INTERFACIAL STUDIES OF NEURO-POTENT SUBSTANCES

by

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INTRODUCTION

Until recently the only narcotics in use in the
medical world were the various preparations of opium.
Opium and its derivatives were not the most efficient nar-
cotics desired, because they suffered the serious drawbacks
of being dangerous in doses large enough to produce sleep,
and they sometimes led to unpleasant after-effects. So
when synthetic substances were discovered that had powerful
narcotic action, but were almost free from the dangers and
the other draw-backs of morphine-containing compounds,
great advances were made in the application of synthetic
chemistry to pharmacology.

Similar to the narcotics are the compounds used for
anaesthetics. These substances do not differ greatly from
other narcotics in their chemical constitution or physio-
logical action, except that such compounds are usually very
volatile and administered by inhalation, so that effects
can be rapidly produced and their duration regulated. Sub-
stances that are to be used as narcotics are usually non-
volatile ones, capable of offering resistance to oxidation
by the body. Such substances would act slower, and the
effects would be noticed over a longer length of time.

A large number of substances are now used as narcotics and anaesthetics, but, upon examination, their constitution shows no structure in common. Aliphatic hydrocarbons possess narcotic properties, these properties being increased by the introduction of hydroxyl groups to form alcohols. But upon further introduction of hydroxyl groups, as in glycerol, the narcotic action disappears. Many substances owe their narcotic action to alkyl groups; the introduction of ethyl groups, particularly, produce sedative action. Halogen substitution products, especially chlorine, greatly add to narcotic power, the narcotic power increasing with increase in number of halogen atoms substituted in the molecule. Carbonyl groups (-CO-), and in some cases ring structures containing nitrogen, possess narcotic power. Certainly no chemical structure is common to this dissimilar list of the classes of compounds comprising narcotics and anaesthetics.

The action of narcotics is obscure, and many theories have been advanced to explain the physiological action of a hypnotic once administered to produce or to prolong sleep. As yet no single theory, whether physical or chemical, has been successful in explaining all the phenomena of sleep. The theory that will be the successful one will probably be one that combines both chemical and physical explanations.

Pharmacologists hold that drug action is principally physical, and disregard entirely the chemical character of the substance; but the poisonous property of an arsenic compound is due not to its physical structure so much as to the presence of arsenic in the molecule.

EHRLICH'S THEORY OF SELECTIVE ACTION

The selective action of certain compounds is considered by Ehrlich (1) to be dependent upon "the coming together of certain groups in the molecule in some sort of chemical connection with the cell substance. It is only when the compound is held to the tissues (anchored) by the groups, that the whole complex molecule can take effect and exert its characteristic physiological action." Ehrlich's view will only permit a compound, then, to be a drug when it has within its molecule a so-called "anchoring" group, which group when anchored to the body cell will then allow the remainder of the molecule to exert its physiological action.

SLEEP AND ITS RELATION TO NARCOSIS

A compound to be a narcotic must produce and maintain profound sleep. This insensibility produced by narcotics seems to differ from natural sleep in many ways. In normal

sleep, the respirations per minute remain unaltered, but the movement becomes only thoracic and shallow, with the inspired air and output of CO_2 diminished by one-half to two-thirds. The blood becomes congested in the limbs and venous system with a decrease in arterial pressure, pulse-rate, and velocity of blood flow. The body temperature falls, and mental activity decreases. At first nervous excitability decreases; then it begins to increase and becomes almost as great as it is toward the end of the sleep. Consciousness alone seems to be abolished during sleep, although the nerves and special senses continue to transmit impulses and produce reflex movements.

Sleep, as pointed out by Verworm (2), is entirely different from narcosis. Sleep comes because of lessened irritability (fatigue) of the brain cells due to work, and because of the removal of external stimuli, as noise, lights, clothing pressure, etc. Narcosis comes from direct and intentional depression of the cells of the brain and central nervous system. In sleep the cells recover from the fatigue and are restored to their full capacity for work, but in narcosis no such reparation takes place; instead the cells continue to lose irritability and become more fatigues, very often requiring, later, very prolonged natural sleep for restitution. Narcotics do not directly

or primarily induce natural sleep.

THE MEYER AND OVERTON THEORY OF NARCOSIS

In an effort to explain the action of hypnotics and the manner in which they depress the brain cells and central nervous system, Meyer and Overton in 1901 (loc. cit.) published their theory. It was a theory that was predominately physical and was based on the solubility of the drug in aqueous solution and in fat solution. They showed that substances can be divided into different groups according to the rapidity with which they diffuse into protoplasm, this rate of diffusion being dependent on their solubility in fat, lecithin, and other lipoid tissue. If S_f is the solubility of a substance in fat, and S_w the solubility of the same substance in water, then S_f/S_w equals a constant and is called the distribution coefficient of the substance. The value of this distribution coefficient, according to Overton, determines the velocity of diffusion of the substance into the cell protoplasm; the higher the distribution coefficient, the more rapidly will the substance diffuse. In comparing narcotics, it was found that the narcotic power was roughly proportional to the value of the distribution coefficient; or in other words, that the narcotic power of a drug is dependent and roughly measured by the ratio of its solubility in lipoid tissue to its

solubility in water.

Meyer determined the smallest concentration of these substances which would produce a definite physiological effect, and expressed the values as fractions of the normal solution, calling these fractions liminal values. When these liminal values were compared with the distribution coefficients for the same substances, it was found that when the liminal value was small the distribution coefficient was large, and vice versa. In the series that Meyer ran, the distribution coefficients decreased in regular order as the liminal value increased, with two slight exceptions, namely tetronal and bromal hydrate.

INTERFACIAL SURFACE TENSIONS AND THEIR RELATION TO NARCOSIS

This work of Meyer and Overton suggested that perhaps the solubilities of these drugs in water and fats were not the only controlling or contributing factors in narcotic action. Interfacial surface tension might perhaps be a factor even as important as the solubilities. In the body there are known to be innumerable interfaces of all kinds, such as solid-liquid, liquid-liquid, liquid-gas, and solid-gas interfaces. The blood contains colloids, and interfacial tensions are of fundamental importance in colloid formation. Body cells offer interfaces to other cells and to

blood constituents; and each interface would therefore ex-
ert its own interfacial tension. Correct functioning of
body tissues means health; impaired functioning of body
tissues means poor health, disease, or even death. Any
changes, then, in the normal interfacial tensions at any or
all of the multitude of interfaces would exert a decided
physiological action.

DEFINITION OF SURFACE TENSION

Molecules in the bulk of a liquid exert an attraction
for all other molecules in the liquid,- especially for those
near it. Because this attraction is uniform in all direc-
tions, these molecules will be under the influence of a
balance of forces. But the molecules in the surface show
plainly this molecular attraction because here they are
subject to unbalanced forces. Because there are many more
molecules below the surface exerting their attraction than
there are above the surface, the result is unbalanced sur-
face forces that tend to diminish the surface to a minimum.
That is, the contraction of the surface of a liquid involves
the expenditure of energy by the liquid, and the surface
film of a liquid is consequently in a state of tension.
This tension is known as surface tension, the surface be-
having as if it were composed of an elastic membrane. The

phenomenon of surface tension can be demonstrated beyond a
doubt by the use of an arrangement suggested by Maxwell (3).
Imagine a rectangular wire frame, one side of which is made
of a movable wire that slides always parallel to the oppo-
site side and at right angles to the adjacent sides. If the
rectangle is now filled with a film of liquid, this will
contract and pull the movable side with it. If weights are
now fastened to the movable side, a weight can be found
which will just stretch the film - within certain limits -
indefinitely. Since there are two film surfaces, this
weight is twice the value of surface tension; and if half
this weight is divided by the length of the movable side,
the surface tension per unit length is obtained. The units
generally used to express the pull of surface tension are
dynes per centimeter. This pull exerted multiplied by the
distance through which it moves gives work units, i. e.
dynes x centimeters = ergs. Surface tension is then defined
as the force in dynes per unit length of surface of a liquid
in a direction parallel to the surface.

Some liquids wet the walls of glass tubes and others do
not. When one end of a glass tube is placed in a liquid
that wets the walls of the glass, the surface of the liquid
is concave, and it rises in the tube; when the liquid does
not wet the walls of the tube, the surface is convex, and

the liquid is depressed in the tube. Jurin discovered the law governing the elevation or depression of a liquid in a capillary tube. It may be stated thus: ''The elevation or depression of a liquid in a capillary tube is inversely proportional to the diameter of the tube.'' This law thus makes available two accurate methods for the determination of surface tension in absolute values: the rise in the capillary tube of the liquid, and the drop weight method.(4)

THE CAPILLARY RISE METHOD

Let a capillary tube of radius r be immersed in a vessel of liquid whose density is d, and let the elevation of the liquid in the capillary (from the bottom of the large meniscus to the bottom of the small meniscus) be denoted by h. The weight of the column of liquid in the capillary will be $\pi r^2 hdg$, where g is the acceleration due to gravity. The force sustaining this weight is the vertical component, $2\pi r \gamma \cos\theta$, of the force due to the tension of the liquid surface at the walls of the tube, γ being the surface tension and θ the angle of contact of the liquid surface with the walls of the tube. At equilibrium, the weight and the force sustaining this weight are equal; therefore $\pi r^2 hdg = 2\pi r \gamma \cos\theta$, or $\gamma = hdgr/2 \cos\theta$.

In 1919 Harkins and Brown (5) gave convincing but

indirect evidence that the angle of contact is zero for four liquids: water, benzene, carbon tetrachloride, and ethylene dibromide. Richards and Carver (6) added chloroform and ether to this list of liquids with zero contact angles. For other liquids the angle of contact is unknown, although it is probable that it is zero for most liquids.

Because the angle of contact is so important in the development of this method, the lack of exact proof of the angles is a big barrier to attaining accuracy by this manner; but for lack of better evidence, the contact angle is considered zero for all liquids.

THE DROP WEIGHT METHOD

The other method in most common use in determining surface tension is the drop weight method. This method has one big advantage over the capillary rise method in that it is independent of the angle of contact the liquid might make with the walls of the glass tube. It also lends itself to the determination of interfacial surface tensions much more readily than the previous method, is more simple experimentally, and has about the same degree of precision.

The principle of the drop weight method is a simple one. If a drop of liquid, forced to hang from the end of a

perfectly round cylindrical tip, is cylindrical in shape
and of the same diameter as the tip, the maximum weight of
the liquid upheld is exactly equal to the weight of the
liquid upheld in a capillary tube of the same diameter.
This is because in both cases the force of surface tension
acts on a line $2\pi r$ long, so the force is $2\pi r\gamma$. This force
holds up the weight of the drop. If the hanging drop is
allowed to form and hang on as long as the surface tension
will hold it, at the time the drop breaks loose from the
tip the weight is entirely supported by the component of
the surface tension, $W=2\pi r\gamma$; where $W=mg$. Or $\gamma=mg/2\pi r$.

This equation would hold, provided the drop broke at
the rim of the tip; but actually the drop does not break
away from the exact end of the tip, but leaves behind a
residual or pendant drop. Before the drop breaks free, it
is constricted to a diameter less than that of the tip some
distance below the edge. Thus the drop that falls would
have a smaller weight than that in the equation, which
would result in smaller values for the surface tension.
Harkins and Brown determined the values of the corrections
required for this pendant drop by comparing the results of
the drop weight method with those of the capillary height
method, and derived a correction in terms of the radius and
the volume of the drop.(loc. cit.)

As r is a linear dimension of the hanging drop, and if l is some other linear dimension, r/l will remain constant if the form of the hanging drop is kept constant while the volume changes. Since $l = V^{1/3}$, then $r/l = r/V^{1/3}$. Now if the form of the drop determines the amount that will fall, then the actual weight of the falling drop is

$$W = 2\pi r \gamma f(r/l) = 2\pi r \gamma f(r/V^{1/3}).$$

Solving for γ, when $W = mg$,

$$\gamma = \frac{mg}{2\pi r f(r/V^{1/3})}$$

When this correction is made on the weight of the ideal drop, values in nearly perfect agreement with those determined by the capillary rise method are obtained. If the drop forms in dilute vapor, no buoyancy correction needs to be made, and m then represents the weight in grams of one drop. The weight of the drop divided by the density gives the volume V.

To determine γ, calculate $V^{1/3}$, look up the value of f from Harkins data (loc. cit.), and divide the value of mg, where g is acceleration of gravity, by $2\pi r f$. If m is expressed in grams and r in centimeters and g in dynes, γ will then be calculated in dynes per centimeter.

INTERFACIAL TENSIONS BY THE DROP VOLUME METHOD

One of the big advantages of the drop weight method is the ease with which it can be adapted to the determination of the interfacial surface tension of two immiscible liquids. In principle, interfacial tensions are determined similarly to the method for free surface tensions by the drop weight method. A slight modification of the usual drop weight apparatus is necessary. Since in this method the weight of the drops cannot be obtained directly by weighing, the solution to be dropped is run from an accurately calibrated pipette, and the volume dropped thus determined. If the density is known, the weight can then be easily calculated. The receiving cup contains the second liquid, into which the first liquid is dropped, either upwards or downwards dependent on the density and on the phase that best wets the tip. From the volume of the drops thus obtained, the surface tension can be calculated by a modification of the equation for the drop weight method, namely:

$$\gamma = \frac{V(d-d_1)g}{2\pi r f(r/V^{\frac{1}{3}})}$$

Here γ is expressed in dynes per centimeter when r is expressed in centimeters, g in dynes, and $V(d-d_1)$ in grams. V is the volume of each drop, d the density of the heavier

phase, d_1 the density of the lighter phase, and $f(r/V^{\frac{1}{3}})$ the same correction for the pendant drop as described for the drop weight method.

OTHER METHODS OF DETERMINING SURFACE TENSION

There are many other methods of determining surface tension. Rideal (7) divides all surface tension determination methods into two general types: dynamic and static. Two methods are listed under the dynamic methods, namely the vibrating jet method and the ripple method. The methods listed under the static methods include the two already described, the maximum gas bubble pressure method, the measurement of curved surfaces or bubles, direct pull of a soap film or a ring from off the surface of a liquid, Langmuir's differential method for thin insoluble films on liquid surfaces, vibrating drops, and rate of flow of liquids in capillaries. There are many modifications of some of these methods that allow of easier or more accurate work in certain fields and in certain problems. In general, for pure unassociated liquids in contact with their own vapors, these methods check fairly well, and any great differences are usually due to inexperience of operator or to slow attainment, by diffusion, of surface equilibrium.

ADSORPTION AT INTERFACES

From studies of surface tension, it is easily to be
seen that due to the unbalanced molecular attraction, the
surface of a liquid behaves like a tightly stretched mem-
brane. This contractile force, then, causes the pressure
to be greater at the surface than in the bulk of the liquid.
It is well known that unequal heating of a dilute solution
disturbs homogeneity with respect to concentration; so also,
inequality of pressure may be assumed to cause differences
in concentration in the solution. Although direct experi-
mental evidence is difficult to obtain, there is abundance
of evidence for the view that the concentration at the sur-
face of a solution differs from the bulk concentration in
consequence of the greater surface pressure.

In general the addition of a solute to a solvent will
affect the surface tension of the latter, and since thermo-
dynamically it is known that the energy of a system strives
towards a minimum there will be a tendency, if the solute
lowers the surface tension of the solvent, for the solute
to accumulate in the surface. Likewise, if the solute
raises the surface tension of the solvent, the reverse ac-
tion will occur and the surface phase will be poorer in

solute than in the bulk. This increase or decrease in surface concentration does not continue indefinitely, for a point is soon reached when the action is balanced by the return, due to diffusion, of solute molecules from the higher to the lower solute concentration.

The quantity of solute transferred from the bulk to surface is called the adsorption per unit of surface. This adsorption may be either positive or negative, according to whether the solute lowers or raises the surface tension of the solution.

The exact mathematical treatment of the amount of adsorption in the surface layer was first made by Gibbs (8) in 1876 from thermodynamical consideration of solutions and surfaces. Many derivations have since been made. The following simplified derivation is due to Oswalt (4) with the writer's modification to account for activity.

DERIVATION OF GIBBS EQUATION

Let s be the surface of a solution whose surface tension is γ, and let it be assumed that the surface contain one mol of the solute in excess. If a very small portion of the solute enters the surface layer from the solution, thereby causing a diminution, $d\gamma$, in the surface tension, the

corresponding change in energy will be sdγ. But this amount
of energy which is set free must be equivalent to the osmo-
tic work absorbed in effecting the removal of the same
weight of solute from the solution. Let V be the volume of
solution containing unit weight of solute, and let dp be the
difference in the osmotic pressures of the solution before
and after its removal; the osmotic work will be -Vdp. Since
the gain in surface energy and the osmotic work are equal,
we have sdγ = -Vdp.

The solutions being dilute, we may assume that the gas
laws hold, and since $V = RT/p$, we may write $sd\gamma = -(RT/P)dp$,
or $\frac{d\gamma}{dp} = -\frac{RT}{SP}$

Since pressure is directly proportional to concentra-
tion, the preceding equation becomes $\frac{d\gamma}{dc} = -\frac{RT}{sc}$.

But s has already been defined as the surface which
contains one mol of solute in excess; therefore it follows
that the excess of solute in unit surface is 1/s. Writing
u = 1/s, we have

$$u = -\frac{c}{RT}\frac{d\gamma}{dc}$$

But $c/dc = 1/d\ln c$. Then

$$u = -\frac{1}{RT}\frac{d\gamma}{d\ln c}.$$

Let f = activity coefficient, and a = activity = fc. Substituting these in the above equation,

$$u = -\frac{1}{RT}\frac{d\gamma}{d\ln fc} = -\frac{1}{RT}\frac{d\gamma}{d\ln a}$$

which is the equation of Gibbs.

From this equation it is evident that if the surface tension γ, increases with the concentration, then u is negative and the surface concentration is less than the concentration of the bulk of the solution. This is clearly negative adsorption. On the other hand, if γ decreases as the concentration increases, u is positive and the surface concentration is greater than the concentration of the bulk of the solution, or the adsorption is positive. Finally, if the surface tension is independent of the concentration, then the concentration of the solute in both the surface layer and the bulk of the solution will be the same.

EXPERIMENTAL VERIFICATION OF GIBBS EQUATION

Although Donnan and Barker (9) attempted to prove that this equation was valid, very many difficulties must be over‡ come before accurate quantitative verification is possible. Donnan and Barker employed a solution of nonylic acid up through which a slow stream of air bubbles was blown, and the number and diameter of the bubbles determined. Adsorption of the solute occurred at the bubble interface, and the

quantity so adsorbed was carried into the upper layers of
the solution. Baffle plates in the solution prevented back
diffusion, so the upper part of the solution gradually in-
creased in concentration. The change in concentration being
exceedingly small, it was determined by determining the
change in surface tension, because small changes in concen-
tration produce large changes in the surface tension. Sim-
ilar experiments were made with other solvents; and, al-
though the results did not check the values calculated from
the Gibbs equation, they were within the right order of the
calculated values. From so many other sources like quanti-
tative verification of the Gibbs equation has been obtained
that at least its qualitative truth is apparent, and the
equation has come to be accepted as a scientific law.

MOLECULAR ORIENTATION AND MONOMOLECULAR FILMS

Harkins and Langmuir (loc. cit.) independently devel-
oped the theory of molecular orientation at surfaces. It
was first reasoned from the physics of many floating logs on
the surface of a lake. If a number of similar uniform logs
be indiscriminately thrown upon the surface of a body of
water, they will not orient themselves in any particular
manner but lie in all directions. If now one end of each
log be weighted with a heavy weight, it is found that the

logs will be oriented in a definite manner with their heavy ends turned downward and the lighter ends pointed upward, due to gravity. In like manner, it is assumed that molecules orient themselves on the surface of liquids, due to the polar groups within the molecule.

The idea that molecules possess polar groups is not a new one. The basis of this idea is that the field of molecular attraction does not proceed uniformly from the center of the molecule, but may be concentrated in the neighborhood of one or more atoms composing the molecule. These atoms or atomic groups (polar) are known to possess residual attractions that are apparent at a distance around the molecule. Other atoms or atomic groups (non-polar) possess a residual attraction, but not to such a high degree. Therefore, if a molecule in the surface of a polar liquid had one end a highly polar group and the other end a non-polar group, it is easy to see how such a molecule would become oriented in the surface with its polar group toward the bulk of the liquid and its non-polar end turned outwards toward the surrounding phase. A solution of propane would therefore have its molecules unoriented in the surface, because the entire molecule would be surrounded by a uniform field of attraction, it being entirely non-polar. But propionic acid, with its non-polar methyl end and highly polar carboxyl end,

would be oriented with the molecule standing upright on the surface with its polar end immersed in the polar liquid (water) and its non-polar end turned toward the external phase. If benzene were the external phase, the methyl groups would be immersed in it and the carboxyl groups in the water, but in any case the external surface of the water solution would be a surface of methyl groups.

There is much proof of this theory. If this theory be true, the surface tension of solutions of the fatty acids should be nearly the same, and this was verified by King (10) to be about 45 to 50 dynes per centimeter. The same would hold true for any aliphatic compound that had a polar group, such as NO_2, CN, COOH, COOM, COOR, NH_2, $NHCH_3$, NCS, COR, CHO, I, OH, or groups which contain N, S, O, I, or double or triple bonds. Solutions of aliphatic compounds containing these groups will all give approximately the same surface tension, providing the molecule is long enough to overcome the solubility (pulling) effect of the polar group and remain above the surface.

That molecules do orient in the surface film was proven by another means by Langmuir (18). He also proved that if this surface film was not a monomolecular layer it behaved as one, and that each molecule was oriented in this surface.

His work on expanded films proved conclusively that mole-
cules do orient themselves in the water and are present in a
monomolecular layer. His determinations of the cross sec-
tional areas of each molecule were in agreement with the
areas determined by other means, such as Bragg's (loc. cit.)
determination of the area of a benzene molecule from its
crystal structure.

THE SPREADING OF LIQUIDS ON OTHER LIQUIDS

Many theories have been advanced trying to explain the
spreading of one liquid on another, and the best of these is
probably due to Harkins. Let W_a be the work of adhesion, or
the work necessary to pull apart 1 sq. cm. of the interface
between two liquids ($\gamma a + \gamma b - \gamma ab$); and W_c be the work of
cohesion, or the work necessary to break apart a bar of
liquid 1 sq. cm. in area in such a way as to give two sur-
faces (2γ); and let S designate the spreading coefficient;
then

$$S = W_a - W_c$$

If S is positive, the top liquid will spread on the
other; if S is negative, the liquid will not spread but will
form into lenses on the liquid surface.

The coefficient for liquid a to spread on liquid b is

$S = \gamma b - (\gamma a + \gamma ab)$, so a high surface energy for the liquid a acts in favor of spreading when a is the lower liquid, and against spreading when b is the lower liquid. To prove this, it is found that almost all organic liquids will spread on water, but water spreads upon very few organic liquids. The great effect of polar groups is to increase the work of adhesion toward water much more than it increases the work of cohesion. But a polar group is not essential to spreading, because Harkins found that the spreading coefficient for many non-polar compounds was positive, such as benzene, octane, toluene, p- and m- xylene, and ethyl benzene, and that these compounds would spread on water.

It is possible by means of this spreading of one liquid on another to determine the thickness of the surface film. A dilute solution of oil in benzene is prepared and a drop or two placed on the surface of water. Knowing the volume of the oil placed on the water and the area over which it spreads, it is possible to calculate the thickness of the surface as well as the number of molecules per unit area and the cross section or diameter of the molecules. This furnishes considerable evidence that the surface is only one molecule in thickness.

SELECTIVE AND PREFERENTIAL ADSORPTION

"By preferential adsorption we mean the adsorption or
condensation or loose union of ions of one kind upon a col-
loid surface to the exclusion, partial or entire, of the
other kinds of ions." (11) In aqueous solutions the hydrox-
yl ions are adsorbed in preference to hydrogen ions, and
ions with higher valences are generally more completely ad-
sorbed than ones with lower valences. Ions opposite in
charge to the colloid particles are selectively adsorbed.
Preferential adsorption plays an important part in the field
of colloidal chemistry. It is of importance as a partial or
complete explanation of the following: the charge on the
colloid particles, coagulation, peptization, emulsification,
endosmosis, and emulsion and colloid stability. Selective
adsorption is the basis of a patented process for the separ-
ation of the radioactive salts, and also for ore concentra-
tion processes, collectively called "Froth Floatation."

ADSORPTION AS A PHYSIOLOGICAL FACTOR

The difference of concentration between the surface
film and the bulk of the liquid may be of considerable im-
portance in protoplasm. Thus it is suggested that in the

surface of contact of protoplasm with water, lipin sub-
stances will accumulate and thus make an interface of a
lower surface tension and of a fatty nature. The formation
of this interface with its lower interfacial tension will
then tend to adsorb into the surface dissolved substances
from the blood fluids and from surrounding liquid tissues.
Such adsorbed materials would thus be harmful or harmless
according to their character. This, then, would afford an
excellent opportunity for harmful substances to exert their
influence; and, because of the great amount of interfacial
surface within a body, great harm could be done by this one
process alone.

Traube made a study of the relation of surface tension
to osmosis. He found that the more a dissolved substance
reduced the surface tension of water the greater would be
the velocity of osmosis of the solution. He concluded that
it was a difference in the surface tensions of separated
solutions that determined the direction and velocity of
osmosis, and its direction was from a solution of low sur-
face tension to one of high surface tension. Therefore, at
the body interfaces, if Traube's theory is valid and if neg-
ative adsorption occurs, it means the cell will have a high-
er surface tension, osmosis flow will be greater into the

cell, and swelling may result. If positive adsorption takes place at the interface, it means a lower surface tension for the cell, resulting in unusual osmosis out of the cell and a subsequent drying of tissues and cells (3).

This was partly verified by the work of Czapek (13). Czapek, in a study of the toxic effect of organic solutions on plant cells, found that exosmosis and cell death regularly took place when the surface tension of the solution reached approximately the same value, or about two-thirds that of water. It is evident then that when a substance of high surface activity is brought in contact with protoplasm, a surface tension decrease of both cell and water phase occurs, adsorption takes place with further lowering of cell tension until a certain value is reached, when exosmosis takes place. In order to correlate this idea with Traube's theory, it seems necessary to assume that these organic substances by virtue of their high distribution coefficients readily penetrate the lipoid cell walls and reduce surface tension of material within the cell. The equilibrium is thus disturbed in such a manner as to cause exosmosis from the cell. It is certainly apparent that surface tension and interfacial tensions are of importance to correct body functions, especially in the study of the physiological action of neuro-potent substances.

EXPERIMENTAL PROCEDURE

The theory of Meyer-Overton (loc. cit.) was used as a
basis for this work, and the drugs included in their list
were used with the exception of tetronal and the addition of
ethyl methylcarbamate. The interfacial surface tensions of
aqueous solutions of trional, butyl chloral hydrate, sul-
phonal, bromal hydrate, triacetin, diacetin, chloral hydrate,
ethyl carbamate, monacetin, methyl carbamate, and ethyl
methylcarbamate were determined against pure Nujol and
against a 0.0005 molar lecithin - Nujol solution. All meas-
urements were made at $20^{\circ}C$. The apparatus used was Hall's
modification of the Morgan drop weight apparatus for drop
volume measurements. This apparatus consisted of an accu-
rately graduated pipette which could be closed at the top by
means of a three-way stopcock, or opened to the air, or
opened to a source of suction (mouth). This pipette held
the aqueous drug solution. The end of the pipette was an
accurately ground dropping tip of capillary tubing, the diam-
eter of which was determined by a travelling microscope.
The dropping tip was immersed in a small weighing bottle con-
taining the oil phase, and the drops of solution formed in
it. When not in use the apparatus was allowed to stand full
of $H_2SO_4-K_2CrO_4$ cleaning solution, and before using was

washed with conductivity water. Between solutions the appa-
ratus was repeatedly washed with ether and then with conduc-
tivity water.

MATERIALS AND SOLUTIONS

The compounds used were obtained from many sources.
Trional, butyl chloral hydrate, and sulphonal were
Mallinckrodt's especially purified chemicals. The bromal
hydrate and ethyl carbamate were obtained from Parke Davis,
and were the best quality to be procured. The triacetin,
diacetin, monacetin, and ethyl methylcarbamate were obtained
from Eastman, and, with the exception of diacetin, were of
their highest grade of purity. The chloral hydrate was
Kahlbaum's best. All these compounds were used just as pur-
chased except the diacetin, which was purchased as "Practi-
cal" diacetin, then purified by distillation, and that
fraction used that boiled at 147.5 - 148.5° C under 14 mm.
pressure. The methyl carbamate was prepared by us by treat-
ing methyl chlorocarbamate with ammonia gas at 0°C. The
solution was kept covered with toluene at all times, and the
product was re-crystallized from hot toluene five times and
dried by suction filter and in a H_2SO_4 dessicator.

These compounds were made up in 0.1 M, 0.05 M, 0.025 M,
and 0.01 M solutions with the exception of trional and

sulphonal. Due to the insolubility of these two drugs,
0.012 M, 0.008 M, and 0.004 M solutions of trional, and
0.08 M, 0.04 M, and 0.02 M solutions of sulphonal were pre-
pared. Conductivity water with a free surface tension of
72.7 dynes was used in preparing these solutions; likewise,
this same water was used for all washing of bottles and ap-
paratus. The density of each one of these aqueous solutions
was determined by use of an accurate pycnometer.

The Nujol was obtained from Standard Oil Co., and was
used as sold under the trade name of "Stanolind", which is a
colorless, odorless, white mineral oil. The lecithin was
prepared by the method described by Mathews (14), and fur-
ther separated from cephalin by the method of Levene and
Rolf (15). A 0.0005 M solution was made up in Nujol. In
making this solution, it was assumed that lecithin had a
molecular weight of 777.71, corresponding to a formula of
$C_{42}H_{84}PO_9N$.

All solutions were kept in glass stoppered bottles, and
capped to exclude all dust.

MANIPULATION OF APPARATUS

The apparatus was cleaned and thoroughly rinsed with
conductivity water and then with the solution to be run.

The apparatus was then filled and immersed in the thermostat at 20° C, and time was allowed for it to come to the temperature of the thermostat. Drops of the solution were then allowed to form and drop off in the oil. The drop time was kept as near as possible to fifteen minutes to allow time for surface equilibrium to be attained and orientation to be complete. A definite number of drops was run out, and the individual volume of each determined from the total volume used.

CALCULATION OF RESULTS

The interfacial tension of each solution was calculated by the formula for calculations involving drop volumes, namely

$$\gamma = \frac{V(d-d_1)g}{2\pi r(f\ r/V^{\frac{1}{3}})}$$

where γ is the interfacial tension expressed in dynes per cm., V is the average volume per drop in cc., d is the density of the aqueous solution, d_1 is the density of the oil phase, g is acceleration of gravity in dynes, r is the radius of dropping tip in cm., and $(f\ r/V^{\frac{1}{3}})$ is the value obtained by interpolating Harkins' data (loc. cit.), when the radius of the tip r is divided by the cube root of the volume of each drop.

These values of γ for the different concentrations of each compound were then plotted against the natural logarithm of the concentration expressed in mols per liter of solute. The tangent to the curve at the concentration indicated in the data tables was determined and substituted directly into the Gibbs equation in order to determine the adsorption coefficient of that compound:

$$u = - \frac{d\gamma}{RTd\ \ln(c)}$$

In this equation u is the excess of solute adsorbed in the surface in mols per sq. cm., R is gas constant or 8.316×10^7 ergs, T is the temperature or $293^\circ K$, and $d\gamma/d\ln(c)$ is the slope of the curve at the point the adsorption is desired.

Using these adsorption coefficients, the area occupied by each molecule in the surface at equilibrium was calculated. Assuming Avogadro's number to be 6.06×10^{23} molecules in one mol, this would give 6.06×10^{20} molecules in one cc. of molar solution. Taking a point at 0.025 M as an example, then in one cc. of 0.025 M solution there would be $0.025 \times 6.06 \times 10^{20}$ molecules, or 1.515×10^{19} molecules. Since volume equals L^3, then $(1.515 \times 10^{19})^{2/3}$ molecules would be the number of molecules in one sq. cm. of surface,

provided there was no adsorption. Then, to determine the number adsorbed in the surface, the adsorption value u is multiplied by Avogadro's number, giving the actual number of molecules in excess on the surface. The adsorbed molecules plus the molecules in one sq. cm. of internal area gives the total number of molecules in one sq. cm. of surface. The area occupied by each molecule is then obtained by dividing 1 sq. cm. by the total number of molecules in one sq. cm.

All data and calculated values are arranged in the tables. Certain parts of this data have been rearranged and combined with distribution coefficients and liminal values of Meyer-Overton for the sake of comparison.

CONCLUSIONS

The interfacial tension values obtained for each inter-face are much lower than the free surface tension obtained by Cole (16), which is to be expected of interfacial values. It will easily be seen that in every case the interfacial values for the lecithin - Nujol interface are much lower than those for the pure Nujol interface. This also is to be expected if surface tension is at all associated with nar-cotic action. Great changes in the interfacial tensions are noticed against lecithin - Nujol, with many of the most

concentrated values being very low. Especially is this true
of butyl chloral hydrate, where the 0.1 M solution shows an
interfacial tension value of about 5.74 dynes. The curves
for the lecithin - Nujol interface tend to assume normal ad-
sorption curve shape, but they are quite irregular in some
cases. This probably can be partly explained from a study
of the structure of lecithin. Lecithin, although its exact
structural formula is in doubt, is known to be a complex
molecule containing a choline base probably hooked through
phosphoric acid to glycerine, the other two hydroxyl groups
of glycerine being esterfied by fatty acids. Lecithin then
is amphoteric in nature, and it is very easily hydrolyzed.
Such a combination of chemical properties allows of much
surface reaction between the drug, water, and lecithin.
This would require an indeterminate time for the surface to
reach equilibrium, if it ever did so. This possible inabil-
ity to reach equilibrium may account in part for the irreg-
ular adsorption curves.

The adsorption curves against the pure Nujol are more
regular, probably because there is not the chance for chem-
ical reaction between it and the drug and water. Nujol was
chosen because it was immiscible with water, and probably
would not react with the drug or undergo hydrolysis. These

values could be used as a standard of comparison of the
values obtained from the lecithin – Nujol interface. Leci-
thin was chosen because it is one of the principal constit-
uents of the brain and nervous system; and in narcotic
action the nerves and nerve centers are among the first body
tissues to be affected. Therefore, the interfacial action
of lecithin against these drugs might be an indication of
narcotic action.

From a study of Table III, it is found that the adsorp-
tion values do follow the order of distribution coefficients
and liminal values very closely,– much more so than in Table
IV where the values are irregular. But in Table III it is
seen that when the liminal value is low, the adsorption co-
efficient is high, and vice versa. This certainly indicates
that interfacial tension is important in narcotic action.

When the distribution coefficient is high, so is the
adsorption coefficient. This might be explained by studying
the interfacial boundary at high adsorptions (low interfac-
ial tensions). A low interfacial tension would tend to make
the change from one phase to the other less abrupt. This
would decrease the surface energy and the toughness of the
surface film. If the surface film becomes less tense with

less boundary pressure, more drug will be adsorbed into the surface, there getting the opportunity to exert its physiological action. Also, this lessening of the surface tension will increase the ease with which the drug can leave the aqueous phase and penetrate the oil phase, thus increasing the drug concentration of the oil phase. This increase in oil phase concentration will show up in the distribution coefficient calculations. This distribution coefficient is the ratio of the solubility of the drug in the fat to that in water, or S_f/S_w. To increase the numerator will increase the value of the ratio (distribution coefficient); and it is those drugs that give high distribution coefficients that give the greatest physiological action, according to the Meyer-Overton theory.

A study of the areas occupied by each molecule in the surface shows that the areas increase fairly regularly as the distribution coefficient decreases and as the liminal value increases. Evidently the more powerful a compound acts as a narcotic, the more it will be adsorbed at body interfaces and the closer will the molecules be packed in the surface. The apparently big exception of trional is due to the fact that it was impossible to compare it at the same molar concentration as the other compounds because of its limited solubility.

TABLE I.

Interfacial Tensions between Aqueous Solutions of Narcotics and Nujol

Concentration (molar)	Ave. Drop Vol. (cc)	Density Aqueous Solution	$d - d_1$	Tip Radius (cm)	$\frac{f(r)}{(V^{\frac{1}{3}})}$	Interfacial Tension (Dynes per cm)
Trional						
0.012	0.21211	0.99930	0.11948	0.15008	0.7613	34.59	34.60
0.008	0.23272	0.99890	0.11908	0.15008	0.7655	37.62	
0.004	0.26016	0.99860	0.11878	0.15008	0.7738	41.50	
Butyl Chloral Hydrate						
0.100	0.14905	1.00556	0.12574	0.15008	0.7368	26.36	26.51
0.050	0.19286	1.00188	0.12206	0.15008	0.7543	32.38	32.48
0.025	0.23221	1.00004	0.12022	0.15008	0.7664	37.80	37.91
0.010	0.27306	0.99894	0.11912	0.15008	0.7774	43.49	43.47
Sulphonal						
0.080	0.24698	0.99894	0.11912	0.15008	0.7703	39.66	39.72
0.040	0.26802	0.99860	0.11878	0.15008	0.7737	42.73	42.80
0.020	0.28892	0.99840	0.11858	0.15008	0.7803	45.72	45.58
Bromal Hydrate						
0.100	0.18751	1.01710	0.13762	0.15008	0.7520	35.72	35.60
0.050	0.22186	1.00765	0.12817	0.15008	0.7655	39.85	39.73
0.025	0.26547	1.00267	0.12319	0.15008	0.7750	43.83	43.89
0.010	0.29649	1.00009	0.12061	0.15008	0.7817	47.54	47.54
Triacetin						
0.100	0.17003	1.00230	0.12282	0.15019	0.7463	28.97	28.15
0.050	0.20163	1.00025	0.12077	0.15019	0.7560	33.45	33.45
0.025	0.22989	0.99922	0.11974	0.15008	0.7663	37.30	37.36
0.010	0.25780	0.99861	0.11913	0.15019	0.7733	41.31	41.18

TABLE I. (Continued)

Diacetin

0.100	:	0.19528	:	1.00160	:	0.12212	:	0.15019	:	0.7550	:	32.76	:	32.86
0.050	:	0.22007	:	0.99990	:	0.12042	:	0.15019	:	0.7630	:	36.01	:	36.12
0.025	:	0.23615	:	0.99905	:	0.11957	:	0.15019	:	0.7673	:	38.21	:	38.21
0.010	:	0.25504	:	0.99854	:	0.11906	:	0.15019	:	0.7725	:	40.82	:	40.82

Chloral Hydrate

0.100	:	0.20690	:	1.01280	:	0.13298	:	0.15008	:	0.7590	:	37.67	:
0.050	:	0.24415	:	1.00550	:	0.12568	:	0.15008	:	0.7697	:	41.43	:
0.025	:	0.27542	:	1.00185	:	0.12203	:	0.15008	:	0.7772	:	44.94	:
0.010	:	0.29937	:	0.99970	:	0.11988	:	0.15008	:	0.7823	:	47.68	:

Ethyl Carbamate

0.100	:	0.27195	:	0.99932	:	0.11984	:	0.15019	:	0.7773	:	43.54	:	43.54
0.050	:	0.28950	:	0.99876	:	0.11928	:	0.15019	:	0.7805	:	45.95	:	45.95
0.025	:	0.30064	:	0.99848	:	0.11900	:	0.15019	:	0.7826	:	47.58	:	47.37
0.010	:	0.30654	:	0.99831	:	0.11883	:	0.15019	:	0.7838	:	48.34	:	48.20

Monacetin

0.100	:	0.23221	:	1.00090	:	0.12142	:	0.15019	:	0.7661	:	38.17	:	38.28
0.050	:	0.24973	:	0.99905	:	0.11957	:	0.15019	:	0.7707	:	40.20	:	40.27
0.025	:	0.26016	:	0.99862	:	0.11914	:	0.15019	:	0.7737	:	41.60	:	41.60
0.010	:	0.27246	:	0.99837	:	0.11889	:	0.15019	:	0.7776	:	43.33	:	43.19

Methyl Carbamate

0.100	:	0.17740	:	0.99935	:	0.11987	:	0.15019	:	0.7487	:	29.45	:	29.54
0.050	:	0.18007	:	0.99877	:	0.11929	:	0.15019	:	0.7495	:	29.65	:	29.87
0.025	:	0.18498	:	0.99848	:	0.11900	:	0.15019	:	0.7512	:	30.34	:	30.52
0.010	:	0.18807	:	0.99831	:	0.11883	:	0.15019	:	0.7522	:	30.81	:	30.89

Ethyl Methylcarbamate

0.100	:	0.23400	:	0.99896	:	0.11948	:	0.15019	:	0.7674	:	37.84	:	37.84
0.050	:	0.25701	:	0.99858	:	0.11910	:	0.15019	:	0.7728	:	41.07	:	41.20
0.025	:	0.27857	:	0.99839	:	0.11891	:	0.15019	:	0.7780	:	44.02	:	44.43
0.010	:	0.29343	:	0.99827	:	0.11879	:	0.15019	:	0.7810	:	46.28	:	46.41

TABLE II.

Interfacial Tensions between Aqueous Solutions of Narcotics and Nujol Solution of Lecithin

Concentration (molar)	Ave. Drop Vol. (cc)	Density Aqueous Solution	$d - d_1$	Tip Radius (cm)	$f\left(\frac{r}{\sqrt[3]{V}}\right)$	Interfacial Tension (Dynes per cm)	
Trional							
0.012	0.13667	0.99930	0.12001	0.15019	0.7310	23.14	23.46
0.008	0.14650	0.99890	0.11961	0.15019	0.7357	24.57	24.90
0.004	0.16060	0.99860	0.11931	0.15019	0.7415	26.94	26.28
Butyl Chloral Hydrate							
0.100	0.02865	1.00556	0.12627	0.15019	0.6545	5.85	5.63
0.050	0.08969	1.00188	0.12257	0.15019	0.7075	16.14	16.14
0.025	0.12838	1.00004	0.12075	0.15019	0.7272	22.07	22.19
0.010	0.17014	0.99894	0.11965	0.15019	0.7457	28.35	28.35
Sulphonal							
0.080	0.14847	0.99894	0.11965	0.15019	0.7462	24.56	24.88
0.040	0.15437	0.99860	0.11931	0.15019	0.7390	26.04	25.72
0.020	0.18092	0.99840	0.11911	0.15019	0.7498	29.84	29.84
Bromal Hydrate							
0.100	0.05900	1.01710	0.13781	0.15019	0.6877	12.28	12.28
0.050	0.08063	1.00765	0.12836	0.15019	0.7022	15.31	15.31
0.025	0.09964	1.00267	0.12338	0.15019	0.7125	18.39	17.68
0.010	0.11995	1.00009	0.12080	0.15019	0.7254	21.08	20.41
Triacetin							
0.100	0.10521	1.00230	0.12301	0.15019	0.7155	18.60	18.96
0.050	0.13044	1.00025	0.12096	0.15019	0.7278	22.40	22.51
0.025	0.14618	0.99922	0.11993	0.15019	0.7355	24.64	24.75
0.010	0.15797	0.99861	0.11932	0.15019	0.7407	26.32	26.32

TABLE II. (Continued)

Diacetin

0.100	:	0.11307	:	1.00160	: 0.12231	: 0.15019	: 0.7198	:	19.78	:	20.12
0.050	:	0.13634	:	0.99990	: 0.12061	: 0.15019	: 0.7307	:	23.26	:	23.26
0.025	:	0.14306	:	0.99905	: 0.11976	: 0.15019	: 0.7340	:	24.65	:	24.65
0.010	:	0.15142	:	0.99854	: 0.11925	: 0.15019	: 0.7378	:	25.09	:	25.09

Chloral Hydrate

0.100	:	0.12979	:	1.01280	: 0.13351	: 0.15019	: 0.7279	:	24.72	:	24.72
0.050	:	0.14454	:	1.00550	: 0.12621	: 0.15019	: 0.7345	:	25.62	:	25.96
0.025	:	0.14945	:	1.00185	: 0.12256	: 0.15019	: 0.7368	:	25.82	:	25.82
0.010	:	0.16027	:	0.99970	: 0.12041	: 0.15019	: 0.7415	:	26.86	:	27.19

Ethyl Carbamate

0.100	:	0.10816	:	0.99932	: 0.12003	: 0.15019	: 0.7195	:	18.74	:	18.74
0.050	:	0.14552	:	0.99876	: 0.11947	: 0.15019	: 0.7350	:	24.34	:	24.78
0.025	:	0.16322	:	0.99848	: 0.11919	: 0.15019	: 0.7428	:	27.53	:	26.87
0.010	:	0.16781	:	0.99831	: 0.11902	: 0.15019	: 0.7447	:	27.74	:	27.85

Monacetin

0.100	:	0.14306	:	1.00090	: 0.12161	: 0.15019	: 0.7337	:	25.04	:	24.37
0.050	:	0.15142	:	0.99905	: 0.11976	: 0.15019	: 0.7378	:	25.52	:	25.52
0.025	:	0.15850	:	0.99862	: 0.11933	: 0.15019	: 0.7410	:	26.31	:	26.44
0.010	:	0.16453	:	0.99837	: 0.11908	: 0.15019	: 0.7432	:	27.16	:	27.50

Methyl Carbamate

0.100	:	0.20090	:	0.99935	: 0.12006	: 0.15019	: 0.7565	:	32.86	:	33.34
0.050	:	0.22980	:	0.99877	: 0.11948	: 0.15019	: 0.7657	:	37.40	:	37.08
0.025	:	0.23373	:	0.99848	: 0.11919	: 0.15019	: 0.7663	:	37.58	:	37.91
0.010	:	0.23996	:	0.99831	: 0.11902	: 0.15019	: 0.7695	:	38.32	:	38.23

Ethyl Methylcarbamate

0.100	:	0.13864	:	0.99896	: 0.11967	: 0.15019	: 0.7318	:	23.38	:	23.71
0.050	:	0.15339	:	0.99858	: 0.11929	: 0.15019	: 0.7387	:	25.72	:	25.72
0.025	:	0.16519	:	0.99839	: 0.11910	: 0.15019	: 0.7437	:	27.47	:	27.47
0.010	:	0.16781	:	0.99827	: 0.11898	: 0.15019	: 0.7447	:	28.06	:	27.66

TABLE III.

Correlation between Interfacial Tensions, Adsorptions, Distribution Coefficients,
and Liminal Values of Narcotics against Nujol

Substance	Distribu- tion Coef- ficient (1)	Liminal Value (1)	Adsorption Mols per sq. cm. at 0.025 M	Interfacial Tension at 0.025 M		Area of Molecule in Surface per sq. cm.
Trional (2)	4.46	0.0018	2.9140×10^{-10}	37.62		5.572×10^{-15}
Tetronal (3)	4.04	0.0013				
Butyl Chloral Hydrate	1.59	0.0020	2.9315×10^{-10}	37.80	37.91	5.441×10^{-15}
Sulphonal	1.11	0.0060	1.7635×10^{-10}	42.73	42.80	8.851×10^{-15}
Bromal Hydrate	0.66	0.0020	2.0410×10^{-10}	43.83	43.89	7.704×10^{-15}
Triacetin	0.30	0.0100	1.7960×10^{-10}	37.30	37.36	8.699×10^{-15}
Diacetin	0.23	0.0150	1.7240×10^{-10}	38.21	38.21	9.042×10^{-15}
Chloral Hydrate	0.22	0.0200	1.6240×10^{-10}	44.94		9.566×10^{-15}
Ethyl Methyl- Carbamate (4)			1.5490×10^{-10}	44.05	44.46	10.001×10^{-15}
Ethyl Carbamate	0.14	0.0400	0.6665×10^{-10}	47.58	47.37	21.500×10^{-15}
Monacetin	0.06	0.0500	0.7448×10^{-10}	41.60	41.60	19.510×10^{-15}
Methyl Carbamate	0.04	0.4000	0.2709×10^{-10}	30.41	30.59	44.370×10^{-15}
Water				54.26		

(1) Values taken from May, " The Chemistry of Synthetic Drugs", p. 47.
(2) Adsorption value, interfacial tension, and area determined at 0.008 M concentration.
(3) Could not be obtained for use.
(4) May does not include this compound.

TABLE IV.

Correlation between Interfacial Tensions, Adsorptions, Distribution Coefficients,
and Liminal Values of Narcotics against Nujol Solution of Lecithin

Substance	:Distribu- :tion Coef- :ficient (1)	: Liminal :Value (1)	: Adsorption :Mols per sq. cm.: : at 0.025 M :	Interfacial Tension at 0.025 M		:Area of Molecule : in Surface : per sq. cm.
Trional (2)	: 4.46	: 0.0018	: 1.3500×10^{-10} :	24.57	24.90	: 11.810×10^{-15}
Tetronal (3)	: 4.04	: 0.0013	:			:
Butyl Chloral	:	:	:			:
Hydrate	: 1.59	: 0.0020	: 3.3040×10^{-10} :	22.07	22.19	: 4.846×10^{-15}
Sulphonal	: 1.11	: 0.0060	: 3.0030×10^{-10} :	26.04	25.72	: 5.316×10^{-15}
Bromal Hydrate	: 0.66	: 0.0020	: 1.5785×10^{-10} :	18.39	17.68	: 9.825×10^{-15}
Triacetin	: 0.30	: 0.0100	: 1.0045×10^{-10} :	24.64	24.75	: 14.926×10^{-15}
Diacetin	: 0.23	: 0.0150	: 0.4420×10^{-10} :	24.65	24.65	: 30.389×10^{-15}
Chloral Hydrate	: 0.22	: 0.0200	: 0.2336×10^{-10} :	25.82	25.82	: 49.315×10^{-15}
Ethyl Methyl-	:	:	:			:
Carbamate (4)	:	:	: 0.7904×10^{-10} :	27.47	27.47	: 18.511×10^{-15}
Ethyl Carbamate	: 0.14	: 0.0400	: 0.8715×10^{-10} :	27.53	26.87	: 16.969×10^{-15}
Monacetin	: 0.06	: 0.0500	: 0.4746×10^{-10} :	26.31	26.44	: 28.668×10^{-15}
Methyl Carbamate	: 0.04	: 0.4000	: 0.2368×10^{-10} :	37.58	37.91	: 48.852×10^{-15}
Water	:	:	:	29.05	29.00	:

(1) Values taken from May, "The Chemistry of Synthetic Drugs", p. 47.
(2) Adsorption value, interfacial tension, and area determined at 0.008 M concentration.
(3) Could not be obtained for use.
(4) May does not include this compound.
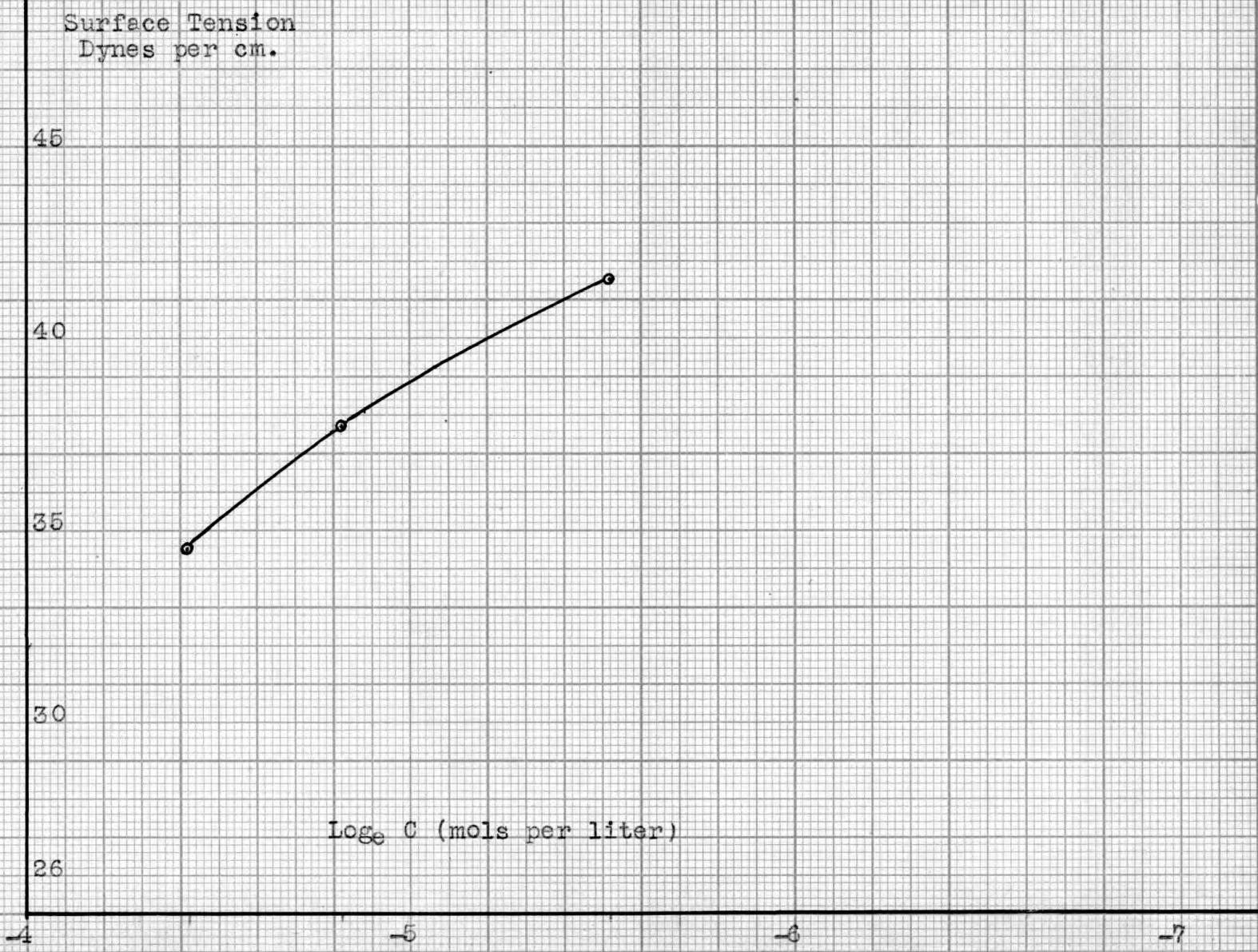
Fig. 1.   AQUEOUS TRIONAL — NUJOL INTERFACE
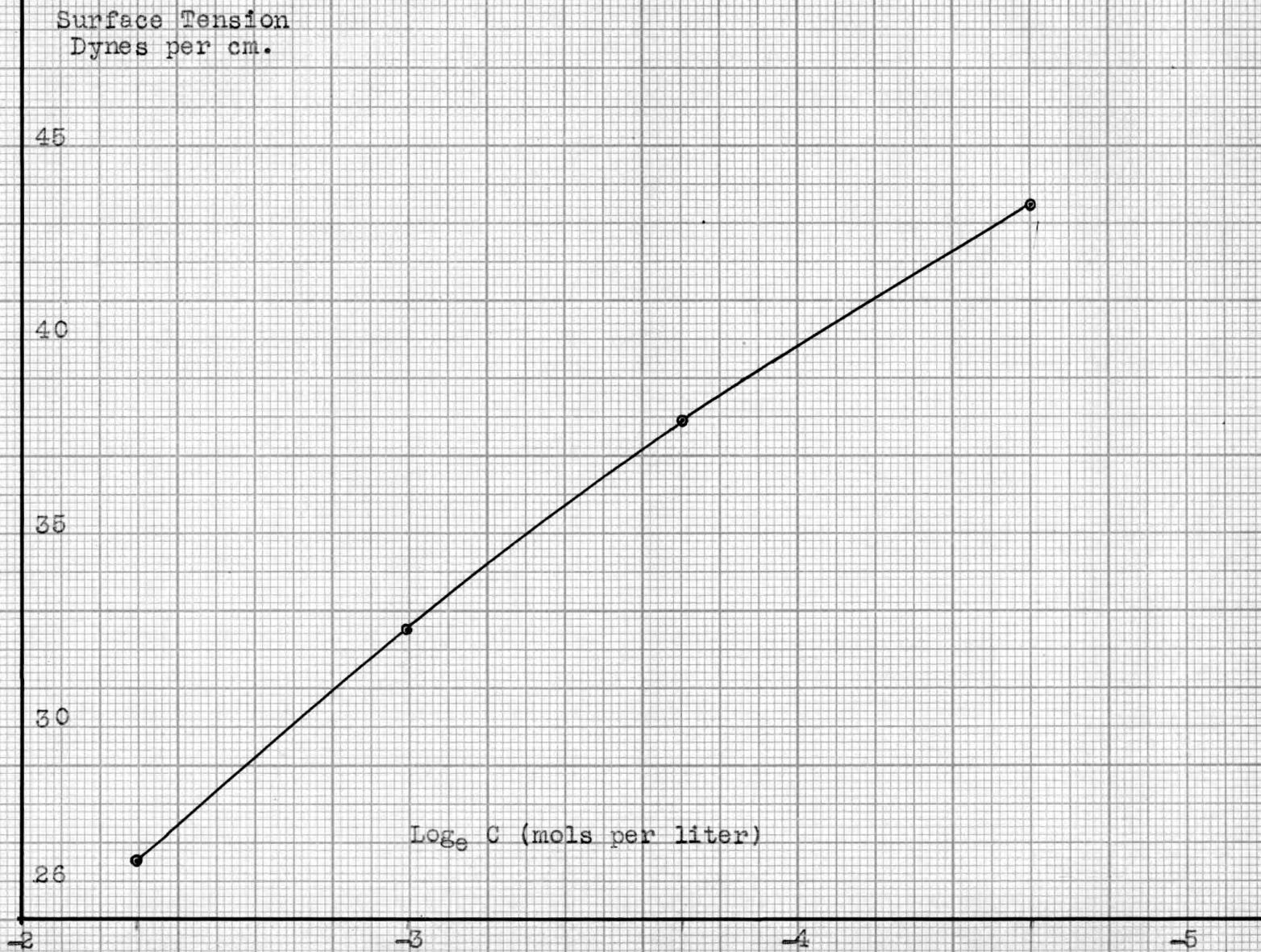
Fig. 2. AQUEOUS BUTYL CHLORAL HYDRATE – NUJOL INTERFACE
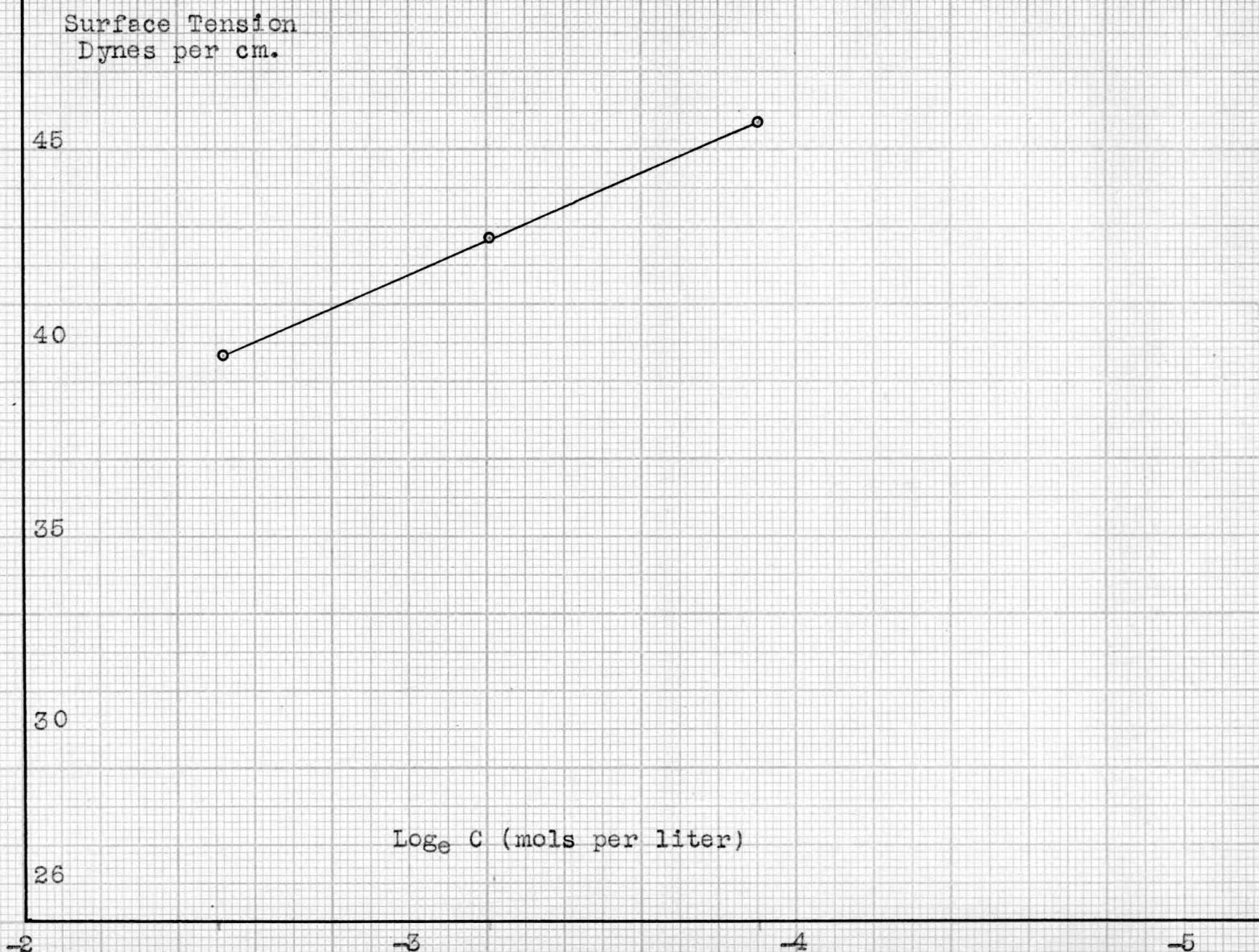
Fig. 3. AQUEOUS SULPHONAL — NUJOL INTERFACE

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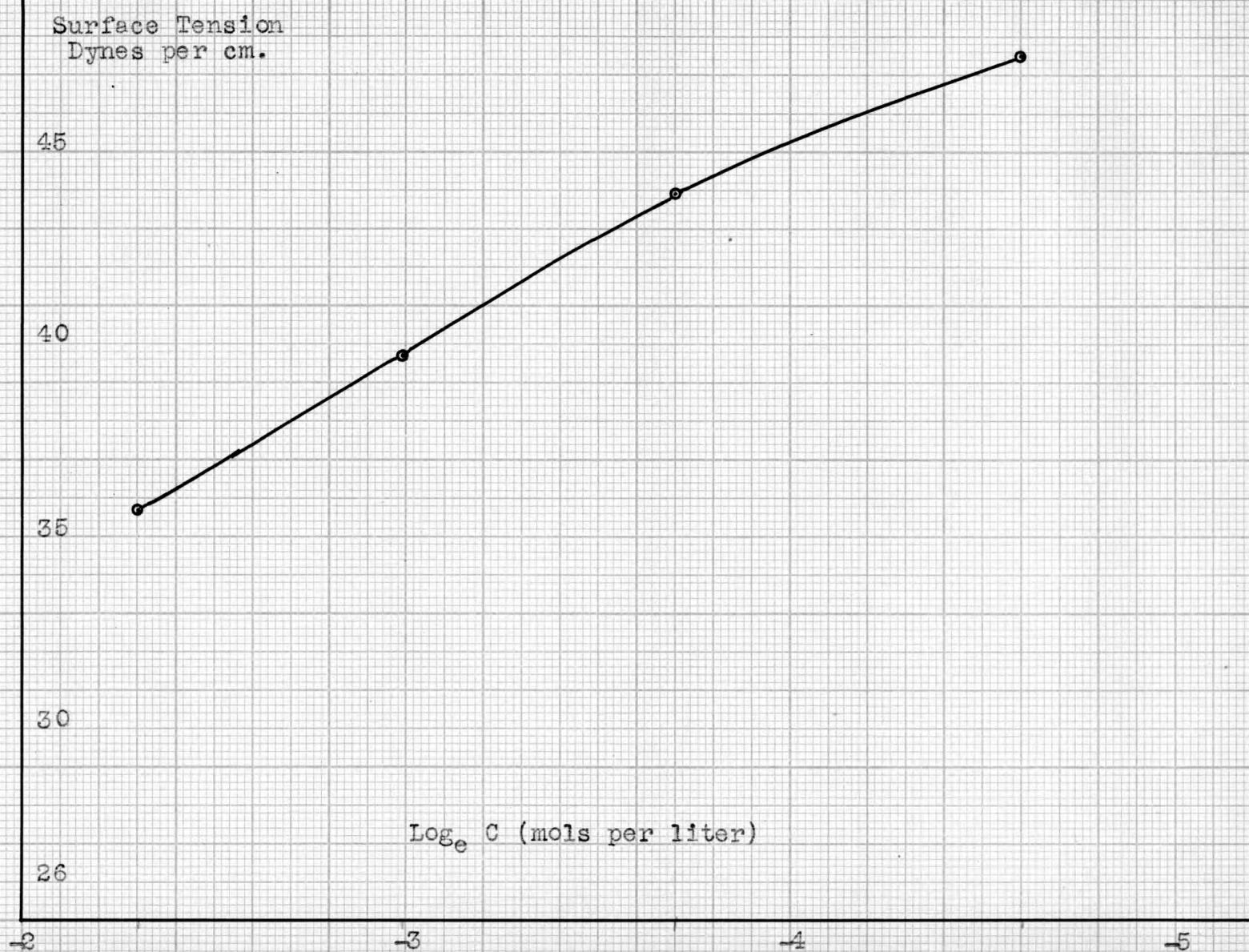
Fig. 4. AQUEOUS BROMAL HYDRATE — NUJOL INTERFACE
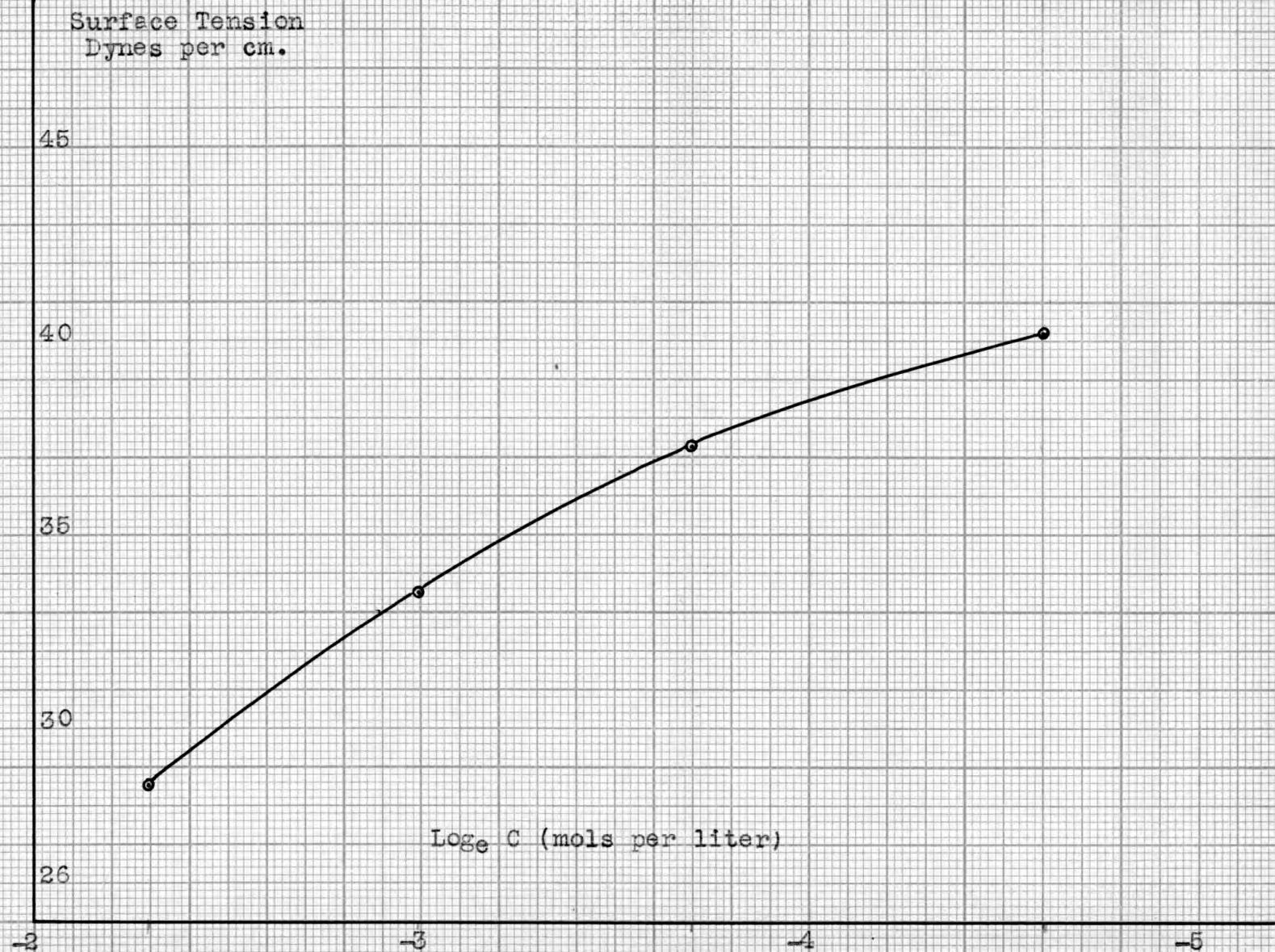
Fig. 5. AQUEOUS TRIACETIN — NUJOL INTERFACE
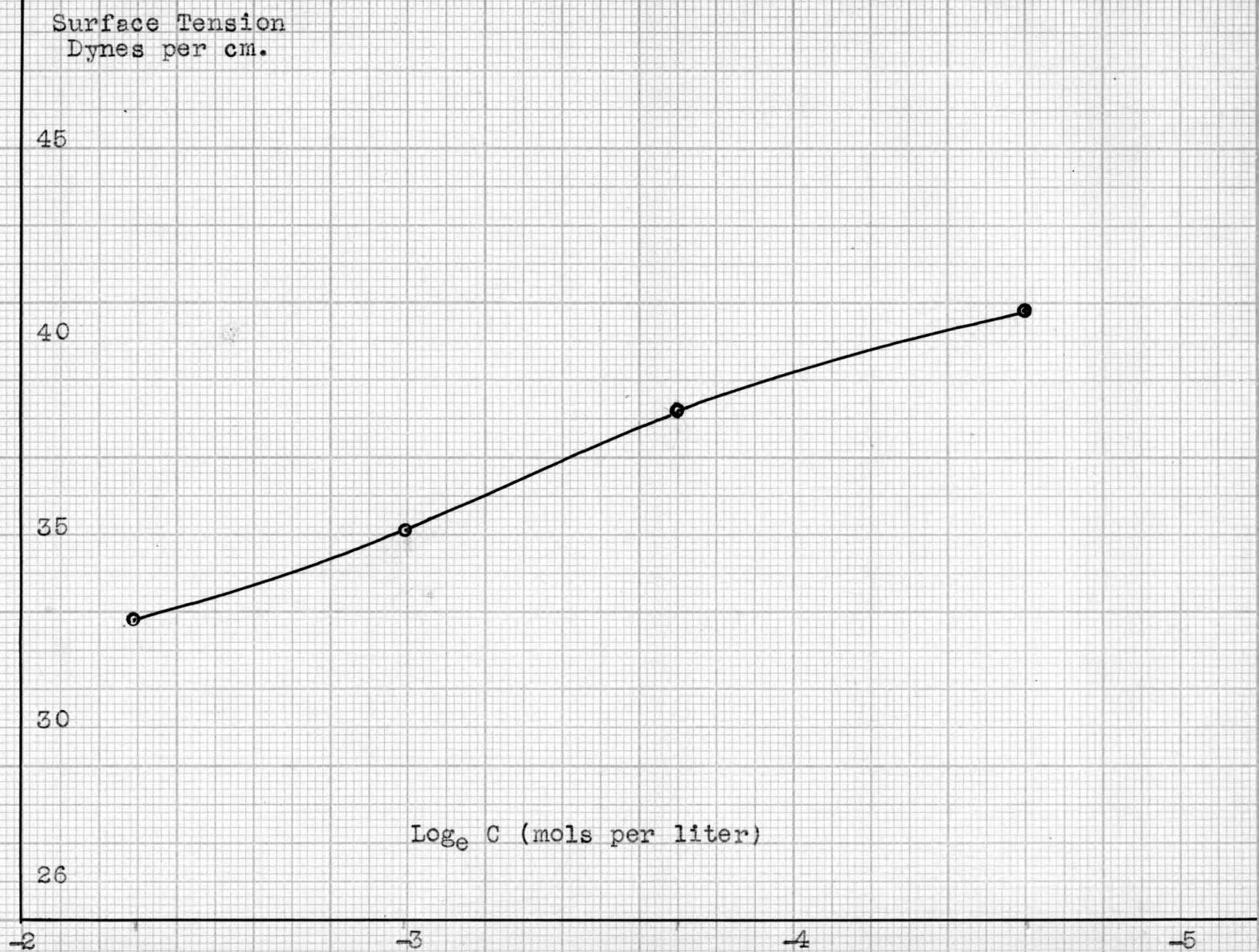
Fig. 6. AQUEOUS DIACETIN — NUJOL INTERFACE
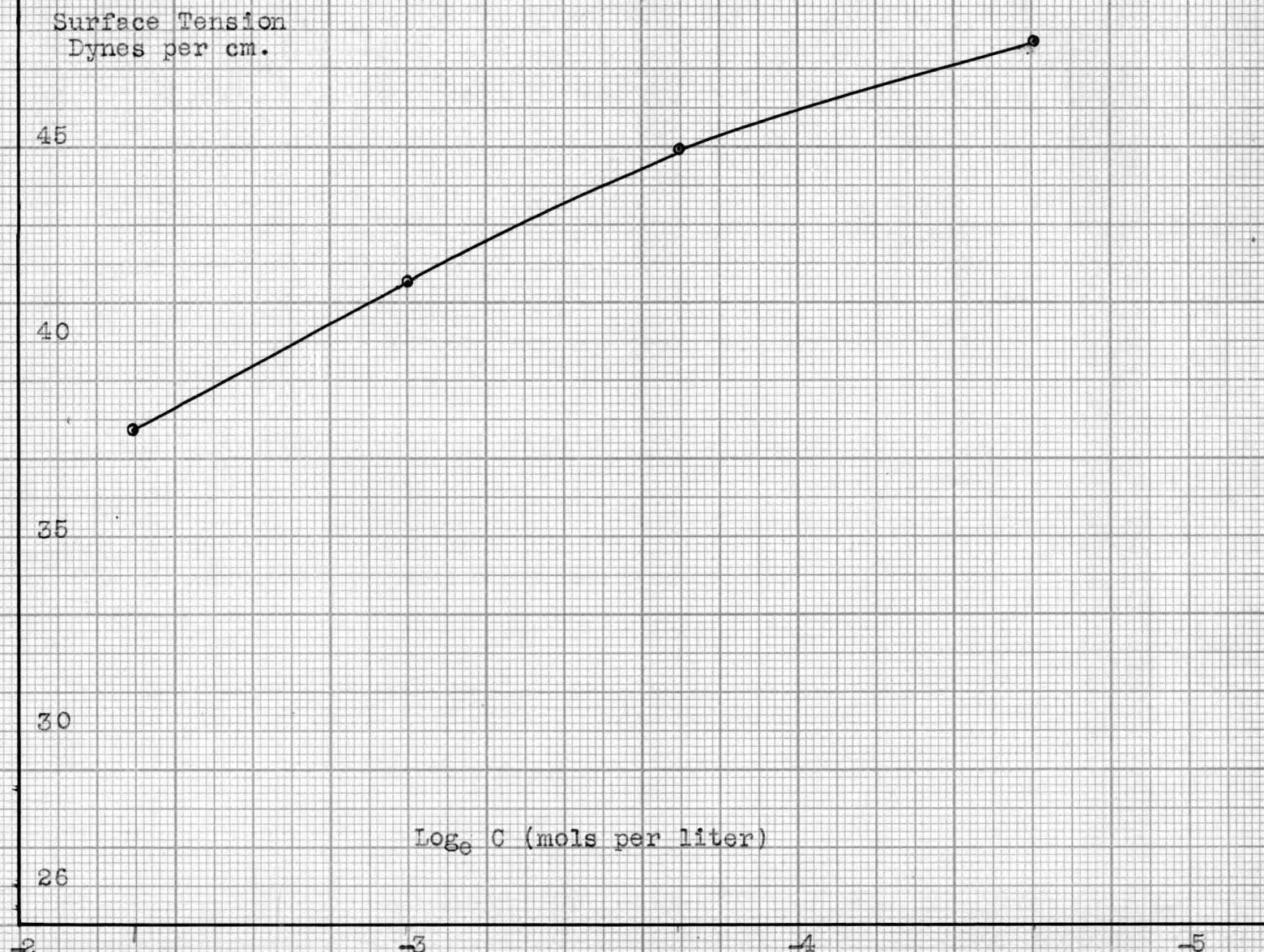
Fig. 7. AQUEOUS CHLORAL HYDRATE — NUJOL INTERFACE

Fig. 8. AQUEOUS ETHYL METHYLCARBAMATE — NUJOL INTERFACE

Fig. 9.   AQUEOUS ETHYL CARBAMATE - NUJOL INTERFACE

Fig.10. AQUEOUS MONACETIN — NUJOL INTERFACE

Fig. 11.   AQUEOUS METHYL CARBAMATE - NUJOL INTERFACE

Surface Tension
Dynes per cm.

30

25

20

Log$_e$ C (mols per liter)

15

11

-4   -5   -6   -7
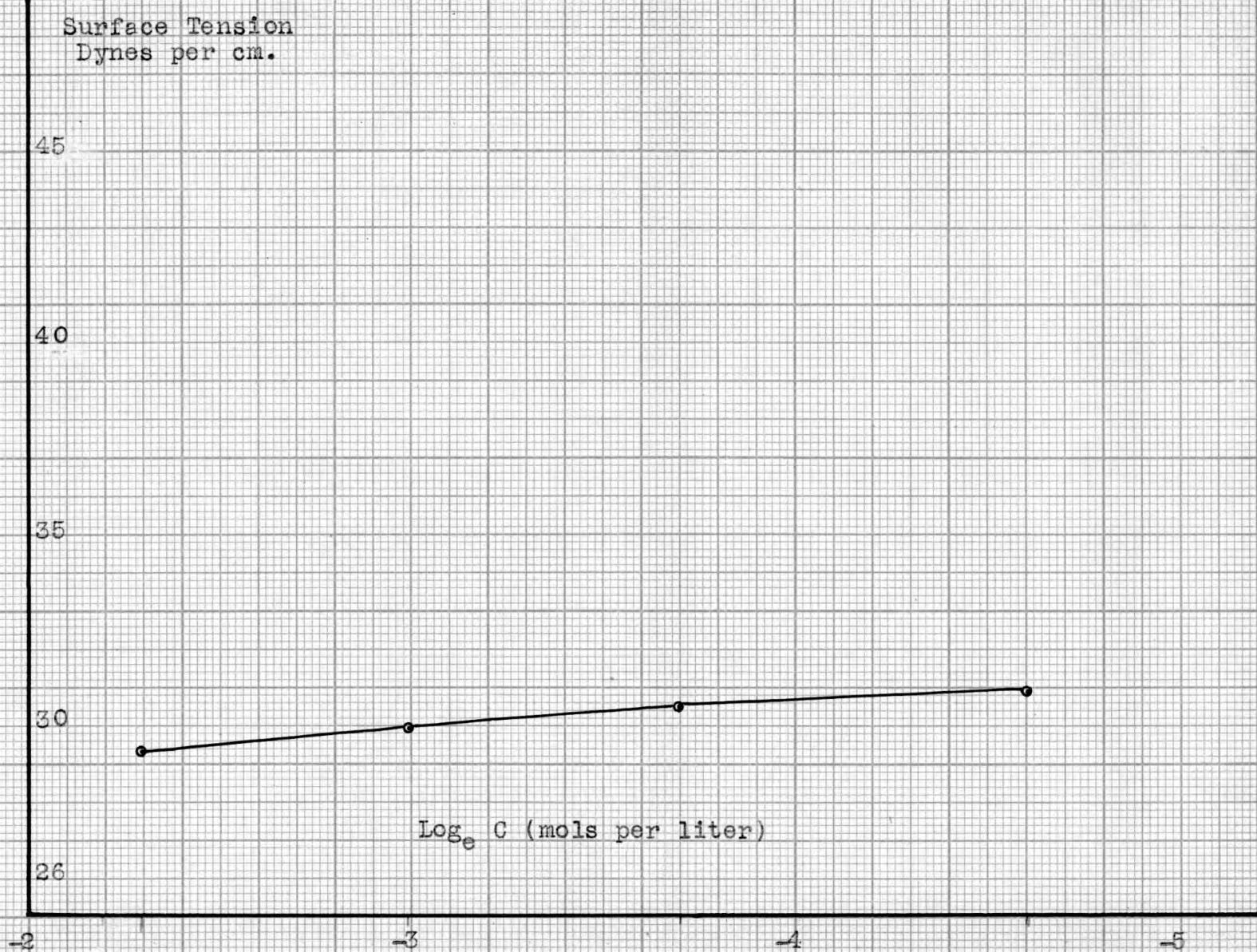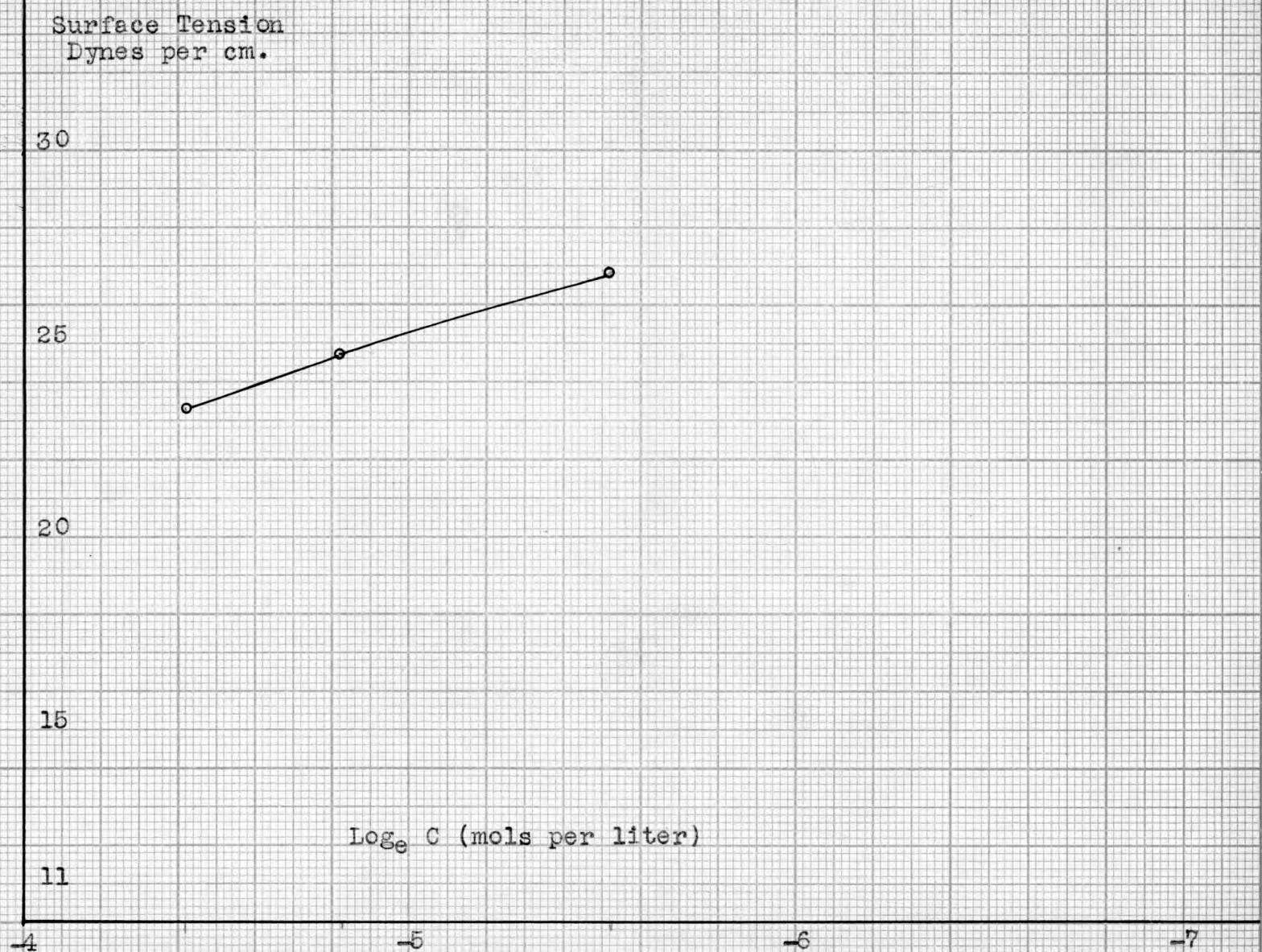
Fig. 12.   AQUEOUS TRIONAL — NUJOL LECITHIN INTERFACE
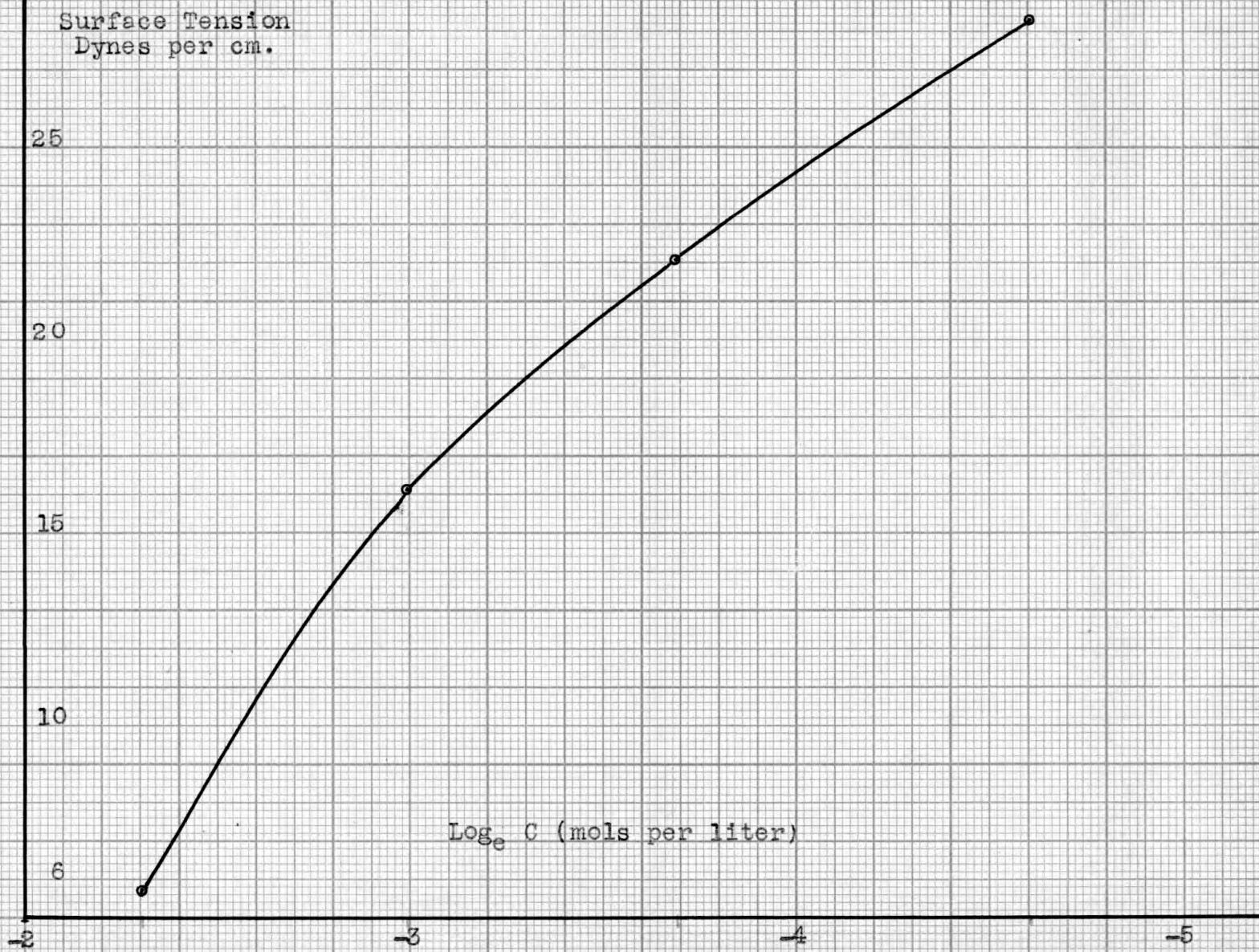
Fig. 13. AQUEOUS CHLORAL BUTYL HYDRATE — NUJOL LECITHIN INTERFACE
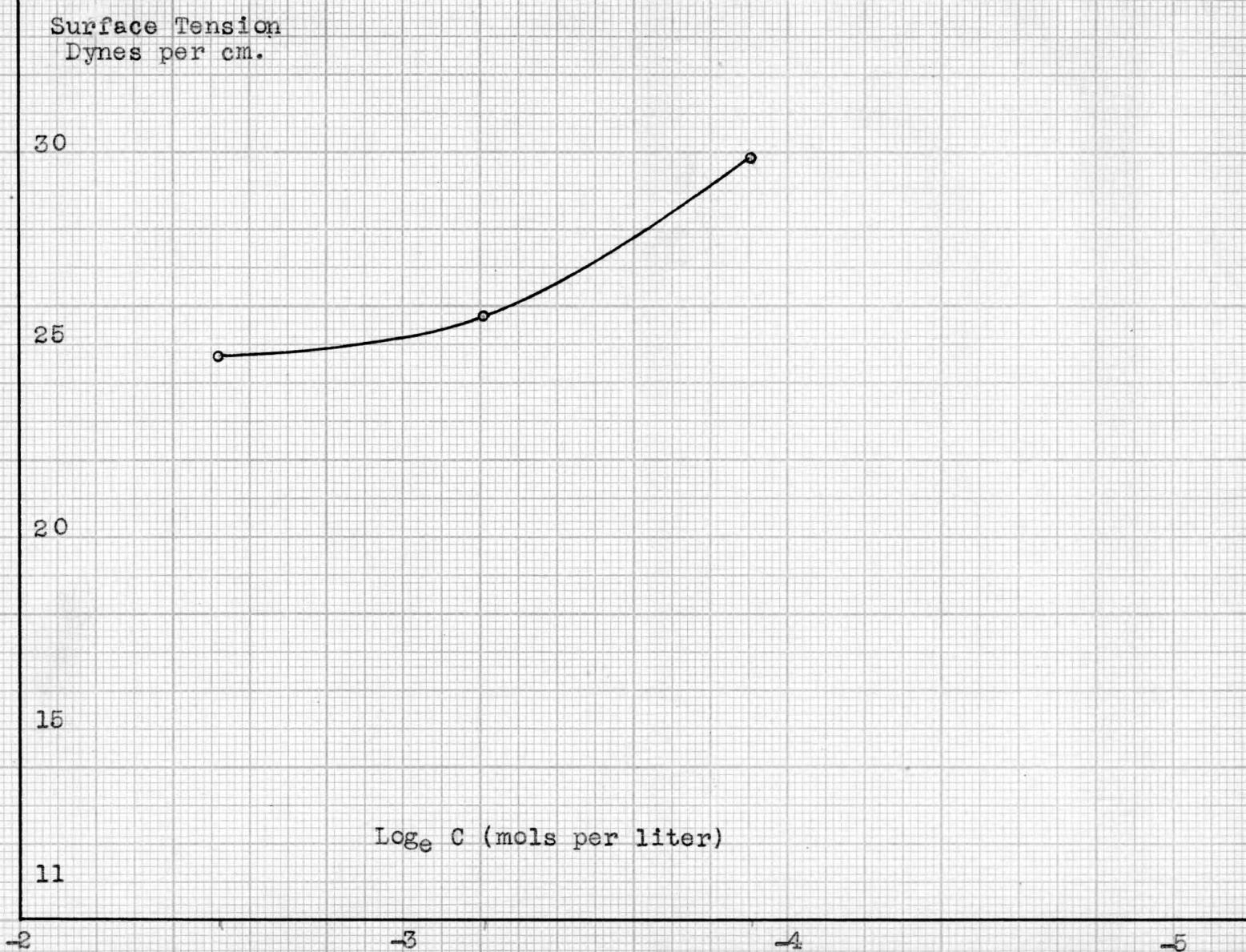
Fig.14. AQUEOUS SULPHONAL — NUJOL LECITHIN INTERFACE
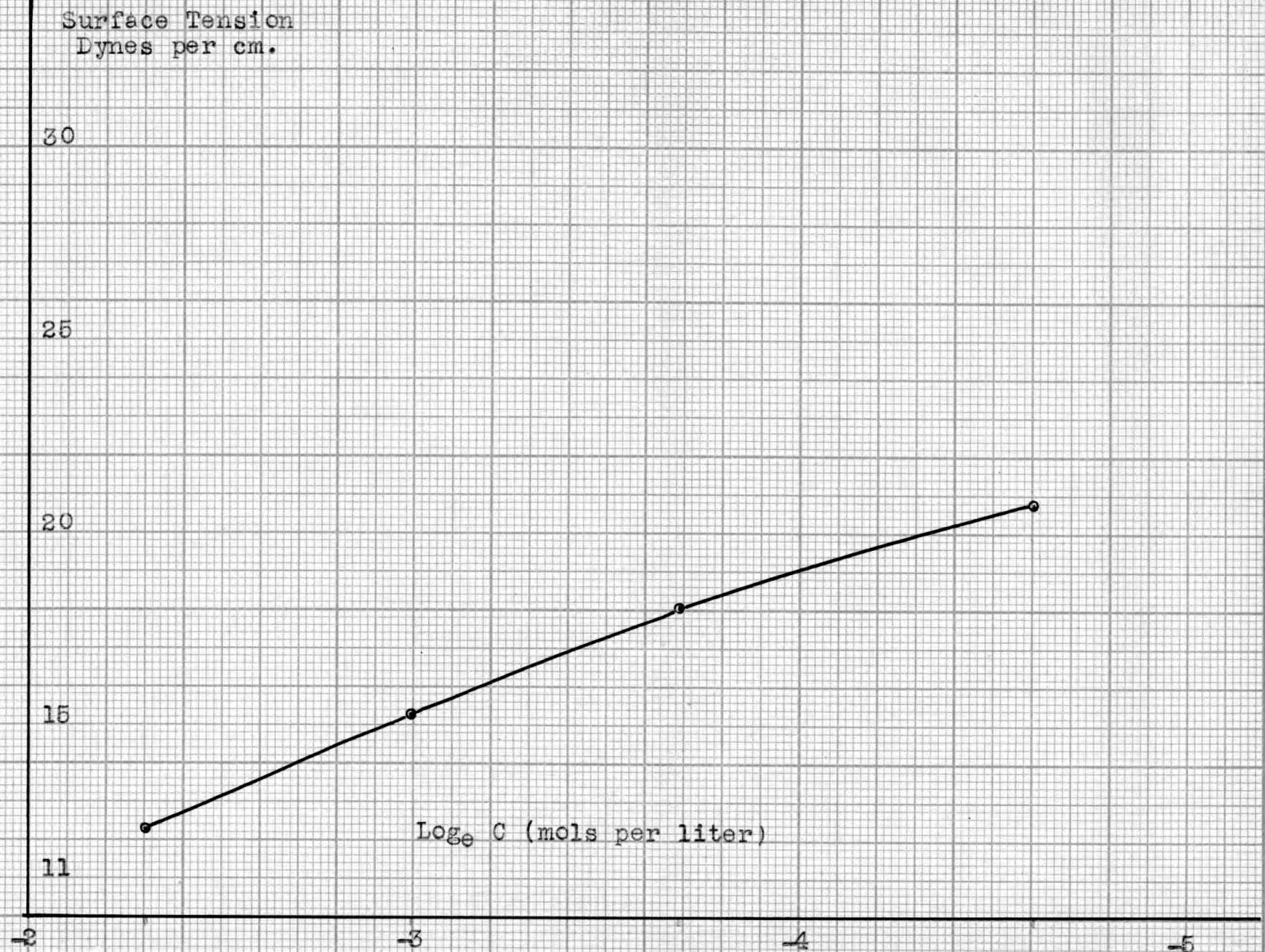
Fig.15. AQUEOUS BROMAL HYDRATE — NUJOL LECITHIN INTERFACE
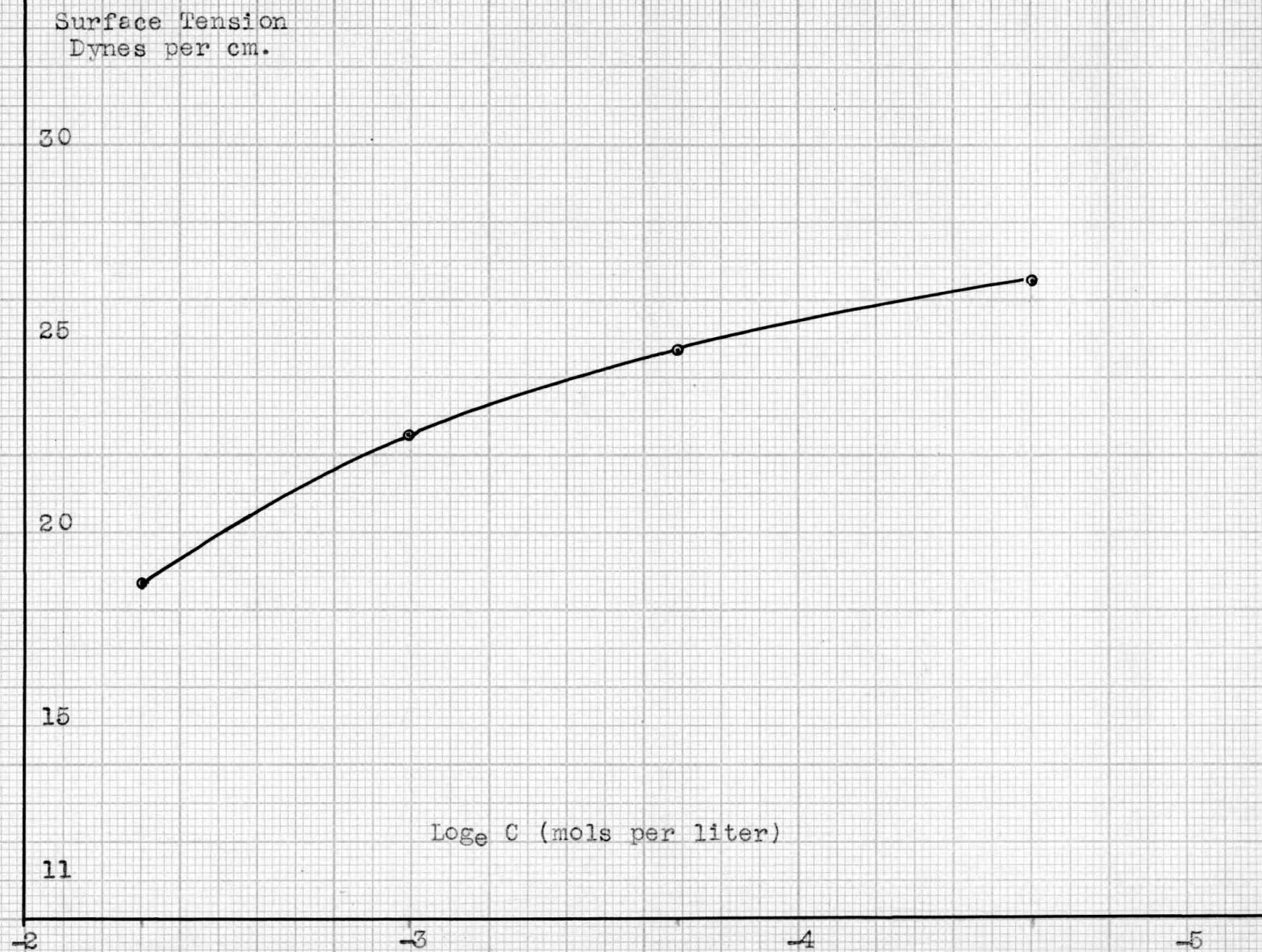
Fig. 16. AQUEOUS TRIACETIN — NUJOL LECITHIN INTERFACE
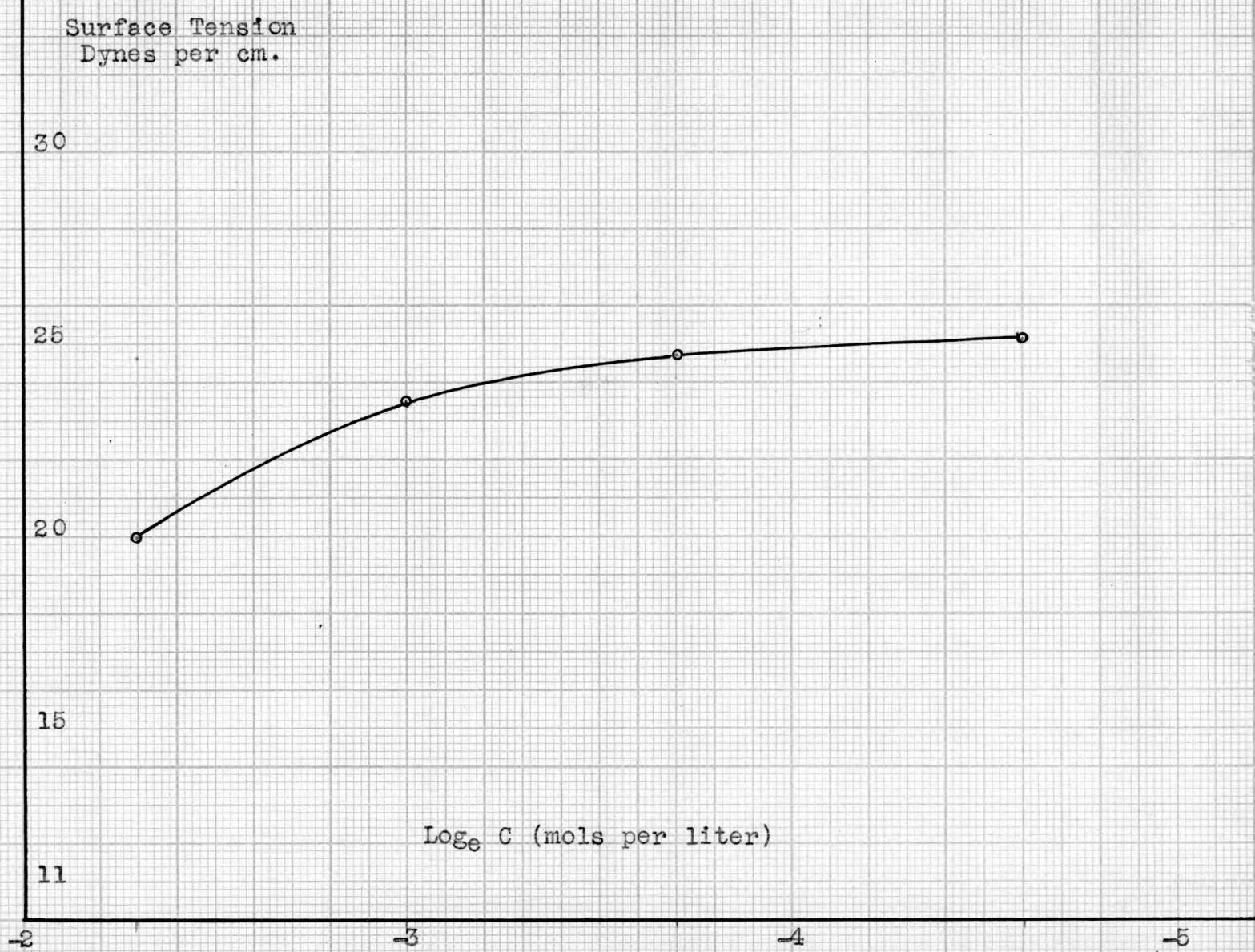
Fig.17. AQUEOUS DIACETIN — NUJOL LECITHIN INTERFACE
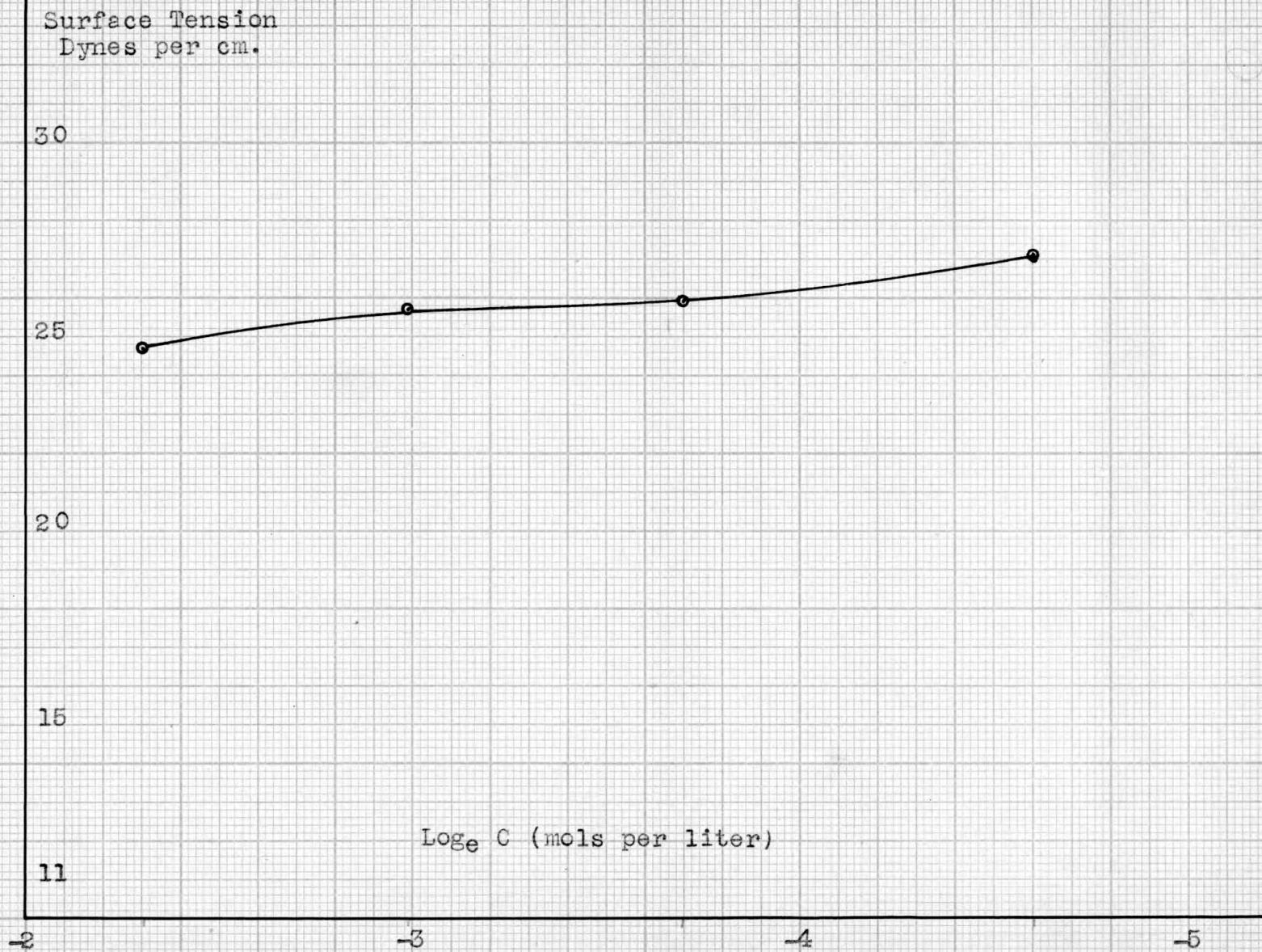
Fig.18.   AQUEOUS CHLORAL HYDRATE — NUJOL LECITHIN INTERFACE

Fig.19. AQUEOUS ETHYL METHYLCARBAMATE — NUJOL LECITHIN INTERFACE
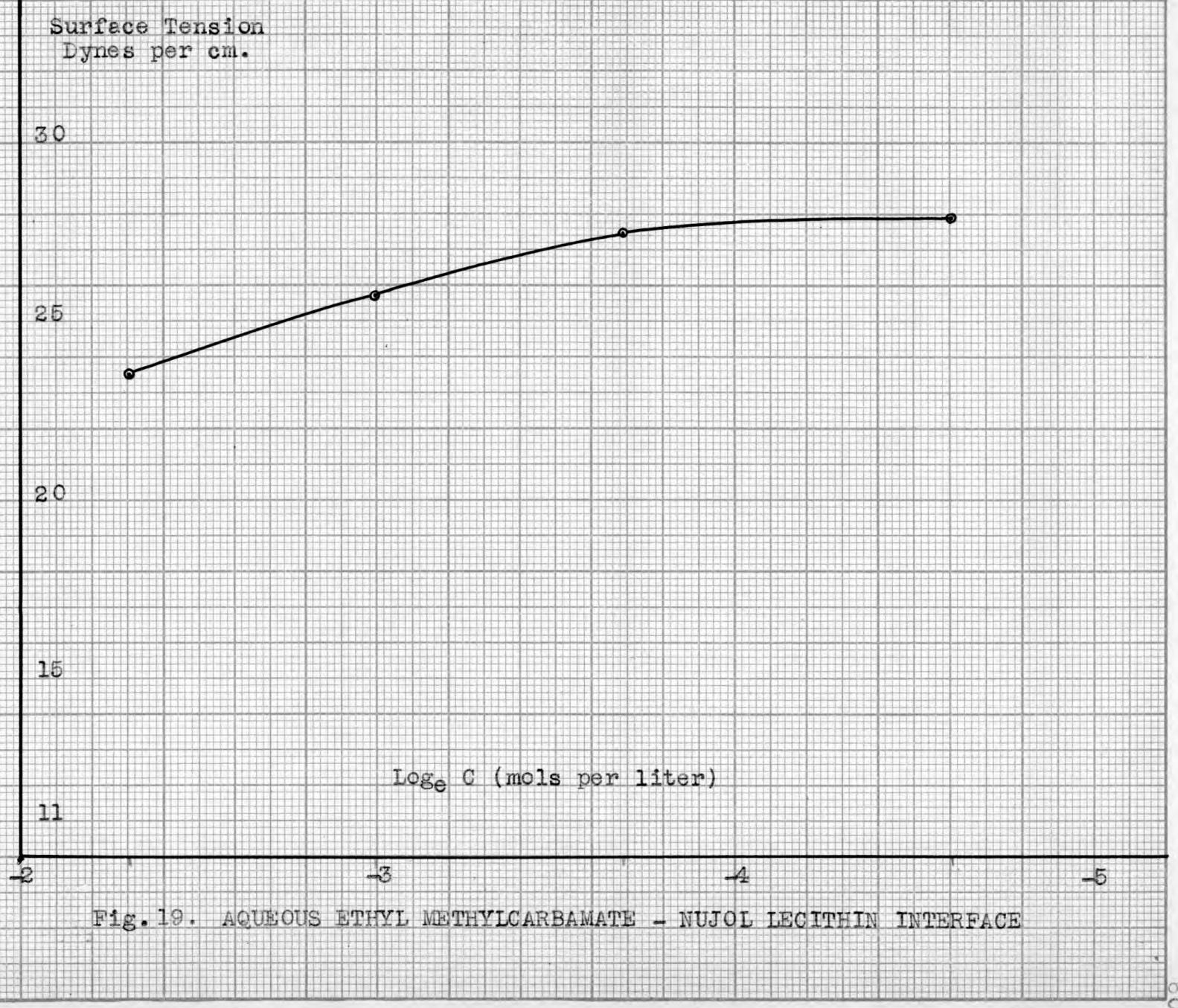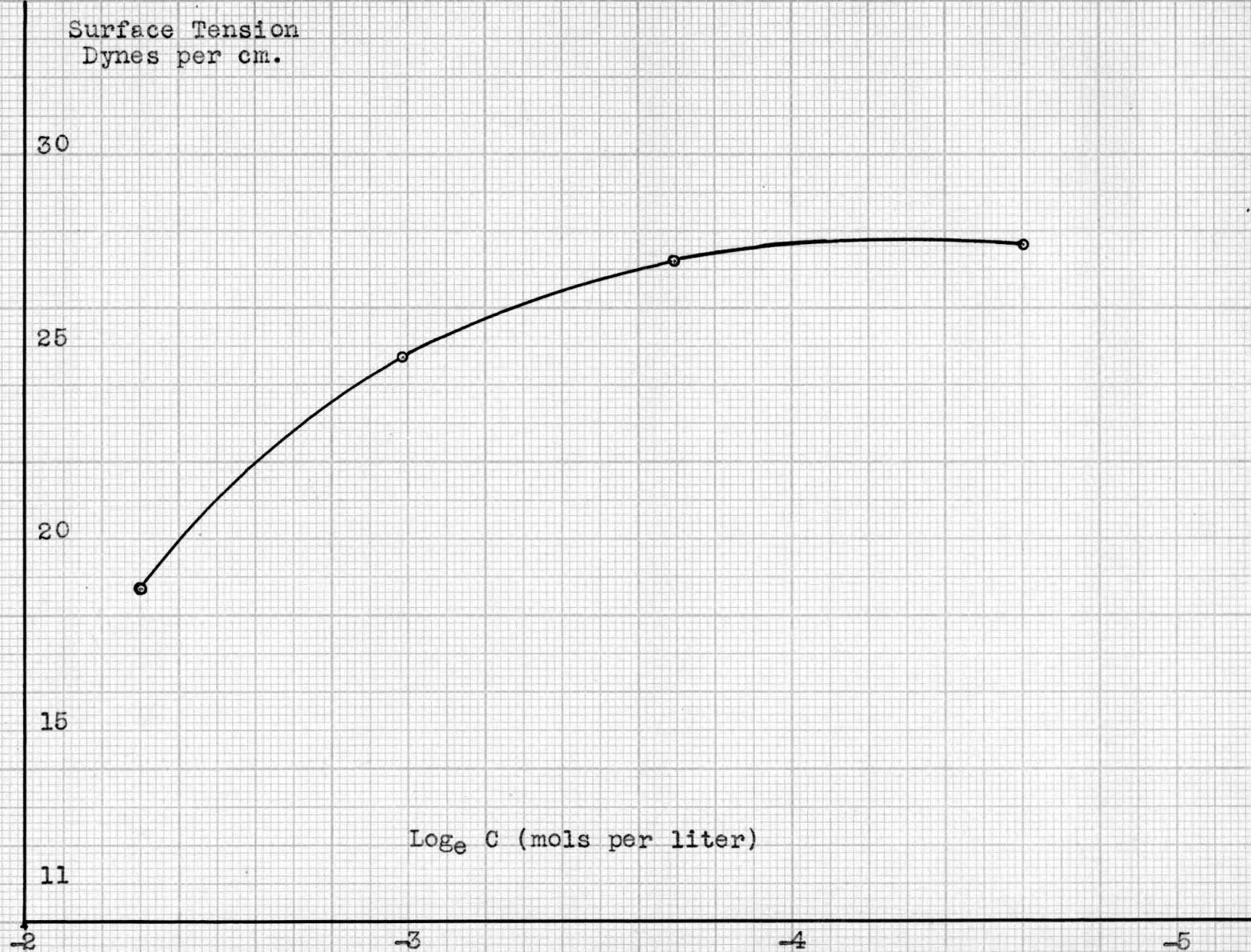
Fig.20. AQUEOUS ETHYL CARBAMATE – NUJOL LECITHIN INTERFACE
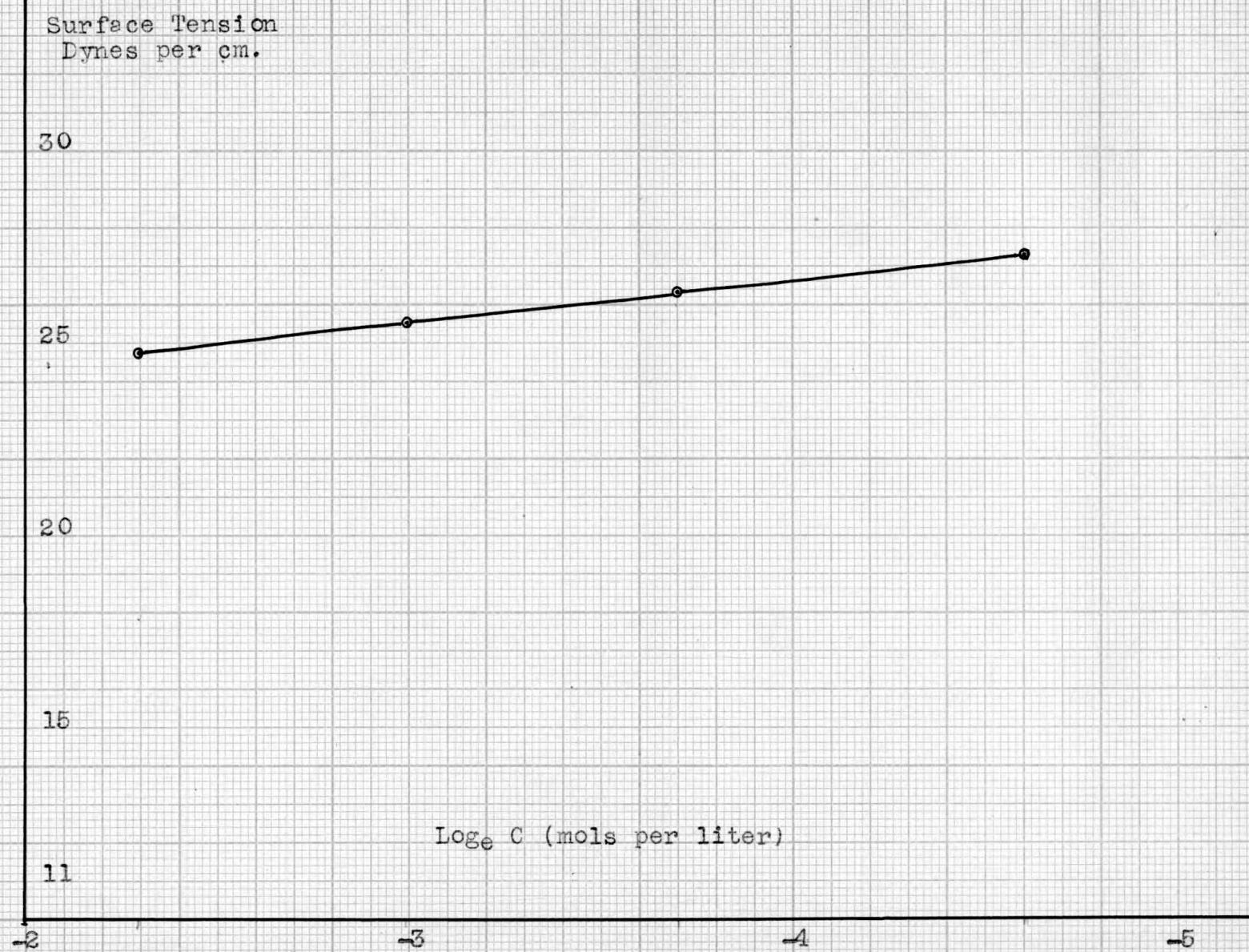
Fig.21. AQUEOUS MONACETIN — NUJOL LECITHIN INTERFACE
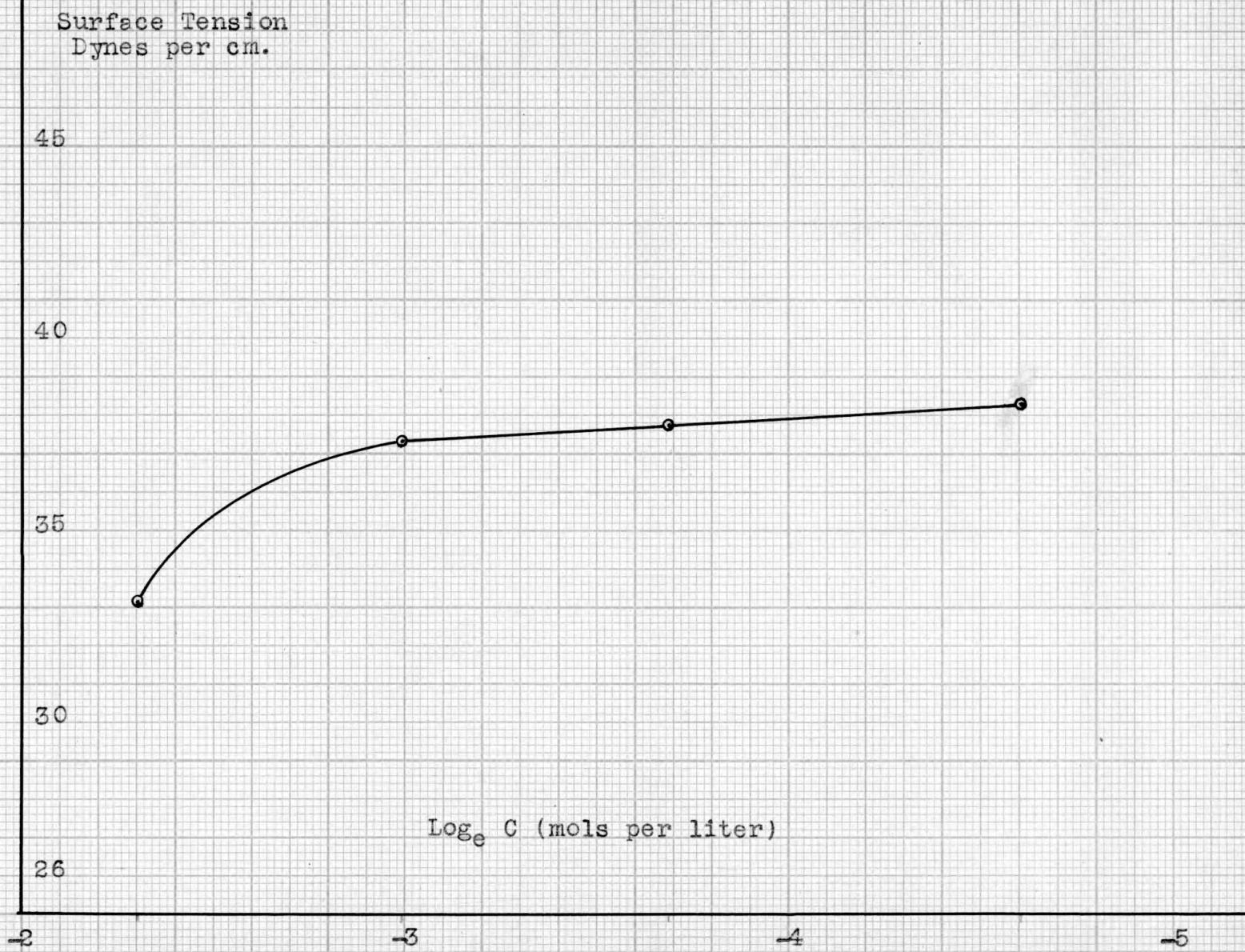
Fig.22. AQUEOUS METHYL CARBAMATE — NUJOL LECITHIN INTERFACE

SUMMARY

1. A short description of narcotics and anaesthetics
is given, and their nature and chemical structure is dis-
cussed, showing their great dissimilarity in molecular
structure. The effect on narcotic power of adding chemical
groups to molecules is discussed briefly, using a few prin-
cipal groups as examples.

2. The many theories of narcotic action are so far
inadequate or wholly untenable. There are both chemical and
physical theories of narcotic action, with Ehrlich's and
Meyer-Overton's theories respective examples.

3. The Verworm theory of sleep is given and natural
sleep is compared with the narcotic insensibility. It is
found that narcotic sleep can not replace natural sleep be-
cause it lacks the restitution properties of natural sleep.

4. The theory of Meyer-Overton for narcotic action is
advanced. It states that a drug's neuro-potent action de-
pends on the ratio of its solubility in fats to that in
water, or what is termed its distribution coefficient.
When the distribution coefficient is large, so is the drug

power. Meyer's liminal values are described.

5. Interfacial surface tensions are discussed with their relationship to narcosis.

6. Surface tension is defined and briefly described.

7. The capillary rise, drop weight, and drop volume methods for determining surface tensions are described, and equations developed for the calculation of data. Other methods of determining surface tension are listed.

8. Harkins' correction of the weight of the ideal drop is explained and applied to the drop weight formula.

9. Adsorption at interfaces is described along with orientation theories, monomolecular layers, selective and preferential adsorption.

10. The adsorption equation of Gibbs is developed after the manner of Oswalt.

11. The theory of Harkins, explaining the spreading of one liquid on another, is probably the best of those so far developed, and its mathematical statement is given.

12. A relation between adsorption, surface tension, and physiological functions is given.

13. The interfacial surface tensions of Meyer-Overton's series of drugs against Nujol and lecithin - Nujol solution are determined, and adsorption coefficients are calculated by the Gibbs equation. These values are used in calculating the area occupied by one molecule in the surface.

14. The adsorption curves for the aqueous phase against pure Nujol are quite regular, but those against lecithin - Nujol are more irregular.

15. A decrease in interfacial tensions of the same solutions at the different interfaces is found, showing great surface activity between drug and lecithin.

16. The adsorption values against pure Nujol follow Meyer-Overton's order nearly exactly. However, those against lecithin - Nujol are not so regular.

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