.9			24.7
	126	31, 31			
<i>cis</i> -1,3-cyclohexanediol (15)	69.0	47.0		36.4	22.2
	113	60, 60		57	
<i>trans</i> -1,3-cyclohexanediol (16)	66.6	43.9		35.5	20.4
	120	57, 57		53, 11	
polyols					
glycerol (17)	64.7	74.1			
	119, 33	105, 26, 26			
trimethylolpropane (18)	63.5	44.9	23.0	9.1	
	120	21 (3)			
pentaerythritol (19)	62.7	47.1			
	121	21 (4)			
2,2,6,6-tetramethylcyclohexanol (20)	76.8	45.0	29.3	18.5	68.2; 62.7
	95, 12 (4)	23, 11, 11			134; 136, -17

^a In ppm, rounded to the nearest tenth. ^b In ppb ± 3 ; upfield shifts are positive.

slow chemical exchange, the ^{13}C resonance of a hydroxylated atom will be a doublet with a spacing of Δ_β . The relative intensities of the doublet components correspond to the mole fractions of protons and deuterons. The γ -isotope effect due to a hydroxyl group on a vicinal carbon, i.e., CCOH vs. CCO, is usually smaller: $\Delta_\gamma < 70$ ppb,

The isotope state of a hydroxyl group (light or heavy) is analogous to the spin state ($+1/2$ or $-1/2$) of a spin $1/2$ nucleus. The isotopic multiplets are thus similar to those due to spin-spin couplings. The multiplet types can be designated according to the kind and number of isotope effects affecting the atom.³ Thus, e.g., the resonance of a hydroxylated carbon atom with a hydroxyl on a vicinal carbon will be a $\beta\gamma$ -quartet with components corresponding to the HH, HD, DH, and DD species. A hydroxylated carbon atom flanked by two hydroxylated carbons, such as carbon-2 of glycerol, will give rise to a $\beta\gamma_2$ -sextet with components corresponding to the HHH, HHD and HDH, HDD, DHH, DHD and DDH, and DDD species. Examples of such multiplets are shown in Figure 1 with the spectrum of glycerol.

The isotopic multiplets for the nonhydroxylated central carbon atoms in a series of β -polyols are shown in Figure 2. As can be seen in the figure, the analogy with spin-spin multiplets is born out rather well. The γ_3 , $\gamma_2\gamma'$, and γ_4 multiplets are first examples of three and four γ -effects on the same carbon atom. It can be shown that the relative intensity of the m 'th component in a multiplet due to n equivalent isotope effects is given by

$$\frac{n! R^{m-1}}{(m-1)!(n-m+1)!} \quad (1)$$

where R is the deuterium/proton mole ratio and the first component is the protio form. Thus, the relative intensities of the γ_4 -quintet of pentaerythritol are $1:4R:6R^2:4R^3:R^4$. It has been suggested that the isotopic multiplets in the cobalt-59 NMR spectra of aqueous solutions of $\text{Co}(\text{NH}_3)_6^{2+}$ could be used for the determination of the isotopic composition of heavy water.⁹ The isotopic multiplets in the ^{13}C NMR spectra of polyols in $\text{Me}_2\text{SO}-d_6$ solutions could be used for the same purpose. They offer the advantage of requiring only very small (a few μL) samples for analysis.

Structural Trends. The isotope effects on ^{13}C chemical shifts due to hydroxyl deuteration for the series of β -diols and related alcohols and polyols investigated in this work are summarized in Table I. Also given in the table are the chemical shift values. The magnitude of the β -isotope effect seems to show no clear general structural trends. However, for molecules with non-equivalent hydroxyls, the β -effect is greater for the less-substituted carbon atom. Thus, Δ_β for CH_2OH is greater than that for CHOH in **8**, **17**, and **20**. Similar trends have been observed in carbohydrates.^{4,5} More clearly cut trends are exhibited in the γ -effect. A plot of Δ_γ against the number of hydrogens bonded to the affected carbon atom is shown in Figure 3. The trend of smaller γ -effect with increasing degree of substitution is rather clear. It seems significant that in cyclic and strained molecules, Δ_γ is larger than in acyclic systems. Also, the values of α -diols are at the lower end of the respective ranges. Intrinsic isotope effects on chemical shifts are usually discussed in terms of contributions from intramolecular electric field effects, changes in bond hybridization, and isotopic perturbation of the thermal

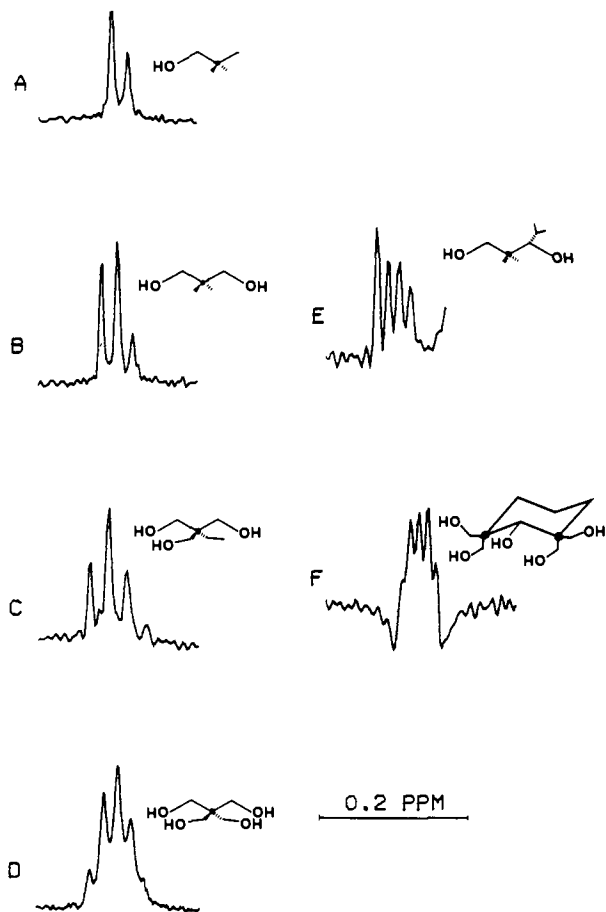


Figure 2. Isotopic multiplets in the ^{13}C resonances of the quaternary carbons of neopentanol (3) (A), neopentane glycol (7) (B), trimethylpropane (18) (C), pentaerythritol (19) (D), 2,2,4-trimethyl-1,3-pentanediol (8) (E), and 2,2,6,6-tetramethylcyclohexanol (20) (F) with partially deuterated hydroxyls.

distribution of molecules over excited vibrational states.¹⁰ The vibrational modes involving a carbon atom attached to several heavy atoms are likely to be less sensitive to isotopic perturbation than the ones involving a carbon bonded to hydrogens. Thus, the present findings suggest that the latter mechanism is of primary importance for the γ -effect in β -diols and related alcohols and polyols.

Long-Range Effects. Isotope effects extending over four and five chemical bonds were also observed. Isotopic multiplets reflecting such long-range effects are shown in Figure 4. The magnitude of the extra splittings on C1 of 8 was found to be larger (-18 vs. -14 ppb) when acetone was used as the solvent instead of Me_2SO . This finding and the fact that long-range effects are observed only with some substances suggest that these effects are due to isotopic perturbations of rapid chemical equilibria rather than being intrinsic ones. Such equilibria may involve intramolecular hydrogen bonding in 2,2,4-trimethyl-1,3-pentanediol and 2,2,6,6-tetramethylcyclohexanol or a *lax,3eq* to *leq,3ax* conformational equilibrium in *trans*-1,3-cyclohexanediol.

It can be shown⁵ that, for an equilibrium between two states with chemical shifts δ_a and δ_b , the isotope shift, Δ , arising from the isotopic perturbation of the equilibrium [i.e., from modifying the equilibrium constant, K , by the factor k (the magnitude of the equilibrium isotope effects)] is given by

$$\Delta = K(k - 1)(\delta_b - \delta_a) / [(1 + K)(1 + kK)] \quad (2)$$

A maximum in Δ is obtained when $K = k^{-1/2}$. Since k is expected

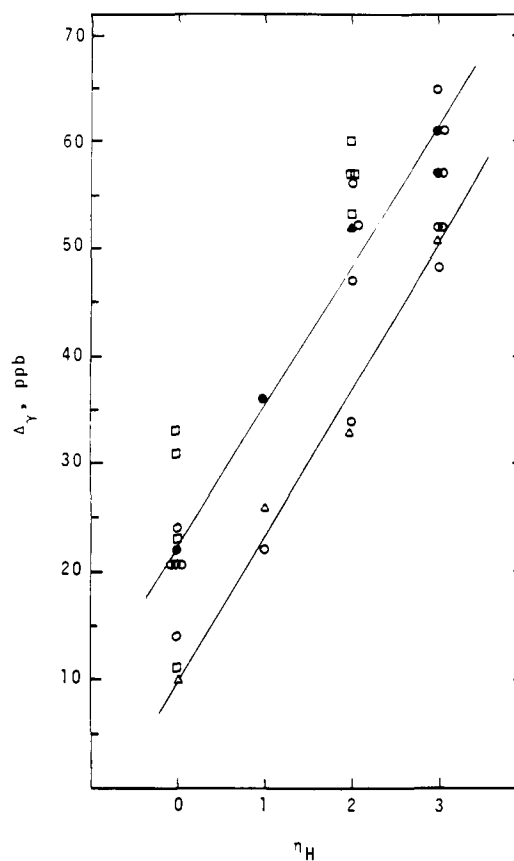


Figure 3. A plot of the three-bond deuterium isotope effect, $\Delta\gamma$, against the number of hydrogens bonded to the affected carbon atom: (●) alcohols, (Δ) α -diols, (\circ) β -diols, (Δ) γ -diol, (\square) cyclic diols. The lines are drawn to guide the eye.

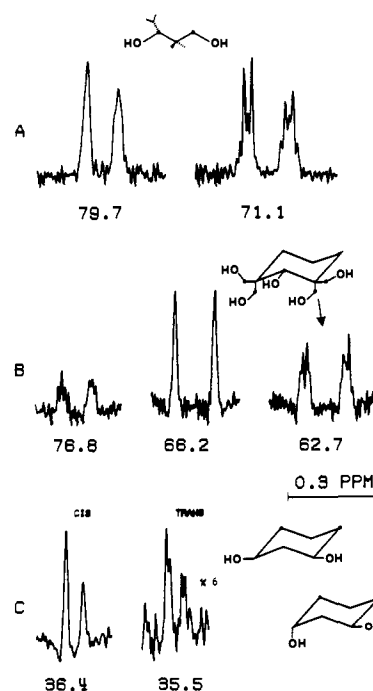


Figure 4. Isotopic multiplets with examples of long-range effects in the spectra of (A) 2,2,4-trimethyl-1,3-pentanediol (8) showing "extra" splittings on C1 but not on C3, (B) 2,2,6,6-tetramethylcyclohexanol (20) showing "extra" splittings on C1 and on the *cis*- CH_2OH groups but not on the *trans* ones, and (C) carbons 4 and 6 of *cis*- and *trans*-1,3-cyclohexanediol (15 and 16) showing "extra" splittings for the *trans* isomer but not for the *cis* one.

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to be close to unity, a maximum isotope effect on the chemical shift will be observed when the equilibrium constant itself is close to unity. Noteworthy in this respect is *trans*-1,3-cyclohexanediol (16), for which $K = P_{1ax,3eq}/P_{1eq,3ax} \approx 1$. The chemical shift difference at C4 between the *cis*-isomer 15, where the hydroxyls are equatorial, and the *trans*-isomer 16, where the hydroxyls are half of the time axial and the other half equatorial, is 0.9 ppm. Thus, the value of $\delta_b - \delta_a$ can be estimated at 1.8 ppm. The observed long-range isotope effect is 0.011 ppm. Solving eq 2 for k and using these values, one obtains $k = 1.025$, i.e., the deuterated hydroxyl prefers the equatorial orientation over the axial one by a factor of 1.025. Isotope effects of similar magnitude have been observed in dimethylcyclohexane derivatives.¹¹ Preference for the axial orientation of trideuteriomethyl groups has been demonstrated.^{11,12} The equatorial preference of the deuteriohydroxyl is probably related to solvation effects.

In 2,2,4-trimethyl-1,3-pentanediol (8) only the carbon resonance of the CH₂OH group exhibits the long-range isotope effect. The most likely origin of this effect is isotopic perturbation of an equilibrium involving the CHOH...*(OH)*CH₂ intramolecular hydrogen bond and a conformation lacking such a bond. Indeed, such equilibria for β -diols are well-known in the literature.^{13,14} The absence of long-range isotope effects in other molecules investigated in this work suggests that in these molecules the equilibrium strongly favors only one of the structures.

The situation in 2,2,6,6-tetramethylcyclohexanol (20) is much more complex. Here C1 experiences long-range isotope effects from all four primary hydroxyls, whereas only the resonance of the *cis*-CH₂OH groups exhibits a long-range effect. The ring hydroxyl, which must be equatorial, is probably involved in intramolecular hydrogen bonding with the hydroxymethyl groups both as a hydrogen donor and as an acceptor. This is probably also true for the *cis*-hydroxymethyls, which are axial.

Conclusions

The isotopic multiplets in the ¹³C NMR spectra of polyols with partially deuterated hydroxyls are analogous to spin-spin multiplets. Their pattern is predictable on statistical grounds. The variation of the γ -effect with the degree of substitution of the carbon atom suggests that the main mechanism for these effects is isotopic perturbation of the thermal distribution of molecules over excited vibrational states. Isotope effects extending over four and five bonds are due to isotopic perturbations of chemical equilibria involving intramolecular hydrogen bonding in β -diols or, in *trans*-1,3-cyclohexanediol, a preference for the equatorial orientation of deuterated hydroxyl groups.

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Registry No. 1, 67-56-1; 2, 64-17-5; 3, 75-84-3; 4, 594-60-5; 5, 110-63-4; 6, 76-09-5; 7, 126-30-7; 8, 144-19-4; 9, 42075-32-1; 10, 3950-21-8; 11, 107-41-5; 12, 24892-49-7; 13, 3039-96-1; 14, 2694-23-7; 15, 823-18-7; 16, 5515-64-0; 17, 56-81-5; 18, 77-99-6; 19, 115-77-5; 20, 5416-55-7; D₂, 7782-39-0.

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Communications to the Editor

Multiple Mixed-Metal Condensation Leading to the Pentagonal Bipyramidal Hexahydride $\text{Ir}_2\text{Cu}_3\text{H}_6(\text{MeCN})_3(\text{PMe}_2\text{Ph})_6^{3+}$

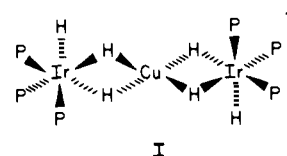
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We have reported earlier that $[\text{Cu}(\text{NCMe})_4]\text{PF}_6$, an operational source of naked "Cu⁺", finds adequate electron density in the hydride ligands of several transition-metal polyhydride complexes to condense to hydride-rich mixed-metal clusters.^{1,2} In the cases of $\text{CuRe}_2\text{H}_{10}(\text{PMe}_2\text{Ph})_6^{+1}$ and the structurally distinct *fac* and *mer* isomers of $\text{CuIr}_2\text{H}_6(\text{PMe}_2\text{Ph})_6^{+2}$ the resulting trimetal backbone is linear. In the case of $\text{Cu}_2\text{Re}_4\text{H}_{16}(\text{PMe}_2\text{Ph})_8^{2+}$,¹ a planar (rhomboidal) raft of six metals is formed in which two coppers are separated by 2.493 Å. Acetonitrile is absent from all of these products.

A surprising feature of $\text{Cu}(\eta^2\text{-fac-IrH}_3\text{P}_3)_2^{2+3}$ (I) is the presence of terminal hydride ligands, not involved in bonding to copper. We have now explored the $\text{Cu}^+/\text{fac-IrH}_3(\text{PMe}_2\text{Ph})_3$ system, at Ir/Cu stoichiometries lower than 2:1, and find evidence for an



unexpected yet isolable aggregate. At a mole ratio of 2:3, *fac*- IrH_3P_3 and $\text{Cu}(\text{NCMe})_4\text{PF}_6$ react in THF (-78°C , subsequently warmed to 25°C) to yield a colorless precipitate.⁴ The ¹H NMR of the precipitated product shows single chemical shifts for MeCN, Me_2PPh , and hydride hydrogens in the *ligand* ratio 1.5:3:3. The Me_2PPh resonance is a doublet, consistent with *cis* disposition of the phosphines, and the hydride resonance is a broad doublet. The ³¹P{¹H} NMR spectrum shows only a singlet, but selective coupling to the hydride hydrogens reveals an AA'A'XXX' pattern. The infrared spectrum (Nujol) shows bands characteristic of coordinated MeCN (2302 and 2272 (s) cm^{-1}) and of bridging hydrides (1759(s), 1789 (sh) cm^{-1}).

The X-ray crystal structure⁵ of this material, crystallized as hexagonal plates by cooling from CH_2Cl_2 , shows it to have the

(4) The ³¹P{¹H} NMR of the filtrate showed the presence of some $\text{Cu}(\eta^2\text{-fac-IrH}_3\text{P}_3)_2^{2+}$.

(5) Crystallographic data (-158°C): space group $R\bar{3}2$, $a = b = 12.317$ (2) Å, $c = 42.629$ (11) Å, $Z = 3$; $R_F = 7.1\%$, $R_wF = 7.6\%$ for 1199 observed ($I > 3\sigma$) reflections. The cation has a crystallographic C_3 axis passing through the iridiums and three crystallographic C_2 axes in the Cu_3 plane. The cations suffer a disorder of the three copper atoms over a planar hexagonal shape (60:40 occupancy); the acetonitrile molecules bound to these coppers lie slightly off the crystallographic C_2 axes and thus suffer additional disorder. The two crystallographically independent PF_6^- ions display high thermal motion.

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