# The Marvellous Properties of Thiotimoline

# Isaac Asimov

## PART I

The correlation of the structure of organic molecules with their various properties, physical and chemical, has in recent years afforded much insight into the mechanism of organic reactions, notably in the theories of resonance and mesomerism. The solubilities of organic compounds in various solvents has become of particular interest in this connection through the recent discovery of the endochronic nature of thiotimoline.[{2}](#a76)

It has been long known that the solubility of organic compounds in polar solvents such as water is enhanced by the presence upon the hydrocarbon nucleus of hydrophilic—i.e. water-loving—groups, such as the hydroxy (-OH), amino (-NH2), or sulfonic acid (-SO3H) groups. Where the physical characteristics of two given compounds—particularly the degree of subdivision of the material—are equal, then the time of solution—expressed in seconds per gram of material per milliliter of solvent—decreases with the number of hydrophilic groups present. Catechol, for instance, with two hydroxy groups on the benzene nucleus dissolves considerably more quickly than does phenol with only one hydroxy group on the nucleus. Feinschreiber and Hravlek[{3}](#a78) in their studies on the problem have contended that with increasing hydrophilism, the time of solution approaches zero. That this analysis is not entirely correct was shown when it was discovered that the compound thiotimoline will dissolve in water—in the proportions of 1 gm./ml.—in minus 1.12 seconds. That is, it will dissolve before the water is added.

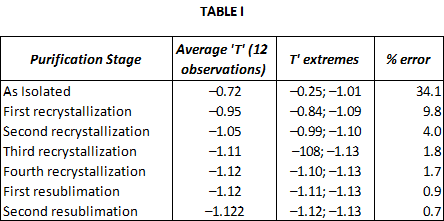
Previous communications from these laboratories indicated thiotimoline to contain at least fourteen hydroxy groups, two amino groups and one sulfonic acid group.[{4}](#a80) The presence of a nitro group (-NO2) in addition has not yet been confirmed and no evidence as yet exists as to the nature of the hydrocarbon nucleus, though an at least partly aromatic structure seems certain.

The Endochronometer—First attempts to measure the time of solution of thiotimoline quantitatively met with considerable difficulty because of the very negative nature of the value. The fact that the chemical dissolved prior to the addition of the water made the attempt natural to withdraw the water after solution and before addition. This, fortunately for the law of Conservation of Mass-Energy, never succeeded since solution never took place unless the water was eventually added. The question is, of course, instantly raised as to how the thiotimoline can ‘know’ in advance whether the water will ultimately be added or not. Though this is not properly within our province as physical chemists, much recent material has been published within the last year upon the psychological and philosophical problems thereby posed.[{5}](#a82) [{6}](#a84)

Nevertheless, the chemical difficulties involved rest in the fact that the time of solution varies enormously with the exact mental state of the experimenter. A period of even slight hesitation in adding the water reduces the negative time of solution, not infrequently wiping it out below the limits of detection. To avoid this, a mechanical device has been constructed, the essential design of which has already been reported in a previous communication.[{7}](#a86) This device, termed the endochronometer, consists of a cell 2 cubic centimeters in size into which a desired weight of thiotimoline is placed, making certain that a small hollow extension at the bottom of the solution cell—1 millimeter in internal diameter—is filled. To the cell is attached an automatic pressure micro-pipette containing a specific volume of the solvent concerned. Five seconds after the circuit is closed, this solvent is automatically delivered into the cell containing the thiotimoline. During the time of action, a ray of light is focused upon the small cell-extension described above, and at the instant of solution, the transmission of this light will no longer be impeded by the presence of solid thiotimoline. Both the instant of solution—at which time the transmission of light is recorded by a photoelectric device—and the instant of solvent addition can be determined with an accuracy of better than 0.01 per cent. If the first value is subtracted from the second, the time of solution (T) can be determined.

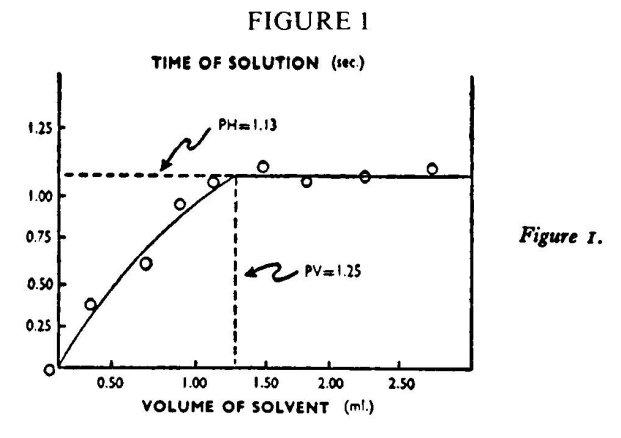
The entire process is conducted in a thermostat maintained at 25.00° C.—to an accuracy of 0.01° C.

Thiotimoline Purity—The extreme sensitivity of this method highlights the deviations resulting from trifling impurities present in thiotimoline. (Since no method of laboratory synthesis of the substance has been devised, it may be practically obtained only through tedious isolation from its natural source, the bark of the shrub Rosacea Karlsbadensis rufo.[{8}](#a88)) Great efforts were therefore made to purify the material through repeated recrystallizations from conductivity water—twice redistilled in an all-tin apparatus—and through final sublimations. A comparison of the solution times (T) at various stages of the purification process is shown in Table I.



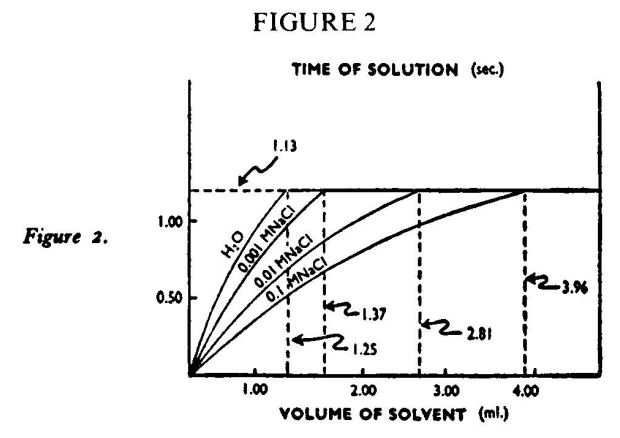
It is obvious from Table I that for truly quantitative significance, thiotimoline purified as described must be used. After the second resublimation, for instance, the error involved in an even dozen determinations is less than 0.7 per cent with the extreme values being -1.119 seconds and -1.126 seconds.

In all experiments described subsequently in this study, thiotimoline so purified has been used.

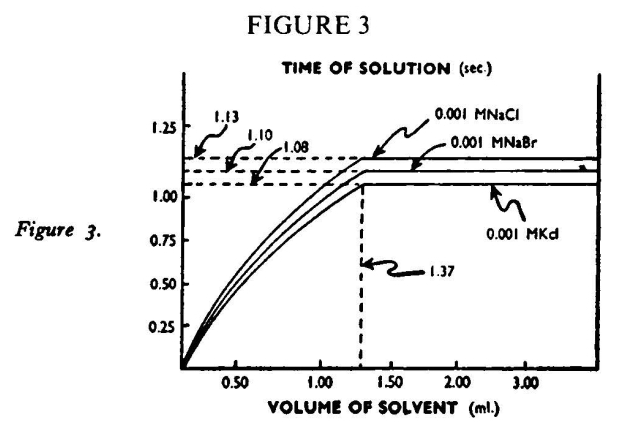


Time of Solution and Volume of Solvent—As would seem reasonable, experiments have shown that increasing the volume of solvent enables the thiotimoline to dissolve more quickly—i.e. with an increasingly negative time of solution. From Figure 1, however, we can see that this increase in endochronic properties levels off rapidly after a volume of solvent of approximately 1.25 ml. This interesting plateau effect has appeared with varying volume of solvent for all varieties of solvents used in these laboratories, just as in all cases the time of solution approaches zero with decreasing volume of solvent.

Time of Solution and Concentration of a Given Ion—In Figure 2, the results are given of the effect of the time of solution (T) of varying the volume of solvent, where the solvent consists of varying concentrations of sodium chloride solution. It can be seen that, although in each case the volume at which this plateau is reached differs markedly with the concentration, the heights of the plateau are constant (i.e. -1.13). The volume at which it is reached, hereinafter termed the Plateau Volume (PV), decreases with decreasing concentration of sodium chloride, approaching the PV for water as the NaCl concentration approaches zero. It is, therefore, obvious that a sodium chloride solution of unknown concentration can be quite accurately characterized by the determination of its PV, where other salts are absent.



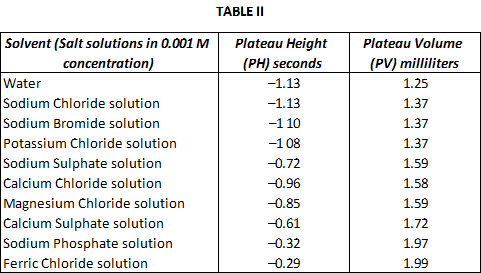
This usefulness of PV extends to other ions as well. Figure 3 gives the endochronic curves for 0.001 molar solutions of sodium chloride, sodium bromide, and potassium chloride. Here, the PV in each case is equal within the limits of experimental error—since the concentrations in each case are equal—but the Plateau Heights (PH) are different.



A tentative conclusion that might be reached from this experimental data is that the PH is characteristic of the nature of the ions present in solution whereas the PV is characteristic of the concentration of these ions. Table II gives the values of Plateau Height and Plateau Volume for a wide variety of salts in equal concentrations, when present alone.

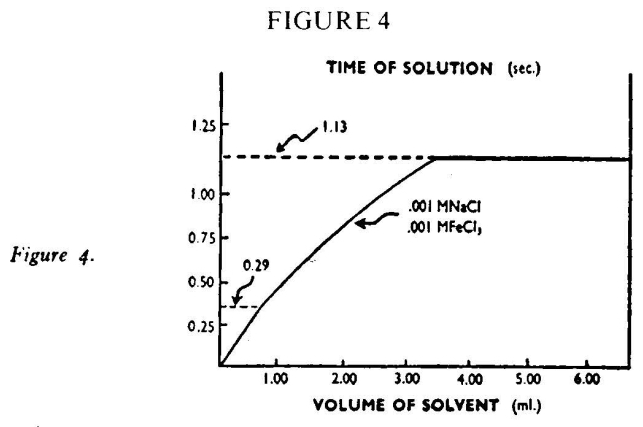
The most interesting variation to be noted in Table II is that of the PV with the valence type of the salt present. In the case of salts containing pairs of singly-charged ions—i.e. sodium chloride, potassium chloride, and sodium bromide—the PV is constant for all. This holds also for those salts containing one singly charged ion and one doubly charged ion—i.e. sodium sulphate, calcium chloride, and magnesium chloride—where the PV, though equal among the three, varies markedly from those of the first set. The PV is, therefore, apparently a function of the ionic strength of the solution.

This effect also exists in connection with the Plateau Height, though less regularly. In the case of singly charged ions, such as in the first three salts listed in Table II, the PH is fairly close to that of water itself. It falls considerably where doubly charged ions such as sulphate or calcium are present. And when the triply charged phosphate ion or ferric ion is present, the value sinks to merely a quarter of its value in water.



Time of Solution and Mixtures of Ions—Experiments currently in progress in these laboratories are concerned with the extremely important question of the variation of these endochronic properties of thiotimoline in the presence of mixtures of ions. The state of our data at present does not warrant very general conclusions, but even our preliminary work gives hope of the further development of the endochronic methods of analysis. Thus, in Figure 4, we have the endochronic curve where a mixture of 0.001 M Sodium Chloride and 0.001 Ferric Chloride solutions is the solvent. Here, two sharp changes in slope can be seen: the first at a solution time of -0.29, and the second at -1.13, these being the PH’s characteristic of Ferric Chloride and Sodium Chloride respectively—see Table II. The PH for a given salt would thus appear not to be affected by the presence of other salts.

This is definitely not the case, however, for the PV, and it is to a quantitative elucidation of the variation of PV with impurities in the solvent that our major efforts are now directed.



Summary—Investigations of the endochronic qualities of thiotimoline have shown that:

a—Careful purification of the material is necessary for obtaining quantitative results.

b—Increasing the volume of solvent results in increasing the negative time of solution to a constant value known as the Plateau Height (PH), at a volume of solvent known as the Plateau Volume (PV).

c—The value of the PH is characteristic of the nature of the ions present in the solvent, varying with the ionic strength of the solution and not varying with the addition of other ions.

d—The value of the PV is characteristic of the concentration of the ions present in the solvent, being constant for different ions in solution of equal ionic strength, but varying markedly with the admixtures of second varieties of ions.

As a result of all this, it is suggested that endochronic methods offer a means of rapid—2 minutes or less—and accurate—within 0.1 per cent at least—analysis of inorganic, water-soluble materials.

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## PART II

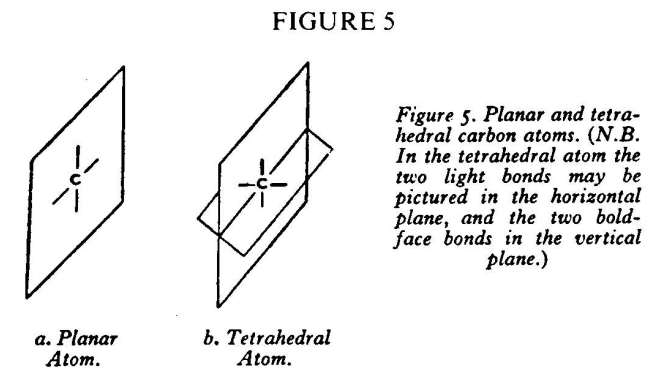
Some years ago, the unusual endochronic properties of purified thiotimoline were first reported in this journal.[{9}](#a90) Despite the fascinating theoretical implications of these properties, thiotimoline research has languished, due largely to the distressing skepticism with which the first reports were met. This laboratory, however, due to the grants-in-aid made available to us by the American Association for the Advancement of Quantitative Psychiatry, has successfully extended its earlier observations in directions which were as unanticipated as they have proven fruitful.

It is the purpose of this present paper, in part, to show that by use of thiotimoline, certain mental disorders can be quantitated and their diagnosis converted from an uncertain art to an exact science.

The Endochronic Carbon Atom—As explained in detail in the previous paper on this subject, the unique property of thiotimoline is its extremely rapid rate of solution in distilled water. So rapid is this rate, indeed, that it dissolves 1.12 seconds before water is added. This endochronicity or ‘negative solution time’ is truly unique, as far as we know. Barosjek and Libnicz[{10}](#a92) report small endochronic effects in certain thiotimoline derivatives but we have been unable to confirm their findings.

Endochronicity is, of necessity, an inevitable consequence of the molecular structure of thiotimoline, and as a first assumption, one may lay the responsibility at the door of the versatile carbon atom. This is not the first time that an advance in our understanding of the carbon atom has led to a major advance in chemistry.

In the nineteenth century, it was pointed out that the four valence bonds of carbon were not distributed toward the points of a square (as, for convenience’s sake, they still are on the blackboard and on the pages of textbooks) but toward the four vertices of a tetrahedron, (see Figure 5). The difference is that in the first case, all four bonds are distributed in a single plane, while in the second, the bonds are divided, two and two, among two mutually perpendicular planes. The second view has made possible an explanation of phenomena such as optical isomerism which had been impossible to understand in the light of the older ‘planar carbon atom’.



Now once more we can broaden our scope. We can pass from the ‘tetrahedral carbon atom’ to the ‘endochronic carbon atom’, in which the two planes of carbon valence bonds are not both spatial in the ordinary sense. One, instead, is temporal. It extends in time, that is. In the temporal plane, one bond extends toward yesterday and one toward tomorrow. Such, a carbon atom cannot be presented on paper in the ordinary way and no effort will be made to do so.

Such an endochronic carbon atom is obviously very unstable and can occur only rarely, in fact only within the molecule of thiotimoline as far as we know. What there is in thiotimoline structure to cause this, what sort of super steric hindrance is as yet unknown, but the endochronic atom undoubtedly exists. As a result of its existence, a small portion of the thiotimoline molecule exists in the past and another small portion in the future.

It is this small portion of the molecule existing in the future which is dissolved by water which also exists in the future (i.e. is about to be added to the thiotimoline but has not yet been added). The remainder of the molecule is dragged into solution in the process and thus ‘dissolves’ in water which to all appearances is not there. Once this is understood, the mystery and apparent paradox disappears from thiotimoline’s behaviour and the whole becomes something quite prosaic and amenable to mathematical analysis.

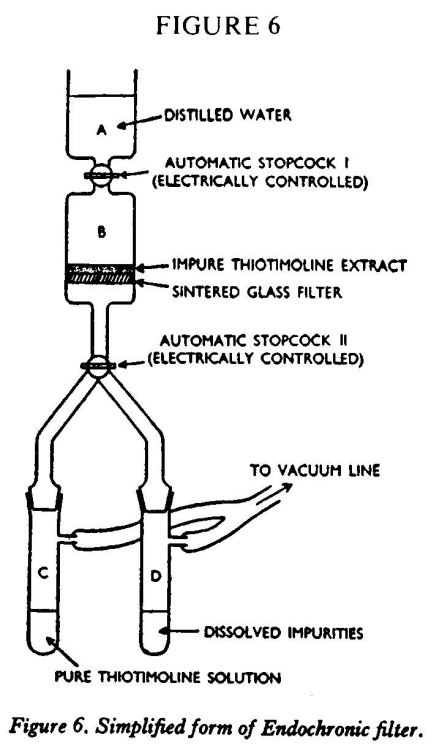
Such a mathematical analysis is now in preparation and will be submitted for publication at a future date. In connection with that, it may be stated briefly at the present time that the possession of endochronic properties necessitates the possession of exochronic properties as well. Considerable effort is being expended at our laboratories now to detect such exochronic properties. If, for instance, a small sample of thiotimoline solution at an original concentration of 1 milligram per milliliter is evaporated exceedingly quickly at temperatures low enough not to damage the molecule, it is obvious that thiotimoline ought to precipitate out of solution only 1.12 seconds after all the water has disappeared and not an instant before. Such phenomena have not yet been observed here, but we feel it to be only a question of developing appropriate techniques.

Endochronic Filtration—No factor has served to retard thiotimoline research as much as the difficulty in obtaining pure substance. Since relatively small traces of impurities mask the endochronic properties of thiotimoline and interfere with the reproducibility of quantitative measurements, considerable effort has perforce been expended on its thorough purification. Repeated recrystallization and resublimations have been necessary. The technique of endochronic filtration has been developed to simplify this procedure enormously.

As described in earlier papers, an extraction of the bark of the shrub, Rosacea Karlsbadensis rufo with distilled water at 5° C., followed by lyophilization (i.e. freeze-drying) of the extract, results in a faintly yellow powder one milligram of which will dissolve in 1 milliliter of water in -0.72 seconds. (It is important that this extraction not be extended for too long a period of time as the gradual extraction of the less soluble, non-endochronic components of the bark will rapidly destroy all traces of endochronicity in the final powder.)

Once an impure powder with significant endochronicity is obtained, only one further step is necessary to obtain extreme purity. The endochronic filter here shown (see Figure 6) is a simplified diagram taken from a detailed report from this laboratory on the principles of its mechanism.[{11}](#a94) It is only necessary here to describe the process briefly. The endochronic filter is essentially a device for rapid suction filtration. Stopcocks 1 and 2 are automatically controlled by an electric circuit not shown in this diagram. At the start of the process, stopcock 1 is in the closed position and 100 milliliters of distilled water are in vessel A. On the sintered glass filter of vessel B, not more than one gram of impure thiotimoline powdered extract is placed. Stopcock 2 (which is a two-way stopcock) is so turned as to connect vessels B and C. The electric circuit is then closed, an action which automatically turns on the vacuum pump. Five seconds after the electric circuit has been closed, a timer activates a relay which opens stopcock 1 and simultaneously turns stopcock 2 into its other position connecting vessels B and D.

The consequences of such a procedure are plain. At 0.72 seconds before stopcock I was opened, the thiotimoline molecules in the impure extract had dissolved in the water that was about to fall upon it while the non-thiotimoline molecules remained, of course, impervious to water whose existence was for them as yet only potential. Under the influence of the vacuum, the dissolved thiotimoline was sucked through the sintered glass filter and into vessel C. When stopcock I was opened, stopcock 2 was turned so as to allow any impurities that dissolved in the water which now actually fell upon the extract to be sucked into vessel D.



The solution in vessel C was lyophilized and one milligram of the white powder thus obtained was found to dissolve in one milliliter of water in -1.124 seconds, a velocity somewhat more negative than had been attained by the use of the most highly purified samples of thiotimoline, as otherwise prepared. Trace ionic impurities present were derived, in all probability, from impurities in the distilled water used and did not interfere with the subsequent investigations.

The Endochronometroscope—The endochronometer, described in my previous communication to this journal, is essentially a device whereby a small cell containing powdered thiotimoline interrupts a light-beam which would otherwise be focused upon a photoelectric cell. Solution of the thiotimoline renders the cell transparent and the photoelectric cell is activated, closing the circuit and recording the exact time of solution. Since the water is added by an electrically-controlled automatic pipette, the time of addition of water can also be determined with great precision. The time of solution minus the time of addition is the ‘endochronic interval’.

It has been increasingly apparent to workers in this laboratory that attention must be paid not only to the time at which thiotimoline dissolves but to its manner of dissolving. Lumbegger and Hophni of this laboratory have recently described a motion picture micro-camera (an ‘endochronometroscope’) attachment, by use of which fine deviations from the solubility norm can be detected.[{12}](#a96) Although the original purpose of this was to test certain theoretical implications of the endochronic carbon atom hypothesis, endochronometroccopy proved of the utmost importance in a series of experiments to be described below.

Willometry—It will be noted that the endochronic filter as well as the endochronometer are adjusted to work with a minimum of human interference. The necessity of this is obvious. Useless speculation has been brought forward in the past as to the possibility of withdrawing water after the thiotimoline has been dissolved and before the water has actually been added, thus ‘fooling’ the thiotimoline into dissolving in water which never arrives. In such a ridiculous attempt, needless to say, only the experimenters are fooled, since what they propose (if indeed they propose it seriously) runs counter to the second law of thermodynamics, as elementary calculation will show.[{13}](#a98)

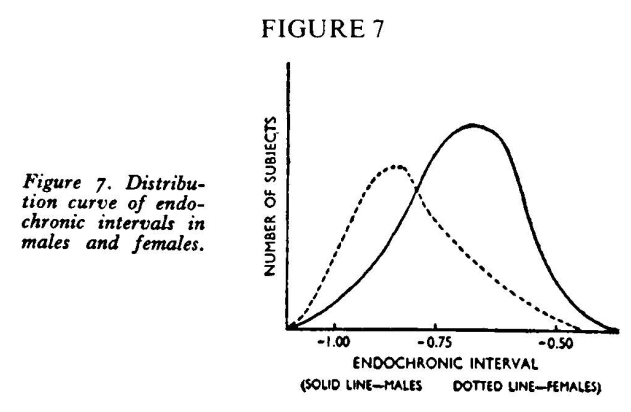
Nevertheless, with ample supplies of thiotimoline of extreme purity finally made available by the use of endochronic filtration, it became possible to determine the effect of human will upon the negative time of solution (i.e. the endochronic interval) and, conversely, to measure the strength of the human will by means of thiotimoline. The resultant technique has been given the name, willometry.

It was early observed, for instance, that strong-willed, incisive personalities achieved the full endochronic interval when adding water by hand. Having made up their minds, in other words, that they were going to add the water no doubts assailed them and the final addition was as certain as though it had been mechanically arranged.

Other individuals, of a more or less hesitating, self-deprecatory nature, yielded quite different results. Even when expressing themselves as entirely determined to add the water in response to a given signal, and though assuring us afterward that they had felt no hesitation, the time of negative solution decreased markedly. Undoubtedly, their inner hesitation was so deeply bound with their unconscious mind and with superego-censored infantile traumas that they were completely unaware of it in any conscious manner. The importance of such physical demonstrations, amenable to quantitative treatment, to the psychiatrist is obvious.

In a mass willometric experiment, 87 male students of the freshman class of Comstock Lode College (Crowded Creek, North Dakota) were used as subjects. It was found that the distribution of willpower varied in the ordinary bell-shaped probability curve. Two students yielded a time of solution of -1.10 seconds or better on all occasions and two students yielded an endochronic interval that was actually positive. It was interesting to note that among the female students (62 of whom were used in a similar experiment) the probability curve was somewhat skewed in the direction of stronger will (see Figure 7). Whereas the observed mean time of solution for all male subjects was -0.625, that for females was -0.811. This confirms a sex difference which has been intuitively apparent (to males, at least) through all of recorded time.

There is reason to think that the endochronic interval may vary with the immediate state of mind of a subject. One student, E. H., having yielded endochronic intervals of from -0.55 to -0.62 over a period of dozens of experiments, suddenly jumped the interval to -0.92. This increase in self-confidence appeared quite remarkable. The technician in charge of the experiment on close questioning insisted that no untoward event had taken place and, indeed, stated that the subject had done nothing more than to express the desire for a walk in the countryside that evening and that the technician had agreed to accompany him. Since E. H. was not particularly athletically inclined, it seemed strange that the prospects of a walk should so affect him. To test whether the effect could be rendered still stronger, the author of this paper voluntarily offered to accompany E. H. as a third member of the party. Unaccountably, the endochronic interval dropped to -0.14 with the very next test. If we may be allowed some speculation, it may be that we are here in the presence of another sex difference made apparent by thiotimoline research, since the author of this paper is male (as was the student) while the technician is female—very pronouncedly female, in fact. Some facets of this obscure situation have been commented upon very recently by McLevinson.[{14}](#a100)



Schizophrenic Willometry—Lumbegger, of this laboratory, in the course of his endochronometroscopic observations on both mechanically and manually induced solutions of thiotimoline was the first to observe the anomalous behavior of thiotimoline under the influence of particular subjects.[{15}](#a102) Ordinarily, the thiotimoline powder dissolved with great rapidity (the time between completely solid state and completely dissolved state being less than a thousandth of a second) and with no perceptible unevenness. In the case of one subject, however, J. G. B., it was found that, strangely enough, there was a perceptible time during which part of the thiotimoline had dissolved and part had not. Dozens of repetitions of the experiments showed beyond all doubt that there was no flaw in the endochrononometer or endochronometroscope. A series of stills published in Lumbegger’s paper, referred to above, make that quite clear.

The subject, however, when subjected to thoroughgoing psychoanalysis, promptly displayed hitherto undetected schizophrenic tendencies. The effect on the endochronic interval of two personalities of differing degrees of self-confidence within a single mind is obvious.

Through the kindness of Dr. Alan E. Windischgraets of the Psychosomatic Institute (Potlikker, Oklahoma) we were able to make use of 150 patients of varying schizophrenic tendencies as subjects for willometric studies.

These studies quickly indicated that three types of schizophrenic deviations from the normal may be detected endochronometroscopically. These may be termed horizontal schizophrenia, vertical schizophrenia, and diffuse schizophrenia. In horizontal schizophrenia, the thiotimoline sample differs in its behavior about a horizontal line of cleavage. More commonly the upper half of the sample dissolves as much as 0.01 seconds before the lower half. This may be referred to as the supra variety. Less frequently it is the lower half that dissolves first and this is the infra variety.

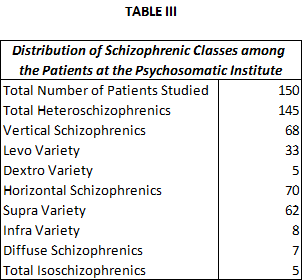
Similarly, vertical schizophrenia evidences itself in variable solubility about a vertical line of cleavage. Here the left half of the sample dissolves first in about half the cases, and the right half in the other half. These are known respectively as the and the dextro variety. It has been a matter of some remark as to why the two varieties of vertical schizophrenia should be of equal occurrence while those of horizontal schizophrenia should be so unevenly represented in favor of the supra variety. There have been suggestions that the gravitational field plays its part in this, but no direct experimental evidence exists.

In diffuse schizophrenia, no neat dividing line exists between early-dissolving thiotimoline and late-dissolving thiotimoline. Rather the substance seems to dissolve in ragged patches randomly distributed through the body of the sample.

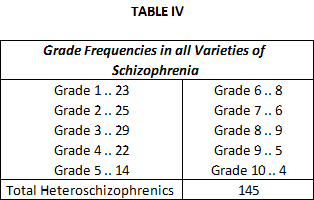
All these varieties of schizophrenia described above may be lumped together under the general name of heteroschizophrenia, since two personalities of different wills are involved. The heteroschizophrenics comprise by far the majority of the subjects tested. There remain, however, a few subjects who, from a psychiatric standpoint, show all the symptoms of schizophrenia, but who nevertheless show no discontinuities in the endochronic interval. The conclusion at which we have arrived is that these subjects possess two personalities of equal will and are, therefore, isoschizophrenic.

A summary of the distribution of patients in the various schizophrenic classes is given in Table III.

Each patient, in addition to being typed as one of the varieties listed above, can be further graded in accordance with the amount of deviation in the endochronic interval of the early-dissolving portions of thiotimoline and the late-dissolving portions. Since the maximum difference observed is about 0.010 seconds and since the endochronometroscope can easily detect time intervals of 0.001 seconds, ten grades may be distinguished, Grade 10 shows 0.010 seconds of deviations, Grade 9 shows 0.009 seconds of deviation and so on down to Grade 1 which shows 0.001 seconds of deviation.



In general, the lower grades are more frequently populated, as may be seen in Table IV. (It will be noted that only 145 patients are listed in Table IV. It is obvious that in the case of the 5 isoschizophrenics, Grade numbers are not applicable.)



The value of such a subdivision of schizophrenia may well be said to be of incalculable potentialities and, indeed, to found a new science of quantitative micropsychiatry. How much more useful it is to say of a patient that he is a vertical schizophrenic, levo variety, Grade 3, than simply to say that he is schizophrenic.

If a small drawback exists in the magnificent structure now being erected, it is that all efforts have been so far unavailing in the attempt to find any medical meaning in our micropsychiatric divisions.[{16}](#a104) This failure of application should not however be allowed to diminish the aesthetic beauty and abstract symmetry of the new technique of endochronometroscopy and the science of quantitative micropsychiatry to which it has given birth.

NOTE

If you have grown interested in thiotimoline, two additional articles dealing with it have appeared since this book was first published. One is “Thiotimoline and the Space Age” which is included in my book Opus 100. The other is “Thiotimoline to the Stars” which appears in my book Buy Jupiter And Other Stories.