Synthesis of Mononitro-, Monoamino- and Monohalo-p-terphenyls, and their Solubility and Specific Gravity

By Tadashi NOZAKI and Yûhei HARADA

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Many physical properties of monosubstituted *p*-terphenyls should vary greatly according to the variety in the nature and the position of the substituent. This is because, since *p*-terphenyl (in general, a para-polyphenyl) is a long planar molecule having many π-electrons, the change in its energy levels caused by a substituent should usually be large, with the mode and degree of the change depending more strongly on the nature and the position of the substituent than in the case of an aliphatic or a condensed aromatic compound. Therefore, various kinds of isomeric monosubstituted *p*-terphenyls seem to be an interesting example regarding the influence of a substituent on physical properties of organic compounds. Studies on their synthesis and physical properties would also be useful for further development in the basic study of organic scintillator and organic semiconductor.

Various synthetic methods for mononitro-, monoamino-, monochloro-, monobromo- and monoiodo-*p*-terphenyls were examined and compared with one another, and suitable methods of preparation are presented in this paper. All isomers of these compounds, including several new compounds, were synthesized and purified. Their solubility and specific gravity were measured, and other physical properties including absorption spectra are now under measurement.

Synthesis.—Ames reviewed the synthesis of substituted terphenyls in 1958[1]. We reported a suitable condition for the mononitration of *p*-terphenyl[2]. In general, the following processes seem to be available for the synthesis of the compounds in question: (1) direct nitration or halogenation of *p*-terphenyl, (2) reaction of 4-(*N*-nitrosoacetamido)-biphenyl (abbreviated as NAB) or *p*-phenylbenzenediazonium oxide (abbreviated as PBDO) with nitrobenzene or halobenzene, (3) reaction of monosubstituted NAB or monosubstituted PBDO with benzene, (4) conversion of another monosubstituted *p*-terphenyl into the desired compound, (5) dehydrogenation of monosubstituted 4-cyclohexylbiphenyl, (6) reaction of monosubstituted *N*-nitrosoacetanilide with biphenyl. The process 1, 2 and in some cases 4 offer a mixture of isomeric monosubstituted *p*-terphenyls. For the separation, column chromatography followed by recrystallization is usually suitable.

The mono-nitration of *p*-terphenyl[2] gave a mixture of 2-nitro-*p*-terphenyl (15∼25%), 4-nitro-*p*-terphenyl (ca. 60%) and 2′-nitro-*p*-terphenyl (15∼20%). This reaction is suitable for preparing 4-nitro-*p*-terphenyl, since it is easily separated from the mixture owing to its low solubility. But, separation of other two isomers required very tedious processes because of their marked similarity in many physical properties. Earlier workers obtained[3] 2-nitro-*p*-terphenyl and 4-nitro-*p*-terphenyl by treating NAB with nitrobenzene and separating the product by fractional recrystallization. According to our experimental result, PBDO could be used in place of NAB to give almost the same yield of the product, and PBDO was prepared much more easily than NAB. Further, 3-nitro-*p*-terphenyl, a new compound, was obtained by column-chromatographic separation of the reaction products, though the yield was poor. 3-nitro-*p*-terphenyl was more conveniently prepared by deacetamidating a nitration product of 4-acetamido-*p*-terphenyl (overall yield, 40% based on 4-amino-*p*-terphenyl). 2′-Nitro-*p*-terphenyl had been obtained by dehydrogenating 3-nitro-4-cyclohexylbiphenyl[4]. This compound was synthesized more conveniently, contrary to the description in a literature[3], by the reaction of nitrosated 3-nitro-4-acetamidobiphenyl with benzene. Although pure 3-nitro-NAB was not obtained, the yield of purified 2′-nitro-*p*-terphenyl was satisfactory (30∼40% based on 3-nitro-4-acetamidobiphenyl).

Nitro-*p*-terphenyl was reduced to amine hydrochloride with tin(II) chloride almost quantitatively, and iodo-*p*-terphenyl was obtained by the Sandmeyer reaction of the diazotized amine with a good yield (50∼60%). The

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[1] R. G. Ames, *Chem. Revs.*, **58**, 895 (1958).

[2] T. Nozaki et al., This Bulletin, **33**, 1331 (1960).

[3] H. France et al., *J. Chem. Soc.*, **1938**, 1368.

[4] F. R. Basford, ibid., **1937**, 1442.

yield of chloro- and bromo-*p*-terphenyls except 4-chloro- and 4-bromo-*p*-terphenyls by this method, however, was poor. Several new compounds, i. e. 2′-chloro-, 2′-bromo-, 2-, 3- and 2′-iodo-*p*-terphenyls, were thus obtained.

The earlier workers[3] also prepared 2-, 3-, 4-chloro-, 2-, 3- and 4-bromo-*p*-terphenyls by similar processes as they used for preparing 2- and 4-nitro-*p*-terphenyls. In these cases, too, PBDO was found to be used preferably to NAB. Separation of isomeric halo-*p*-terphenyls was more tedious than in the case of the nitro-compounds, requiring repeated chromatographic separation and recrystallization. Hence, for preparing a definite quantity of 2- and 3-chloro (or 2- and 3-bromo), it is preferable to separate a part of 2- and 3-chloro (or 2- and 3-bromo) in pure state from a larger quantity of the mixture. Some of the compounds have considerably higher melting points than the values in the literature[5]. The reaction of PBDO or NAB with iodobenzene, however, gave only traces of iodo-*p*-terphenyls with a much larger quantity of 4-iodobiphenyl.

3-Chloro-4-acetamidobiphenyl had been prepared[6] by chlorinating 4-acetamidobiphenyl with sodium hypochlorite and treating the product with hot acetic acid. Crude 3-bromo-4-acetamidobiphenyl had also been prepared[7] by treating 4-acetamido-biphenyl with bromine in acetic acid and removing less soluble by-products. The two halo-acetamidobiphenyls were nitrosated and converted into 2′- (30∼40% yield based on 4-acetamidobiphenyl) and crude 2′-bromo compounds, the latter being purified chromatographically. These processes compare favorably with the syntheses from 2′-nitro-*p*-terphenyl.

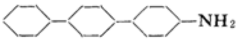
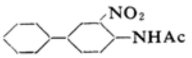
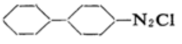
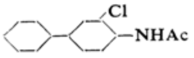
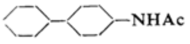
Direct bromination and iodination of *p*-terphenyl under a suitable condition offer 4- and 4-iodo respectively, but the products are contaminated by 4, 4″-dihalo-*p*-terphenyl, which is removed with great difficulty on recrystallization and vacuum sublimation. Column-chromatographic separation with the aid of the absorption technique of a soft γ-ray, however, was very useful for obtaining a small quantity (less than a few grams) of 4-bromo or 4-iodo in pure state, as reported previously[8].

Efforts were made to obtain some kinds of monosubstituted *p*-terphenyl by the reaction of substituted *N*-nitrosoacetanilide with biphenyl in a suitable solvent. The yield of the desired compound, however, was always poor, and by-products were removed with great difficulty.

Suitable processes for preparing the monosubstituted *p*-terphenyls are listed in Table I, and melting points summarized in Table II.

Solubility and Specific Gravity.—Tables III and IV show the solubility, and Fig. 1 shows the relationship between the melting point and the solubility in *n*-hexane at 25°C. Both values are more strongly influenced by the position of the substituent than by its nature. Among 2-halo-*p*-terphenyls, the melting point becomes lower in the order of chloro- iodo-

TABLE I. SUITABLE PREPARATION METHODS FOR MONONITRO-, MONOAMINO- AND MONOHALO-*p*-TERPHENYLS

Substituent	Position			
	2	3	4	2′
NO_2	 $\xrightarrow{NaOH}\xrightarrow{C_6H_5NO_2}$ $\xrightarrow{Seprn.}$	 $\xrightarrow{Ac_2O}\xrightarrow{HNO_3}$ $\xrightarrow{EtOH,\ H_2SO_4,\ NaNO_2}$	 $\xrightarrow{HNO_3}\xrightarrow{Seprn.}$	 $\xrightarrow{N_2O_3}\xrightarrow{C_6H_6}$
NH_2	the reduction of the nitro-compound			
Cl	 $\xrightarrow{NaOH}\xrightarrow{C_6H_5Cl}\xrightarrow{Seprn.}$		the Sandmeyer reaction	 $\xrightarrow{N_2O_3}\xrightarrow{C_6H_6}$
Br	 $\xrightarrow{NaOH}\xrightarrow{C_6H_5Br}\xrightarrow{Seprn.}$		the Sandmeyer reaction	 $\xrightarrow{Br_2}\xrightarrow{N_2O_3}$ $\xrightarrow{C_6H_6}\xrightarrow{Seprn.}$
I	the Sandmeyer reaction			

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[5] H. France et al., ibid., **1938**, 1368.

[6] F. Bell et al., ibid., **1926**, 1246.

[7] J. Kenyon et al., ibid., **1926**, **3051**.

[8] T. Nozaki, This Bulletin, **35**, 1035 (1962).

Table II. Melting point of substituted *p*-terphenyls (°C)

Substituent	Position 2	3	4	2′
NO_2	129	176~177	213	131
NH_2	162~163	179	201	177
Cl	112~113	142	222	100~101
Br	87~ 88	151~152	234	98
I	101	155~156	247	99~100

p-Terphenyl 213°C

Table III. Solubility of substituted *p*-terphenyls in *n*-hexane at 25°C (g. in 100 ml. solution)

Substituent	Position 2	3	4	2′
NO_2	0.118	0.036	0.015	0.136
NH_2	0.121	0.028	0.019	0.076
Cl	1.59	0.35	0.096	2.19
Br	3.3	0.293	0.073	2.66
I	1.50	0.288	0.038	1.36

Table IV. Solubility of substituted *p*-terphenyls in various solvents at 25°C (g. in 100 ml. solution)

Solute	Solvent *n*-Hexane	Benzene	Ethanol
p-Terphenyl	0.084	1.20	0.056
2-Cl	1.59	27	1.16
3-Cl	0.36	6.5	0.199
4-Cl	0.096	1.74	0.084
2′-Cl	2.19	28	1.18
4-NO_2	0.015	0.75	0.035
4-NH_2	0.018	1.00	0.31
4-Br	0.073	1.34	0.047
4- I	0.038	0.67	0.028

In ethyl acetate: *p*-Terphenyl, 0.500, 4-Cl, 0.719

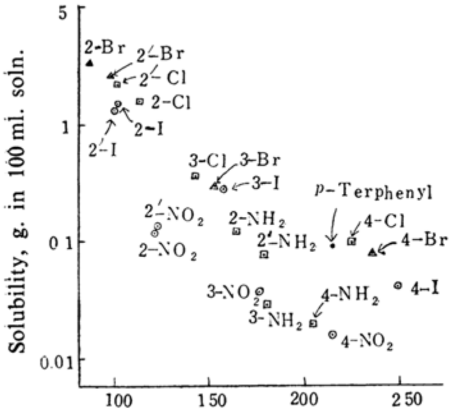

Fig. 1. Relationship between the melting point and the solubility in *n*-hexane at 25°C.

and bromo-*p*-terphenyl. The same order is seen for 2′-halo-*p*-terphenyls, though the differences are small. For 3- or 4-halo-*p*-terphenyls, on the other hand, the order is iodo-, bromo- and chloro-*p*-terphenyl. The 2- and 2′-halo-*p*-terphenyls are apt to form supersaturate solutions. Table V indicates the specific gravity at 25°C. It is, of course, quite sensitive to the nature of the substituent. The influence of the position of the substituent, on the other hand, is less clear and less systematic on the specific gravity than on the melting point and the solubility.

Table V. Specific gravity at 25°C

Substituent	Position 2	3	4	2′
NO_2	1.293	1.296	1.321	1.283
NH_2	1.205	1.225	1.236	1.215
Cl	1.226	1.264	1.271	1.234
Br	1.437	1.439	1.466	1.425
I	1.634	1.596	1.635	1.582

p-Terphenyl 1.236

Figure 2 shows the dependence of the solubility on the temperature. The heat of solution is calculated by the use of the Clapeyron's equation (Eq. 1) with the assumption (Eq. 2):

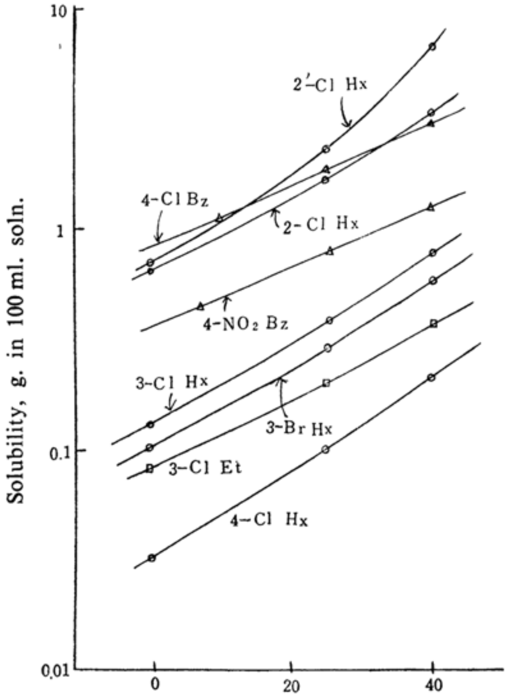

Fig. 2. Temperature dependence of the solubility.

$$\frac{\mathrm{d}P}{\mathrm{d}T}=\frac{\Delta H}{T(V_{\mathrm{L}}-V_{\mathrm{S}})} \qquad (1)$$

$$P=kC,\ V_{\mathrm{L}}\gg V_{\mathrm{S}},\ kCV=\boldsymbol{R}T \qquad (2)$$

where ΔH is the molar heat of the solution, V_{L} the molar dilution, V_{S} the molar volume of solid solute, C the concentration and k a coefficient independent of temperature.

Since

$$\Delta H=\frac{\boldsymbol{R}T^2}{C}\cdot\frac{\mathrm{d}C}{\mathrm{d}T} \qquad (3)$$

and $\mathrm{d}C/\mathrm{d}T$ is known from Fig. 2, ΔH can be calculated. The result is shown in Table VI.

TABLE VI. PARTIAL MOLAR HEAT AND ENTROPY OF SOLUTION AT 25°C FOR THE SATURATION CONCENTRATION (kcal./mol.)

Solute	Solvent	ΔH	TS_{m}	ΔH-TS_{m}
2-Cl	Hx	4.0	2.9	1.1
3-Cl	Hx	4.1	3.8	0.4
4-Cl	Hx	4.1	4.5	−0.4
2′-Cl	Hx	5.1	2.7	2.4
3-Cl	Et	3.5	4.6	−1.1
4-Cl	Bz	3.3	3.0	0.3
3-Br	Hx	3.9	4.0	−0.1
4-NO_2	Bz	3.0	3.6	−0.5

Hx: *n*-Hexane; Et: Ethanol; Bz: Benzene
ΔH: Partial molar heat of solution
S_{m}: Entropy of mixing for perfect gases (cratic quantity)
T: Absolute temperature

Since this ΔH is the partial molar heat of solution at the saturation concentration, the value with the opposite sign is the product of partial molar entropy of solution and the temperature. The partial molar entropy of solution for a dilute solution consists of two terms[9]: (1) a term depending only on the concentration (cratic term or entropy of mixing of perfect gases), (2) terms independent of concentration (unitary quantity). The term 1, S_{m}, is expressed by

$$S_{\mathrm{m}}=-\boldsymbol{R}\ln\{x/(1-x)\} \qquad (4)$$

where x is the molar fraction of the solute to the solution. Table VI also shows the value of TS_{m} and that of $H-TS_{\mathrm{m}}$. The term 2, on the other hand, is dependendent on the various quantities: the degree of symmetry and flexibility of the solute molecule, the shape and size of the solute and of the solvent molecule, the translation and rotation of the solute molecule in solution, the lattice vibration of the solute substance in a solid state and the intramolecular motion of the solute substance both in solution and in solid state. A higher degree of symmetry of 4-substituted compounds is one reason for low solubility. Since the translational and the rotational entropy should not differ largely from compound to compound in question, the difference in the term $H-TS_{\mathrm{m}}$ in Table VI should be due mainly to the degree of flexibility and to a different mode of intramolecular motions. These two are intercorelated.

Studies on absorption spectra, specific heat, X-ray crystallography etc. are necessary for quantitative treatment of such phenomena.

Experimental

Preparation of Nitro-, Chloro- and Bromo-*p*-terphenyls by the Reaction of PBDO with Nitrobenzene, Chlorobenzene and Bromobenzene.—The procedure for the synthesis of 4-bromobiphenyl described in the "Organic Syntheses"[10] was successfully applied to the synthesis of the present compounds with a slight modification: 4-aminobiphenyl was diazotized in a mortar under grinding with a pestle at 8~10°C with occasional addition of ice. When the reaction of PBDO with nitrobenzene, chlorobenzene or bromobenzene was completed, the remaining monosubstituted benzene was removed by distillation. The residue was distilled under reduced pressure, and the distillate subjected to column-chromatographic separation, the solvent and eluant being benzene for nitro-compounds or a mixture of petroleum benzine (b. p., 70~90°C) and benzene for halo-compounds (the molar fraction of benzene being increased with progress of elution). Complete separation was not attained, but the following three fractions were obtained: (1) pure 2-nitro (or 2-chloro or 2-bromo), (2) 3-nitro (or 3-chloro or 3-bromo) containing 2-nitro (or 2-chloro or 2-bromo), (3) 4-nitro (or 4-chloro or 4-bromo) containing the other two isomers. From fractions 2 and 3, 3-nitro (3-chloro or 3-bromo) and 4-nitro (4-chloro or 4-bromo)-*p*-terphenyls were obtained respectively by recrystallization from a mixture of ethanol and ethyl acetate. The compounds in the mother-liquor of the recrystallization were separated by repeating column chromatography and recrystallization. From each 21 g. portion of 4-aminobiphenyl the following products were obtained: 2-nitro, 3.7 g.; 3-nitro, 1.3 g. and 4-nitro, 5.2 g.; 2-chloro, 5 g.; 3-chloro, 2.5 g. and 4-chloro, 4.5 g; 2-bromo, 4 g.; 3-bromo, 2.5 g. and 4-bromo, 5 g.

3-Nitro-*p*-terphenyl was identified as follows: (1) analysis (Found: C, 78.70; H, 4.72; N, 5.00. Calcd. for $C_{18}H_{13}NO_2$: C, 78.53; H, 4.76; N, 5.09%); (2) it gave an amine on reduction, which was converted into 3-chloro by the Sandmeyer reaction.

Synthesis of 3-Nitro from 4-Nitro-*p*-terphenyl.—4-Nitro was reduced to 4-amino (see below). To a warm solution of 4-amino (5 g.) in acetic acid (250 ml.) was added acetic anhydride (30 ml.) to give a fine suspension. This was treated with nitric acid (d=1.38, 20 ml.), gradually warmed to

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[9] e. g. R. W. Gurney, "Ionic Processes in Solution", Chapter 5, McGraw-Hill, New York (1953)

[10] R. Adams, "Organic Syntheses", Vol. 8 (1928), p. 42.

60°C and poured into water. The precipitate was filtered off, boiled in a mixture of ethanol (300 ml.) and sulfuric acid (200 ml.) for 1 hr. Sodium nitrite (20 g.) was added in small portions to the hot mixture, which was then diluted with water. The precipitate was filtered off, distilled in vacuo and purified by column-chromatography. Pure 3-nitro compound (2.3 g.) was obtained in pale yellow plates (from a mixture of ethanol and ethyl acetate).

Synthesis of 2′-Nitro-*p*-terphenyl from 3-Nitro-4-acetamidophenyl. — 3-Nitro-4-acetamidobiphenyl (30 g.) in a mixture of acetic acid (700 ml.) and acetic anhydride (300 ml.) was nitrosated at 10∼15°C by passing nitrous fumes for 4 hr. and adding simultaneously solid sodium nitrite (10 g.). When the green solution was poured into water with stirring, an orange oil separated, which gradually solidified into a hard yellow mass. This material contained slightly less nitrogen than the theoretical value for 3-nitro-NAB. The solid was dried, dissolved in dry benzene (1.5 l.), warmed with care and eventually refluxed for 5 hr. until the evolution of nitrogen ceased. After benzene was removed from the solution, the residue was under reduced pressure, and the distillate subjected to column-chromatography. 2′-Nitro-*p*-terphenyl (12 g.) was obtained as almost colorless plates (from ethanol). A considerable quantity of 3-nitro-4-acetamidobiphenyl was recovered.

Reduction of Nitro-*p*-terphenyls.—Hot solution of 2-nitro, 3-nitro or 2′-nitro compound (3 g.) in ethanol (30 ml.) or in a mixture of ethanol and ethyl acetate was added to a warm solution of tin(II) chloride ($SnCl_2 \cdot 2H_2O$ 15 g.) in hydrochloric acid (11 N, 20 ml.), and boiled for 20 min. On cooling, the amino-*p*-terphenyl hydrochloride precipitated as colorless small crystals in a nearly quantitiative yield. In some cases, the precipitate contained some tin salt, which, however, was easily removed by treatment with dilute hydrochloric acid. Free amine (2-, 3- or 2′-amino compound) was obtained by treating the amine hydrochloride with an aqueous solution of sodium hydroxide. For the reduction of 4-nitro-*p*-terphenyl other solvents were preferably used[2] owing to its low solubility in ethanol, and 4-amino-*p*-terphenyl was obtained by treating the hydrochloride with hot solution of sodium ethylate in a mixture of ethanol and toluene.

The Sandmeyer Reaction.—The amine hydrochloride (2 g.) was dissolved in a mixture of acetic (70 ml.) and sulfuric acid (30 ml.) or suspended in water, diazotized at 5∼10°C and converted into the iodo-*p*-terphenyl with 40∼60% yield. 2′-Chloro and 2′-bromo were also prepared by the Sandmeyer reaction, but the yield was lower. On the other hand, 4-chloro and 4-bromo were synthesized with 40∼60% yield. 2-Iodo: colorless needles from ethanol (Found: C, 60.61; H, 3.80; I, 35.79. Calcd. for $C_{18}H_{13}I$: C, 60.69; H, 3.68; I, 35.63%). 3-Iodo; colorless plates from ethanol (Found: C, 60.54; H, 3.51; I, 35.45%. Calcd.: the same with 2-iodo). 2′-Iodo: colorless plates from ethanol (Found: C, 60.62; H, 3.91; I, 35.76%. Calcd: the same with 2-iodo). 2′-Chloro: colorless needles or plates from ethanol (Found: C, 81.80; H, 5.13; Cl, 13.46. Calcd. for $C_{18}H_{13}Cl$: C, 81.65; H, 4.95; Cl, 13.39%). 2′-Bromo: colorless plates from ethanol (Found: C, 69.84; H, 4.38; Br, 26.06. Calcd. for $C_{18}H_{13}Br$: C, 69.92; H, 4.24; Br, 25.84%).

Synthesis of 2′-Chloro-*p*-terphenyl from 3-Chloro-4-acetamidobiphenyl.—3-Chloro-4-acetamidobiphenyl (20 g.) dissolved in a mixture of acetic acid (150 ml.) and acetic anhydride (50 ml.) was nitrosated by passing nitrous fumes for 2 hr. at 10∼15°C. Stirring the solution into ice water resulted in formation of a milky suspension, from which yellowish hydrophobic powder gradually precipitated. The precipitate was dried and allowed to react with benzene (300 ml.) at 35°C overnight. After benzene was removed from the solution, the residue was distilled under reduced pressure, and the distillate recrystallized from ethanol to give 2′-chloro compound (9 g.).

Preparation of 2′-Bromo-*p*-terphenyl from 4-Acetamidobiphenyl.—4-Acetamidobiphenyl (20 g.) in acetic acid (200 ml.) was treated with bromine (30 g.) at 30∼35°C and poured into water. The separated solid was digested with a mixture of ethanol (100 ml.) and water (100 ml.), the insoluble solid removed, and the solution poured into a large quantity of water. From the precipitate (10 g.), 2′-bromo compound (3 g.) was obtained by a similar process to that for 2′-chloro followed by column-chromatographic separation.

Measurement of the Physical Constants.—Melting point was measured in a capillary tube dipped in a sulfuric acid bath, and the value was corrected with reference to several standard substances. The solubility in a given solvent was measured by weighing the solid that was obtained by drying up a definite volume of the saturated solution. For the measurement of the specific gravity, a small crystal of the compound was prepared using a Bridgeman-type furnace. A portion of the crystal was immersed in water, to which a concentrated aqueous solution of a heavy metal salt was added until the specific gravity of the liquid became equal to that of the crystal.

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The Electrical Communication Laboratory
Musashino, Tokyo