A Stereochemical Study of the Reactions of Trisubstituted Phosphites with Alkyl Hypochlorites[1]

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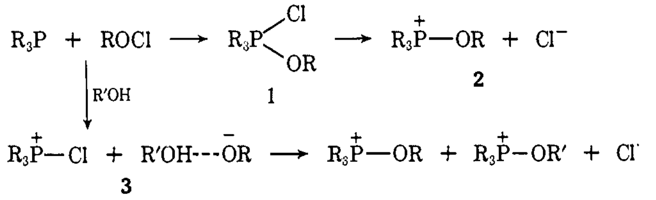
Abstract: The reactions of *cis*- and *trans*-2-methoxy-4-methyl-1,3-dioxaphosphorinans with neopentyl hypochlorite yield *cis* and *trans* six-membered ring phosphates, **6** and **7**. One isomer reacts essentially stereospecifically whereas the other yields mixtures of phosphates whose ratio varies as a function of temperature. These results are explained in terms of the initial formation of pentasubstituted phosphorus intermediates. Trineopentyl and trimethyl phosphite react at −78° to give tetraalkoxyphosphonium chlorides. These salts can be isolated as the relatively stable fluoroborates.

Petrov and Sokolskii[2] showed that trialkyl phosphites react with alkyl hypochlorites to give trialkyl phosphates. It was shown later that these reactions lead to tetraalkoxyphosphonium salts[3–5] as intermediates and that they decompose by an Arbusov reaction to give an alkyl chloride and the trialkyl phosphates.

Reaction of optically active methylpropylphenylphosphine with *t*-butyl hypochlorite gave racemic methylpropylphenylphosphine oxide when the reaction was conducted in pentane. When the reaction was conducted in methanol the oxide was formed with 72% inversion.[6] These and other data suggest[3] that in nonhydroxylic solvents the trisubstituted phosphorus compound reacts with the hypochlorite to give a pentasubstituted phosphorus compound, **1**, which then ionizes to give the alkoxyphosphonium chloride. In hydroxylic solvents displacement by the phosphorus on chlorine to give a chlorophosphonium alkoxide **3** in which the alkoxide ion is stabilized by hydrogen bonding explains the existing data.



$$\mathrm{R_3P + ROCl \longrightarrow \underset{\mathbf{1}}{R_3P\overset{Cl}{\underset{OR}{<}}} \longrightarrow \underset{\mathbf{2}}{R_3\overset{+}{P}{-}OR + Cl^-}}$$

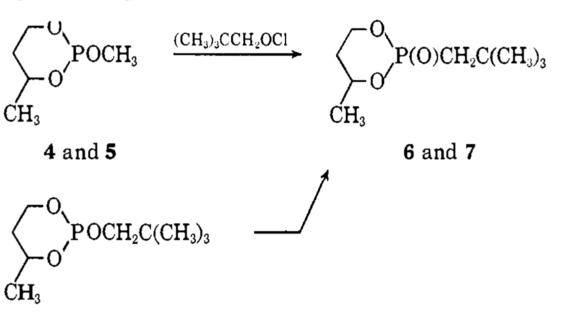
$$\Big\downarrow \mathrm{R'OH}$$

$$\mathrm{\underset{\mathbf{3}}{R_3\overset{+}{P}{-}Cl + R'OH{-}{-}{-}\overset{-}{O}R} \longrightarrow R_3\overset{+}{P}{-}OR + R_3\overset{+}{P}{-}OR' + Cl^-}$$

The need for suggesting a change in mechanism during these reactions and the further requirement that **1** be formed without optical activity or be able to lose it before ionization to **2** prompted further mechanistic investigation.

During the course of this work Cohen[7] reported the isolation of tetramethoxyphosphonium hexachloroantimonate from the reaction of trimethyl phosphite, methyl hypochlorite, and antimony pentachloride. It has also been found that trialkyl phosphate can be alkylated with trialkyloxonium fluoroborates to yield alkoxyphosphonium salts.[8] A discrepancy was noted between the ^{31}P nmr chemical shift reported by Cohen for tetramethoxyphosphonium hexachloroantimonate and that found for tetramethoxy- and tetraethoxyphosphonium fluoroborates. It seemed important therefore to prepare other tetraalkoxyphosphonium salts by the hypochlorite reaction so that their ^{31}P nmr chemical shifts could be compared to those salts prepared by alkylation.

The major effort of this work has been to study whether the intermediates **1** are formed during the reactions of hypochlorites with trisubstituted phosphorus compounds. The isomeric phosphites **4** and **5** have been oxidized with neopentyl hypochlorite to the corresponding phosphates **6** and **7**. The configurations of the phosphates **6** and **7** have been related to the configurations of **4** and **5** by stereospecific oxidation of the phosphites **8** and **9**. One basic assumption has been made in relating the configurations of these substances. It is assumed that the most stable phosphites **4** and **8** of each pair have the same configurations.[9] The ratios **4**:**5** and **8**:**9** are nearly identical with essentially 95% of the most stable phosphites being present at equilibrium. The ^{1}H chemical shifts of the ring methyl groups of **4** and **8** are virtually identical, as are those of **5** and **9**. It should be noted that it is not known which of these isomers is *cis* or *trans* nor is much known about the conformations of the rings.[10] This lack of knowledge does



4 and **5**

6 and **7**

8 and **9**

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[1] This research has been supported by the National Science Foundation under Grant GP-4997X.

[2] K. A. Petrov and G. A. Sokolskii, *Zh. Obshch. Khim.*, **26**, 477 (1956).

[3] D. B. Denney and R. R. DiLeone, *J. Amer. Chem. Soc.*, **84**, 4737 (1962).

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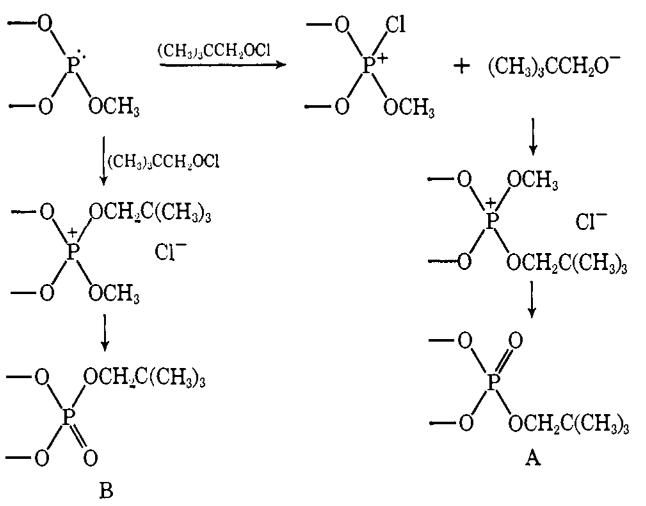

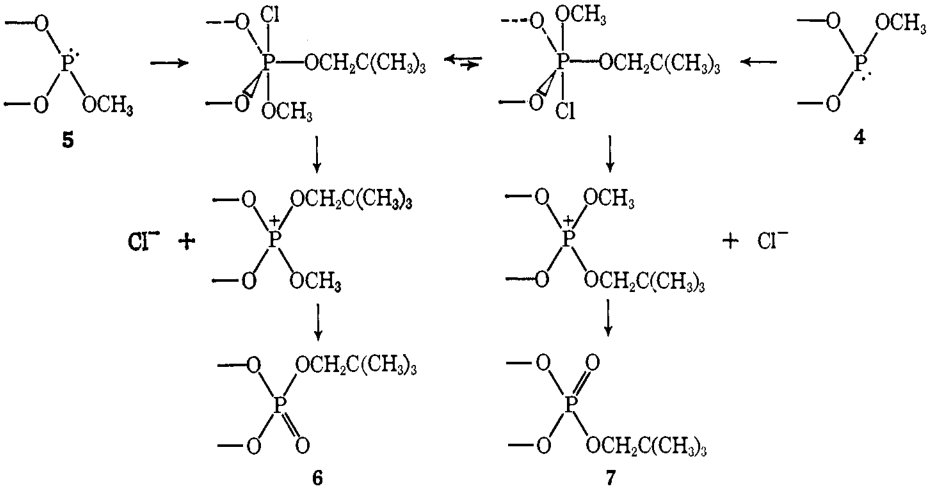

not materially affect the stereochemical studies reported here.

Results and Discussion

The percentages of products **6** and **7** obtained by reaction of **4** and **5** with neopentyl hypochlorite are collected in Table I. Stereospecific oxidation of **8** with retention of configuration yielded **6**, and **9** yielded **7**. The relationship of configurations is then **4**, **6**, and **8**; all have the same relation of the ring methyl group and the alkoxy group and the same is the case with **5**, **7**, and **9**.

Table I. Reactions of **4** and **5** with Neopentyl Hypochlorite

Isomer composition (%)	Product composition (%)	Conditions Temp, °C
5 (84); **4** (16)	**6** (93); **7** (7)	−60 to −78
5 (70); **4** (30)	**6** (81); **7** (19)	−66 to −78
4 ≅ (95)	**6** (40); **7** (60)	−70 to −78
4 ≅ (95)	**6** (46); **7** (54)	−65 to −72
4 ≅ (95)	**6** (41); **7** (59)	−58 to −78
4 ≅ (95)	**6** (66); **7** (34)	+2 to 11

The results show quite conclusively that reaction of **4** and **5** with neopentyl hypochlorite does not yield a common intermediate. Reaction of **4** is not a stereospecific process and the ratio of products **6**:**7** varies as a function of temperature with the trend being toward increasing amounts of **6** as the temperature is raised. Reaction of **5** appears to be very nearly stereospecific; for example, oxidation of the 84:16 mixture of **5** and **4** should yield *ca.* 7% **6** and 9% **7** from the **4** present in the mixture. If these values are subtracted from those found (93% and 7%) it is clear that **5** is converted into **6** as the major product. Similar conclusions are reached using data obtained from the reaction of the 70:30 mixture of **5** and **4**. The stereospecific process results in the substitution of the neopentyloxy group in the opposite relationship to the ring methyl group as the methoxy group had in the starting phosphite.

A stereospecific ionic process in which displacement occurs on chlorine followed by alkoxide attack with inversion does not lead to the observed results (A). An ionic process in which displacement occurs on the neopentyl oxygen of the hypochlorite does predict the proper stereochemistry (B). Previous work has indicated that this kind of displacement does not occur[3,6] and the results obtained with **4** certainly do not support it. There is no reason for supposing that **4** would not also react by a stereospecific process if this kind of mechanism was being followed. In fact if both **4** and **5** react with neopentyl hypochlorite by the same mechanism then it must be able to accommodate a stereospecific and a nonstereospecific product-forming sequence. Formation of a pentasubstituted intermediate can provide such a sequence provided that **5** forms the most thermodynamically stable intermediate directly and **4** forms a less stable intermediate which pseudorotates into the intermediate from **5** with competition from an ionization process which is irreversible.[11] These concepts can be illustrated as shown above.

The proposed mechanism suggests that the chlorine and neopentyloxy group enter into axial and equatorial positions of a trigonal bipyramid; a reversal of positions is just as satisfactory. If **5** forms the most thermodynamically stable pentasubstituted intermediate then ionization and attack by chloride ion on the methyl group will yield the phosphate **6**. The intermediate pentasubstituted phosphorus compound from **5** can probably undergo pseudorotation; however, if the equilibrium constant favors the particular structure no consequence of pseudorotation will be observed. The

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(1968); (b) D. W. White, G. K. McEwen, and J. G. Verkade, *Tetrahedron Lett.*, 5369 (1968).

[11] F. H. Westheimer, *Accounts Chem. Res.*, **1**, 70 (1968), and references therein.

reaction of **4** with neopentyl hypochlorite may form a less stable pentasubstituted intermediate than that from **5**. If this is the case then ionization and displacement by chloride ion will yield **7**. If pseudorotation occurs a more stable intermediate can be formed and this could lead to **6**. This kind of a scheme explains the change in product ratio with a change in temperature.

An alternate mechanism in which the chlorine and neopentyloxy groups enter axial positions does not seem possible. There is no *a priori* reason why the chlorine and neopentyloxy groups could not enter two equatorial positions. If this occurred then either phosphite could in principle give the same pentasubstituted intermediates. It would be strange indeed if this did not occur; however one cannot rule out such a reaction path on the basis of the available evidence. The data support the concept that these reactions occur in nonhydroxylic solvents by the formation of a pentasubstituted intermediate which ionizes to give the tetraalkoxyphosphonium salt.

Trineopentyl phosphite and neopentyl hypochlorite reacted to give tetraneopentyloxyphosphonium chloride as was reported before.[4] The ^{31}P chemical shift of this salt was found to be +2.1 ppm relative to 85% phosphoric acid. The sign and magnitude of the chemical shift do not agree with that found for tetramethoxyphosphonium hexachloroantimonate[7] but does agree with those found for the fluoroborates.[8a,c] It seems likely that tetramethoxyphosphonium hexachloroantimonate was actually prepared by Cohen. The ^{1}H nmr spectra reported for it and tetramethoxyphosphonium fluoroborate are identical.[12] The absorption at −51.1 ppm reported by Cohen may be due to an impurity and the absorption due to the tetramethoxyphosphonium hexachloroantimonate may have been obscured by the external reference. Tetraneopentyloxyphosphonium fluoroborate could be prepared by adding silver fluoroborate to a solution of tetraneopentyloxyphosphonium chloride at −78°. Attempts to detect tetraneopentyloxychlorophosphorane by ^{31}P nmr at −30° on various reaction mixtures showed that only the salt was present.

Reaction of trimethyl phosphite and neopentyl hypochlorite at −78° gave methyl chloride and dimethyl neopentyl phosphate as the major products when the reaction mixture was allowed to warm to room temperature. It had been reported[4] that some neopentyl chloride was formed from this reaction; this result could not be duplicated. When trimethyl phosphite was added to a solution of neopentyl hypochlorite and silver fluoroborate at −78°, the salt trimethoxyneopentyloxyphosphonium fluoroborate could be isolated in *ca.* 50% yield.

Experimental Section

Proton nmr spectra were recorded on a Varian A-60 spectrometer. Chemical shifts are reported in ppm relative to tetramethylsilane as an internal standard. Phosphorus spectra were recorded on a Varian HA-100 operating at 40.5 MHz and are reported in ppm relative to 85% phosphoric acid.

Preparation of 8. Neopentyl alcohol, 5.9 g (0.067 mol), and 10.0 g (0.067 mol) of N,N-diethylaniline in 150 ml of ether were cooled with stirring to 4°. Freshly distilled 2-chloro-4-methyl-1,3-dioxaphosphorinan, 10.4 g (0.067 mol), was added slowly. After stirring for 20 hr the reaction mixture was filtered under nitrogen. The solid residue was washed with three 50-ml portions of ether. The combined ether solutions were evaporated to give 13.2 g of an oil which was distilled to give 8.5 g of material, bp 71–72° (2.3 mm). Glpc analysis showed two components in the relative ratio of 95:5. Other impurities were also present. The ^{1}H nmr spectrum had a singlet at 0.92 and a doublet at 1.17 (J = 6.5 Hz). These absorptions are assigned to the methyls of the neopentyl group and the ring methyl. Another doublet at 3.42 (J = 7 Hz) is assigned to the neopentyl methylene; multiplets at 1.3–2.2 and 3.6–4.7 were also present. The ring methyl absorption is essentially the same, 1.17 *vs.* 1.18, as that found for **4**.

Preparation of 9. The preparation of **9** was accomplished by adding 5.0 g (0.032 mol) of 2-chloro-4-methyl-1,3-dioxaphosphorinan to a mixture of 2.85 g (0.032 mol) of neopentyl alcohol and 3.27 g (0.032 mol) of triethylamine in 12 ml of carbon tetrachloride at 0°. The solution was stirred for 24 hr, filtered, and evaporated. The residue had a singlet at 0.98, neopentyl methyls, a doublet at 1.40 (J = 6.5 Hz), ring methyl, a doublet at 3.45 (J = 7 Hz), neopentyl methylene, and absorptions due to ring protons. The 1.40 shift observed for the ring methyl is in close agreement with the 1.35 found for **5**.

Oxidation of 8. A solution of **8**, 3.0 g (0.015 mol), in 35 ml of benzene was added to a chilled stirred suspension of 6.3 g (0.029 mol) of yellow mercuric oxide in 100 ml of dry benzene. The mixture was stirred for 24 hr, filtered, and evaporated to give 3.3 g of solid. Glpc showed two components in the ratio 95:5. The material was recrystallized from petroleum ether (bp 60–90°; 30–60°) to give 1.3 g (39%) of **6**, mp 91–93°. The ^{1}H nmr spectrum showed an absorption at 0.98, neopentyl methyls, doublet at 3.72 (J = 5 Hz), neopentyl methylenes, a doublet of doublets at 1.36 (J_{HH} = 6 Hz; J_{HP} = 2.5 Hz), and two multiplets at 1.6–2.2 and 4.0–4.9. Integration gave values in agreement with the assignments. The ^{31}P chemical shifts was +7.8.

Anal. Calcd for $C_9H_{19}O_4P$: C, 48.64; H, 8.62. Found: C, 48.42; H, 8.40.

Oxidation of trisubstituted phosphorus compounds with mercuric oxide need not be stereospecific and thus **8** was oxidized with *t*-butyl hydroperoxide which undoubtedly oxidizes with retention of configuration.[6] The same isomer as was obtained above was the major product as evidenced by glpc.

Oxidation of 9. To a chilled solution of 2.0 g (0.01 mol) of **9** in 10 ml of carbon tetrachloride was added a solution of dinitrogen tetroxide in carbon tetrachloride until a permanent green color was obtained. The solvent was removed to give an oil. The ^{1}H nmr spectrum was very similar to that of **6**; however, the ^{31}P chemical shift was +5.2. Glpc analysis showed the same two components as was found from the oxidation of **8**. The major component in this reaction mixture was the minor component in the reaction mixture from **8** and the ratio was 87:13. Addition of **6** augmented the minor component peak.

Reactions of 4 and 5 with Neopentyl Hypochlorite. In a typical experiment, 0.968 g (0.065 mol) of **4** in 10 ml of methylene chloride at −78°, protected from moisture, was treated with an equivalent amount of neopentyl hypochlorite in methylene chloride.[13] The temperature was maintained within the specified limits. The reaction mixture was evaporated *in vacuo* and the residue was analyzed by glpc. The phosphates **6** and **7** comprised *ca.* 80% of the reaction mixture. The individual identities were determined by augmentation with authentic samples. In different experiments the assignments were further examined by ^{1}H and ^{31}P nmr spectral analysis.

Reaction of Neopentyl Hypochlorite and Trineopentyl Phosphite. The reaction gave tetraneopentyloxyphosphonium chloride according to the procedure of Relles.[4,14] The ^{31}P chemical shift was found to be +2.1. As the salt decomposed a new absorption for trineopentyl phosphate appeared at +1.1. The ^{1}H nmr spectrum agreed with that reported earlier.

When silver fluoroborate in 1,2-dichloroethane was added to a reaction mixture from 0.933 g (0.0032 mol) of trineopentyl phosphite and 10.0 ml of 0.32 M neopentyl hypochlorite in methylene chloride at −78° an immediate precipitate of silver chloride formed. The reaction mixture was allowed to warm to room temperature and filtered and the solvent was evaporated to give a solid which was washed 3 times with dry ether and dried *in vacuo*. The salt, 0.9 g (60%), showed in the ^{1}H nmr in methylene chloride a singlet at 1.07, area

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[12] J. Finley, D. Z. Denney, and D. B. Denney, *J. Amer. Chem. Soc.*, **91**, 5826 (1969).

[13] Neopentyl hypochlorite was prepared using the general procedure of E. L. Jenner, *J. Org. Chem.*, **27**, 1032 (1962).

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9, and a doublet at 4.26 (J_{HP} = 4.9 Hz), area 2. Small amounts of impurities were also present. Hydrolysis yielded trineopentyl phosphate and neopentyl alcohol as evidenced by ^{1}H and ^{31}P nmr.

Reaction of Neopentyl Hypochlorite and Trimethyl Phosphite. In a typical experiment, trimethyl phosphite, 0.3117 g (0.0025 mol), was treated at −78° with 68 ml of 0.37 *M* neopentyl hypochlorite solution. The nmr spectrum of the reaction mixture on 100-Hz sweep width indicated neopentyl chloride was not present. When neopentyl chloride was added it could be detected. Other products were those reported before.[4,13]

In another experiment the phosphite, 0.9 g (0.0072 mol), in 5 ml of 1,2-dichloroethane and 10 ml of methylene chloride was added dropwise to a solution of 1.4 g (0.007 mol) of silver fluoroborate and 10 ml of 0.72 *M* neopentyl hypochlorite in 18 ml of 1,2-dichloroethane and 20 ml of methylene chloride maintained between −63 and −70°. The reaction mixture was allowed to warm to room temperature and filtered and the solvent was evaporated to give 1.6 g of oil. The ^{1}H nmr spectrum in methylene chloride showed a singlet at 1.02, doublet at 4.23 (J_{PH} = 11.5 Hz), and doublet at 4.25 (J_{PH} = 5.5 Hz). These absorptions are assigned to the neopentyl methyls, the methoxy methyls, and the neopentyl methylene, respectively. The salt was not too stable and after 6 days in a refrigerator a new singlet at 0.98 and a doublet at 3.95 (J_{PH} = 11.5 Hz) were noted. These absorptions are probably due to the boron trifluoride complex of dimethyl neopentyl phosphate.

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The Determination of the Stereochemical Stability of Organotin Compounds by Nuclear Magnetic Resonance

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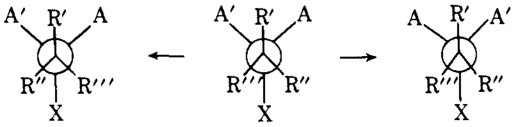
Abstract: The diastereotopic methyl protons in methylneophylphenyltin chloride (**1**) are observably anisochronous in dilute solution in nonpolar solvents. Coalescence of the signals can be produced at a given temperature by addition of a ligand such as DMSO-d_6 or by using a polar solvent such as methylene chloride. The higher the concentration of **1** the lower the temperature required to produce coalescence. Coalescence results from rapid exchange of the diastereotopic nucleii and the observation of a time-averaged signal. The most reasonable mechanism for exchange involves pseudorotation with inversion of configuration at tin. The diastereotopic methyl protons of dimethylphenyl(2-phenylpropyl)tin (**2**) are anisochronous at least up to 222° neat and 160° in the presence of DMSO-d_6–dioxane 1:2. The minimum mean lifetime, at room temperature, for an asymmetric organotin center with four carbon to tin bonds should be greater than 100 days.

In 1900 Pope and Peachey reported the resolution of ethylmethylpropyltin iodide.[1] However subsequent attempts to reproduce this resolution have been unsuccessful.[2,3] In 1928 Kipping attempted unsuccessfully to resolve a number of asymmetric organotin compounds.[4] The recent preparation of optically active, functionally substituted, organosilicon[5] and organogermanium compounds[6] has lead to a resurgence of interest in the resolution of organotin compounds.[3,7] The present study was undertaken to determine if an asymmetric organotin center had sufficient stereochemical stability to allow resolution and to be of use in determining the stereochemistry of substitution at tin.

The method employed was based upon the chemical-shift nonequivalence of diastereotopic nucleii.[8] From the Newman projection formulae of R′R″R‴MM′-A_2X it is obvious that inversion of configuration at either M or M′ will lead to an exchange in the magnetic environment of the two diastereotopic A groups. In the absence of exchange A and A′ will be anisochronous. The magnitude of the chemical shift nonequivalence ($\Delta AA'$) will depend upon the extent of the difference between the magnetic environment of the two sites. The two sites may be sufficiently similar so that the spectrometer cannot resolve the difference between the two signals. In benzylmethylphenylsilane and in α-bromobenzyldimethylchloromethylsilane diastereotopic nucleii which were unresolved at 60 MHz were resolved at 100 MHz, while in methylneophylphenyltin hydride the diastereotopic nucleii are unresolved even at 100 MHz.[9] Alternatively, the failure to observe chemical-shift nonequivalence may be due to rapid exchange between the two sites with the resultant observation of a time-averaged signal.[8]



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