

The Plant Growth Activity of 1-Naphthoic Acid Derivatives and their Related Compounds

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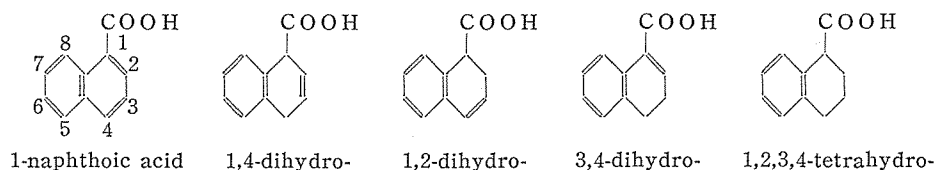
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The plant growth activities of substituted 1-naphthoic and hydro-1-naphthoic acids, and α -alkylphenylacetic and 1,2-benzocyclohexene-3-carboxylic acids are tested in pea straight-growth and callus formation tests. The relationship between structure and activity is discussed. The results seem to conform well with physico-chemical hypothesis of Veldstra. Besides, however, an important role of charge-transfer force in the fixation of the growth substance at the site of action is suggested.

In the last two decades, it has been found that various types of synthetic compounds exhibit the plant growth activity which resembles that of native growth substance, indole-3-acetic acid, and many workers have attempted to gain an insight into the mode of action on the basis of analysis of the relationship between structure and activity of these compounds¹⁻⁴.

In this laboratory, since 1944, a series of studies^{5-19,19a} has been carried out on the activity of a new type of synthetic growth substances, *viz.* 1-naphthoic acid, 1,4-, 1,2-, 3,4-dihydro- and 1,2,3,4-tetrahydro-1-naphthoic acids, stressing



on the following two main themes : one is on absolute configuration and growth activity of optical antipodes of 1,4-dihydro-, 1,2-dihydro- and 1,2,3,4-tetrahydro-1-naphthoic acid^{9,10,14-16}, and the other on structure and activity of a number of their substituted derivatives and structurally related compounds^{17-19,19a}.

In this paper, results obtained in the latter are reviewed, and the structural requirement for activity are discussed. The discussions fall into four subjects.

1) The effect of substituents on the activity of the dihydro- and tetrahydro-1-naphthoic acids.

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2) The effect of modifications of molecular structure appearing in the homologous series of α -alkylphenylacetic acids and 1,2-benzocyclene-3-carboxylic acids.

3) The effect of substituents on the activity of 1-naphthoic acid.

4) The function of aromatic ring in the growth substances.

Measurement of Growth Activity

This was done by pea straight-growth test and callus formation test. The details of the methods have been described in the previous publications by Kato^{20,21}.

Pea straight-growth test is an appropriate method even for the comparison of relatively weakly active growth substances. All points in Figs. 1-10 represent the average of two runs, each of which includes 10 pieces of pea stem section (*var. Alaska*).

Callus formation test gives a measure not of cell elongation but rather of cell division. Decapitated epicotyle of *Vicia faba L.* is the test object. In general, compounds strongly active in the pea straight-growth test are also powerful in the callus formation.

1) Substituted Dihydro- and Tetrahydro-1-naphthoic Acids¹⁷⁾

Activities in the pea straight-growth test of these acids, as well as of their parent acids, are presented in Figs. 1-4.

The results show that the chlorine and the bromine substitutions are similar in the effect of the growth activity. Both the 5- and 8-halogen substitutions, in the 1,4-dihydro-acid series, make the threshold concentration higher. In the 3,4-dihydro-acid series the 5-halogeno-acids are less active and the 8-halogeno-acids are more active than the parent acid. In the tetrahydro-acid series, the 5-halogen substitution depresses the activity considerably, while

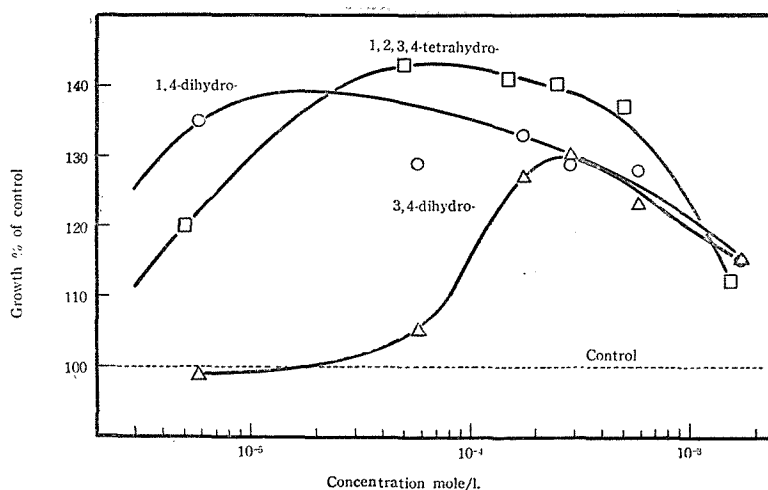


Fig. 1. Activity of hydro-1-naphthoic acids in the straight growth of pea stem section.

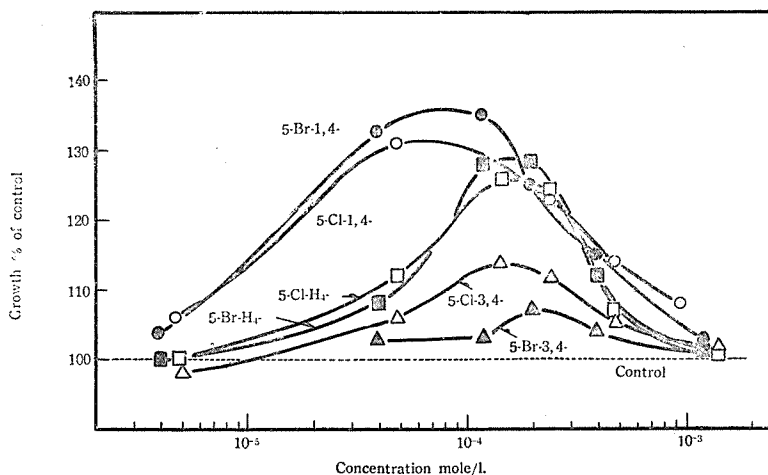


Fig. 2. Activity of 5-halogeno-hydro-1-naphthoic acids in the straight growth of pea stem section

8-halogen substitution does only slightly. The 6-methyl-acids are similar in activity to the corresponding 5-halogeno-acids.

Veldstra¹⁾ has affirmed that the interaction of the growth substances is determined by an adsorption phenomenon at the cellular interface by several weak bonds and that essential requirement for activity is a three dimensional amphipatic structure of the molecule, *i.e.*, a hydrophilic group (H) such as carboxyl group in a very definite spatial relation (as perpendicular and peripheral as possible) to a lipophilic ring system (L), and an appropriate HL-balance. We will discuss the results from this point of view.

Of the non-substituted hydro-1-naphthoic acids, 1,4-dihydro- and 1,2,3,4-tetrahydro-acids are similar in their activities, while 3,4-dihydro-acid is less active than the two. As reported in the previous paper, the surface activities

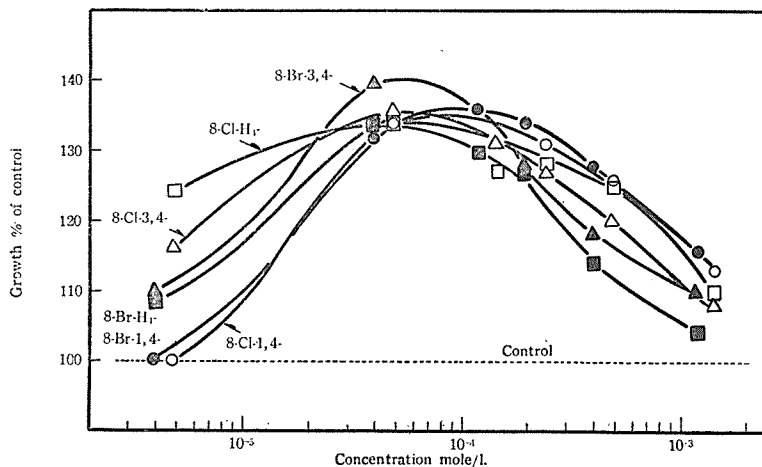


Fig. 3. Activity of 8-halogeno-hydro-1-naphthoic acids in the straight growth of pea stem section.

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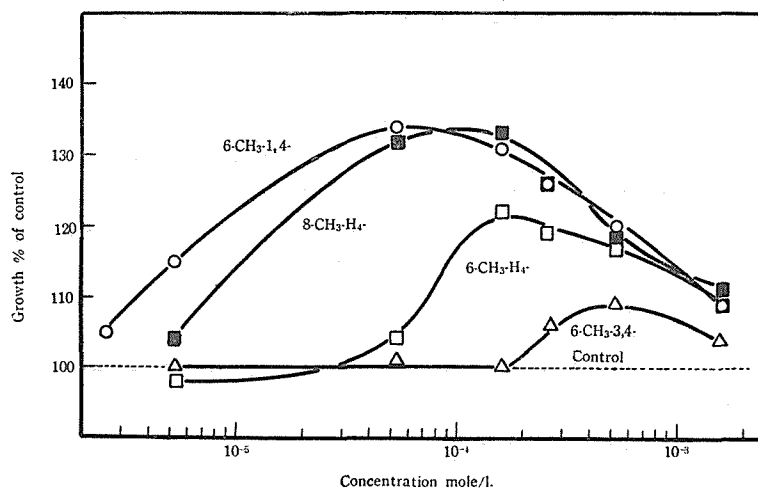


Fig. 4. Activity of methyl-hydro-1-naphthoic acids in the straight growth of pea stem section.

(half suppression value) of the three acids do not differ appreciably from one another, the order being 1,4-dihydro-acid, 3,4-dihydro-acid, 1,2,3,4-tetrahydro-acid¹¹). Therefore, the marked difference in the growth activity may be attributable mainly to difference in the spatial position of carboxyl group with respect to the ring system. In the 3,4-dihydro-acid, the carboxyl group may be nearly coplanar with the ring system because of the conjugated structure, while in the 1,4-dihydro- and 1,2,3,4-tetrahydro-acids the group can take, through interconversion of the alicyclic ring, two positions, in one of which the carboxyl group rises up considerably from the ring plane (*quasi-axial* conformation)^{12, 22}).

Table 1. Callus forming activity of substituted hydro-1-naphthoic acids.

Compounds	Activity	Compounds	Activity
1,4-Dihydro-	++	5-Bromo-tetrahydro-	Inactive
3,4-Dihydro-	+	8-Chloro-1,4-dihydro-	+++
1,2,3,4-Tetrahydro-	+++	8-Chloro-3,4-dihydro-	+++
5-Chloro-1,4-dihydro-	++	8-Chloro-tetrahydro-	+++
5-Chloro-3,4-dihydro-	±	8-Bromo-1,4-dihydro-	+++
5-Chloro-tetrahydro-	±	8-Bromo-3,4-dihydro-	+++
5-Bromo-1,4-dihydro-	++	8-Bromo-tetrahydro-	+++
5-Bromo-3,4-dihydro-	Inactive	Indole-3-acetic acid	++

By the 5-halogen substitution, the activities of the three acids are depressed in parallel with each other. This may be explained by a shift in the HL-balance, because that kind of substitution may have no significant steric effect on the carboxyl group. The fact that the 6-methyl substitution is similar in the effect to the 5-halogen substitution, may be also comprehended on the same basis.

On the other hand, all the 8-substituted acids are nearly equally active.

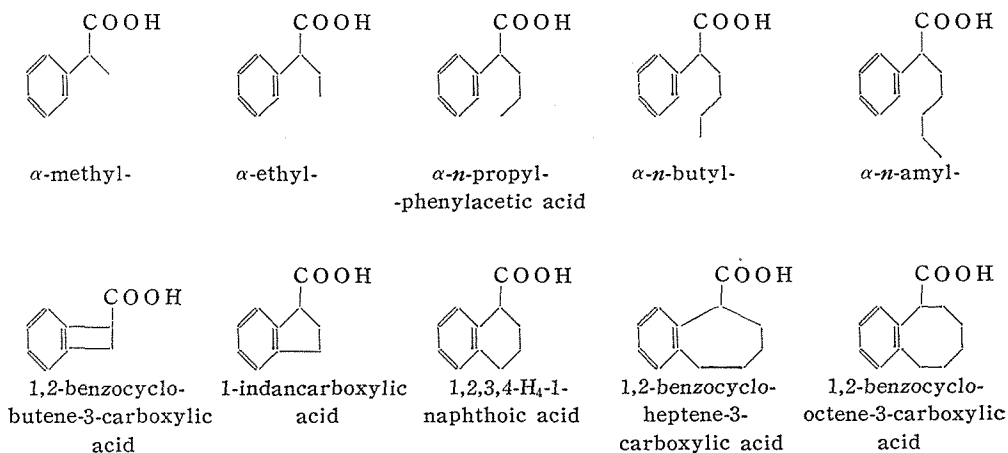
Due to the steric effect of the substituent at 8-position, the carboxyl group may exist predominantly in *quasi-axial* position in 1,4-dihydro- and 1,2,3,4-tetrahydro-acids and it may be forced to twist and rise up more or less from the ring plane in 3,4-dihydro-acid. Such a steric effect may perhaps overcome the suppressive effect of a shift in the HL-balance in 3,4-dihydro-acid and nearly compensate for it in 1,4-dihydro- and 1,2,3,4-tetrahydro-acids.

The results observed in the callus formation test are shown in Table 1. Though the activity of 1,4-dihydro-acid is less than that of 1,2,3,4-tetrahydro-acid in this test, the discussion described above is scarcely affected.

Thus, the present results are consistent with the Veldstra hypothesis. However, syntheses and physiological tests of 6- and 7-halogeno- and 5- and 7-methyl-acids are desirable.

2) α -Alkylphenylacetic Acids and 1,2-Benzocyclene-3-carboxylic Acids¹⁸⁾

1-Indancarboxylic acid, the lower homolog of 1,2,3,4-tetrahydro-1-naphthoic acid, was lately reported to be considerably active²³⁻²⁵⁾. In the homologous series of these two acids, the 1,2-benzocyclene-3-carboxylic acids, the spatial relation of the carboxyl group to the ring system is influenced by the alicyclic ring structure. On the other hand, in the α -alkylphenylacetic acids which may be regarded as the "open forms" of the above acids, such an influence on the carboxyl group is unnecessary to be considered.



In order to examine the effect on the growth activity of such a difference in the molecular structure between the condensed structured 1,2-benzocyclene-3-carboxylic acids and the open formed α -alkylphenylacetic acids, we tested their activities in the pea straight-growth test.

The activities observed are presented in Figs. 5 and 6. Among the α -alkylphenylacetic acids tested, methyl and ethyl acids are the most active, *n*-propyl acid is less active, and *n*-butyl and *n*-amyl acids are inactive. These results agree with those of Veldstra who used the pea curvature test^{26,27)}. Each 1,2-benzocyclene-3-carboxylic acid corresponds in the activity to the α -alkylphenyl-acetic acid which has the same number of carbon atoms as it.

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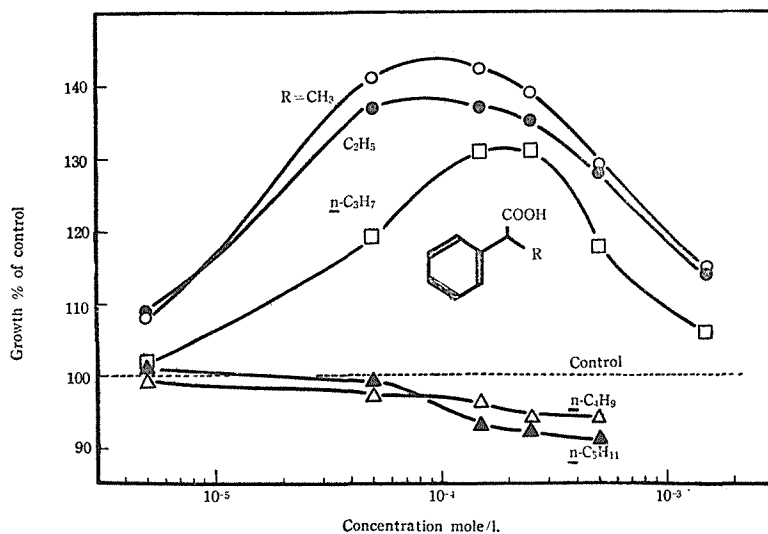


Fig. 5. Activity of α -alkylphenylacetic acids in the straight growth of pea stem section.

The only exception is 1,2,3,4-tetrahydro-1-naphthoic acid, which is more active than *n*-propylphenylacetic acid.

In the α -alkylphenylacetic acids, the terminal of the alkyl chain is considered to lie preferably far from both the benzene ring and the carboxyl group to make the steric repulsions minimum. The chain of *n*-alkanes is demonstrated by Bonham and his coworkers to exist predominantly in all *trans* configuration or in those which involve at least one *gauche* conformation²⁸⁾. Therefore, the spatial relation of the carboxyl group to the ring may not change appreciably

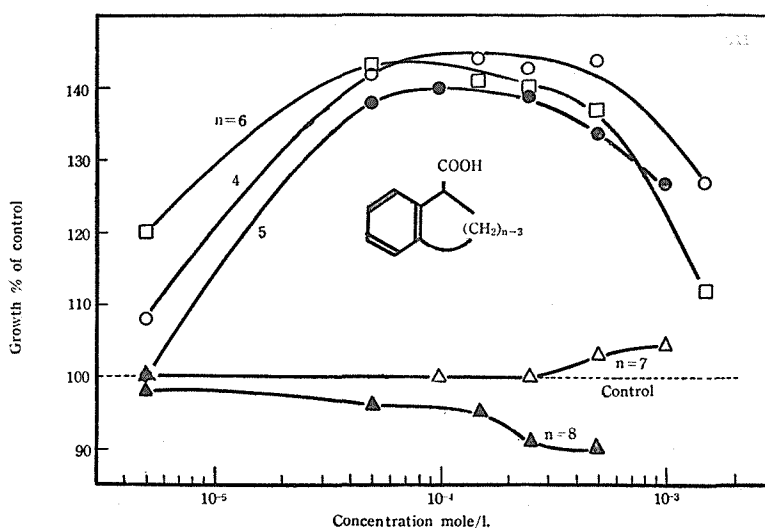


Fig. 6. Activity of 1,2-benzocyclene-3-carboxylic acids in the straight growth of pea stem section.

even if the length of the side chain changes. The carboxyl group in this series emerges considerably from the plane of the benzene ring. Fitting of the molecule to the site of action may, however, be interfered with when the molecular dimension increases due to elongation of the side chain. The molecular dimension of *n*-butylphenylacetic acid may be too large for fitting.

In the 1,2-benzocyclene-3-carboxylic acids, increasing carbon atom in the alicyclic ring may not affect the molecular dimension so remarkably as in the above-mentioned series because of their condensed ring structure. The spatial configuration of the carboxyl group, on the other hand, may be affected considerably. Guessed from the ultraviolet spectra* and the molecular model, the carboxyl group of benzocyclobutene- and indan-carboxylic acids takes a fixed conformation rising considerably from the plane of the benzene ring. The carboxyl of tetrahydronaphthoic acid emerges from the ring plane more conspicuously than in the lower homologs when it takes *quasi-axial* conformation, one of the two conformations inferable^{12,22)}. The carboxyl group of benzo-cycloheptene- and -cycloöctene-carboxylic acids is presumed to be in favorable *equatorial* conformations owing to hydrogen crowding of the ring and restriction of rotation of the group from the argument by Huisgen³⁰⁾ concerning the conformation of 1,2-benzo-cycloheptenyl- and -cycloöctenyl-3-methyltosylates.

1,2,3,4-Tetrahydro-1-naphthoic acid, the carboxyl group of which can emerge from the ring most in this series,** is the most active, and 1,2-benzo-cycloheptene- and -cycloöctene-3-carboxylic acids, the carboxyl group of which lies in the *equatorial* conformations, are inactive. The activity grade of the benzocyclenecarboxylic acids thus may be explained by the spatial relation of the carboxyl group to the ring system, just as in the hydro-1-naphthoic acids discussed in the foregoing section.

On the other hand, because the HL-balance may not significantly differ between the corresponding members of the two series possessing the same number of carbon atoms, the abrupt drop of activity in both series from the C₁₁-acid to the C₁₂-acid may be understood also by an increase of lipophilic nature beyond optimum³²⁾, like the bactericidal activity in the homologous series of *n*-alkylresorcinols³³⁾, *n*-alkanols³⁴⁾, etc.

Consequently, it could not be decided whether this abrupt drop of activity is attributable to molecular form or to HL-balance. However, as presented in the foregoing section, 6-methyl-1,2,3,4-tetrahydro-1-naphthoic acid which is con-

* The ultraviolet spectra of these acids resembling well those of the parent hydrocarbons²⁹⁾ illustrate that the alicyclic ring is transformed from the totally rigid in benzocyclobutene towards the considerably flexible in benzocycloöctene.

** The angle of C-Carboxyl axis to the benzene ring in indancarboxylic acid is considered to be a little larger than that in assumed regular pentagonal cyclopentane derivative, in which it seems to be about 55° (about one-half the tetrahedral angle). It is expected to be larger in benzocyclobutenecarboxylic acid than in indancarboxylic acid, but the upper limit can be regarded as the one in the cyclopropane derivative (60°)³¹⁾. In tetrahydronaphthoic acid, the angle is estimated from the model presented in ref. 22 to be 65-70° in *quasi-axial* and 35-40° in *quasi-equatorial* conformation.

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sidered to have an adequate molecular form is active though its HL-balance does not differ much from those of such acids having the same number of carbon atoms as it as 1,2-benzocycloheptene-3-carboxylic acid and *n*-butylphenylacetic acid. Therefore, these acids are guessed to have their HL-balance not beyond optimum. The abrupt drop of activity can be attributed rather to the inadequate molecular form, though the plant growth activity may be conditioned by the above two factors.

The results obtained in this section are also consistent with Veldstra's view. It is hoped to obtain some informations about the activity of homologs of 1,4-dihydro-1-naphthoic acid, which are considered to have higher chance of having their carboxyl group in the *axial* position, owing to the lower hydrogen crowding.

The analyses of the molecular structure in this discussion suggest that the Jönsson's structural requirement⁽³⁵⁾, "an extended ring system" where the carbon atom of carboxyl group need to situate in the plane of aromatic ring, is quite unreasonable.

3) Substituted 1-Naphthoic Acids¹⁹⁾

1-Naphthoic acid in which the carboxyl group is bound directly to the aromatic ring unlike in its hydrogenated derivatives, 1,4-dihydro- and 1,2,3,4-tetrahydro-acids, is appreciably less active than these two hydro-acids. Because of the conjugated structure, the configuration of the carboxyl group, and also the molecular form of 1-naphthoic acid seem similar to those of 3,4-dihydro-1-naphthoic acid. The similarity of both acids in activity is understood from this point of view.

The growth activity of 1-naphthoic acid is intensified by the halogen substitution at 2- or 8-position, whereas it is reduced by substitution at one of the other positions, the 3- and 5-halogeno-acids being almost inactive (Figs. 7 and 8, Table 2). The activities of methyl substituted 1-naphthoic acids are similar to

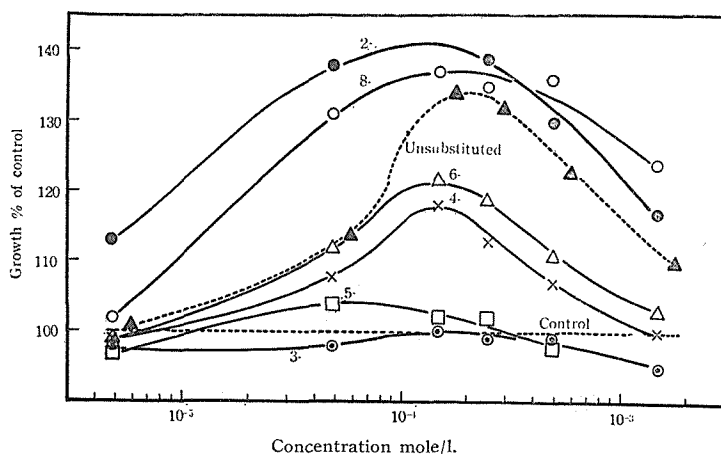


Fig. 7. Activity of chloro-1-naphthoic acids in the straight-growth of pea stem section.

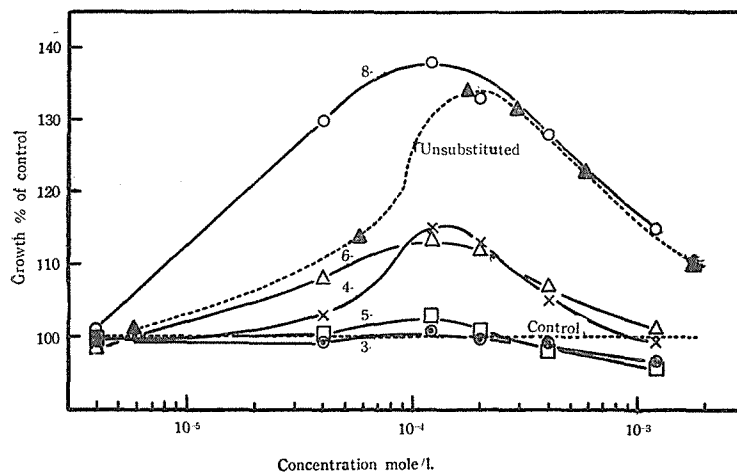


Fig. 8. Activity of bromo-1-naphthoic acids in the straight-growth of pea stem section.

those of the corresponding halogeno-acids (Fig.9, Table 2). In this case, however, unlike the 2-chloro-acid, the 2-methyl-acid is less active than the parent acid. All the nitro-acids tested are less active than the parent acid. (Fig. 10, Table 2).

On the basis that the growth activity of substituted benzoic acids is dependent on a non-planar structure caused by the *ortho* substituent^{27,36,37}, Veldstra has considered that the weak activity of 1-naphthoic acid is attributable to a structure in which the carboxyl group is slightly hindered by the methine group in the *peri*-position, and that the enhanced activities of the 2-chloro-, 8-halogeno- (chloro-, bromo- and iodo-) and 8-methyl-acids result from the carboxyl group being twisted more strongly by these substituents^{27,36}.

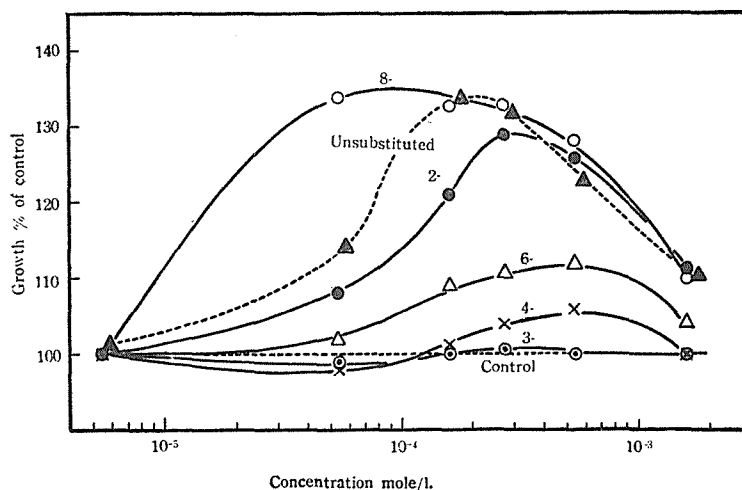


Fig. 9. Activity of methyl-1-naphthoic acids in the straight-growth of pea stem section.

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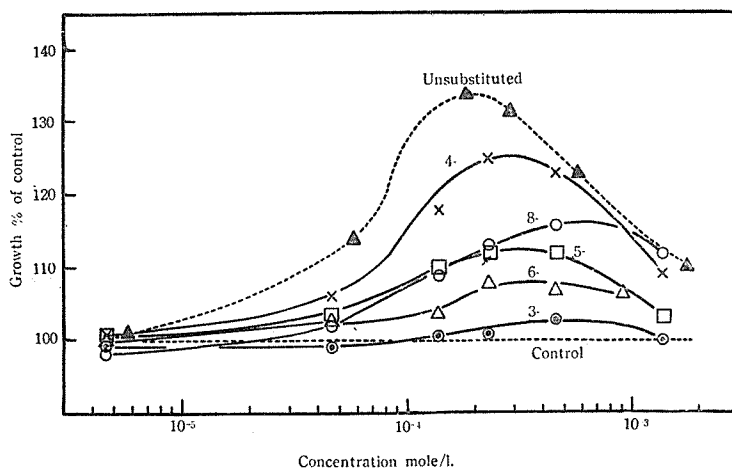


Fig. 10. Activity of nitro-1-naphthoic acids in the straight-growth of pea stem section.

The present results concerning the activities of 2-chloro-, 8-halogeno- and 8-methyl-acids are in good agreement with those of Veldstra in spite of the different test methods. The fact that the 3-, 4-, 5- and 6-substituted halogeno- and methyl-acids are less active than the parent 1-naphthoic acid may be explained by shifts in the HL-balance, and the enhancement of the activity by the 2- and 8-substitutions may be due to the strong steric effect overcoming the suppressive effect of shifts in the HL-balance. That the nitro-acids are less active than the parent acid, may be explained by a shift in the HL-balance, bulkiness of the nitro group and the carboxyl group being less twisted in the 8-nitro-acid than in the 8-halogeno- and 8-methyl acids because of twist of the nitro group itself.

Recently, we confirmed by means of measurements of dipole moment and ultraviolet and infrared spectrum that, in the 2- and 8-halogeno- and methyl-acids, the carboxyl group is considerably twisted from the ring plane, and in

Table 2. Callus forming activity of substituted 1-naphthoic acids.

compounds	activity	compounds	activity
1-Naphthoic	+	8-Bromo-	+++
2-Chloro-	+++	3-Nitro-	Inactive
3-Chloro-	Inactive	4-Nitro-	±
4-Chloro-	±	5-Nitro-	Inactive
5-Chloro-	Inactive	8-Nitro-	±
6-Chloro-	+	2-Methyl-	+
8-Chloro-	+++	3-Methyl-	Inactive
3-Bromo-	Inactive	4-Methyl-	Inactive
4-Bromo-	±	6-Methyl-	Inactive
5-Bromo-	Inactive	8-Methyl-	++
6-Bromo-	+	Indole-3-acetic	++

the 8-nitro acid, the carboxyl and nitro groups are twisted concurrently^{38,39}. Because substitution of naphthoxy compounds generally decreases their activity on the contrary to that of phenoxy compounds^{40,41}, the substitution in naphthalene ring may make the HL-balance improper as suggested by Veldstra⁴². Therefore, the present results also conform to the Veldstra hypothesis except the activity of 2-methyl-1-naphthoic acid in which some other factors may be operative.

4) The Function of Aromatic Ring in the Growth Substances

Recently, emphasizing that the action of growth substances is totally physico-chemical in character, van Overbeek elaborated the Veldstra hypothesis⁴³, and stated the function of the aromatic ring in the growth substance to anchor the molecule to the site of action by *van der Waals'* attraction forces in order for the acid group to interact by hydrogen bond with enzyme system in the right position for which a definite configuration of this group is required. According to this hypothesis, substitution in the aromatic ring would affect the growth activity through the following factors :

- a) regulation of the partition coefficient (HL-balance) to make the molecule arrive at the site of action,
- b) sterical influence on the acid group when substituted at its neighboring positions,
- c) modification of the molecular size required for fitting to the site of action according to the bulkiness and the position of the substituent,
- d) strengthening the anchoring force to the site of action by *van der Waals'* bondings.

As discussed in the foregoing sections, the growth activities of 1-naphthoic acid derivatives and their related compounds are understood very well by the physico-chemical hypothesis. However, by the above-mentioned four factors alone, the complicated effect of substituents appearing in the less active acids than 1-naphthoic acid cannot be explained adequately. Similarly, the positional effect of substituents of benzoic, phenoxyacetic, naphthoxy-2-acetic and phenylacetic acids seems too complex and specific to be understood only by these factors. Therefore, it is forced to be considered that the substitution of the aromatic ring would affect the activity also through some factors proper to π -electron system, because no more than the compounds having aromatic ring or conjugated system are active.

A noticeable hypothesis along this view is advanced by Muir and Hansch^{2,44-46}. They have postulated that the first step of growth promoting action is a definite chemical reaction between the growth substance and the cellular proteinous material. According to this, at least one of the positions on the aromatic ring *ortho* to the carboxyl group or the side chain carrying this group must be capable of reacting with electron-rich plant substrate. Therefore, the *ortho* position must have a proper π -electron density and the group or atom at that position should be prone to be displaced under the conditions of reaction. Recently Fukui and his coworkers have developed the "frontier elec-

tron theory", and found a distinct parallelism between the reactivity index derived from this theory and the experimental chemical reactivity of a number of π -electron systems⁴⁷⁻⁵⁰. Applying this theory, they calculated the π -electron distribution of various benzoic acid derivatives and revealed a parallelism between the indices for nucleophilic replacement reaction at the *ortho* position and the growth activities of these compounds⁵¹.*

Expecting that the growth activity of the substituted 1-naphthoic acids may also correlate to the electronic state at a definite position in the ring, we calculated the reactivity indices by the same method as above, and found that the activity is much affected by the reactivity of radical or nucleophilic replacement at 8-position as well as by dimensional factors and HL-balance of the molecule^{19,19a}). The effects of substituents appearing in the less active acid than the parent acid may be understandable on this basis. The enhanced activity of the 2- and 8-substituted acids may result from their high reactivity as well as from the favorable configuration of the carboxyl group.

Then, further consideration must be required to give a solution to the discrepancy between the chemical reactivity hypothesis which can explain the effect of substituents in the aromatic ring of the 1-naphthoic acids and benzoic acids and the physico-chemical hypothesis which is consistent with activities of the hydro-1-naphthoic acids, 1,2-benzocyclohexene-3-carboxylic acids and α -alkylphenylacetic acids.

Lately, Fukui and his coworkers indicated that the reactivity index derived from the frontier electron theory at a definite position of aromatic compound is an index not only of the reactivity of replacement reaction, but also of total stabilization energy in the formation of charge-transfer complex bonding with another molecule or ion at that position, and explained well the orientational properties of charge-transfer forces⁵²).

Therefore, even if a good correlation between the index and the growth activity is found, it does not mean immediately that the true chemical reaction, such as replacement reaction, is concerned. Thus, the effect of substituents in the aromatic ring system could be elucidated consistently by both physico-chemical and reactivity hypotheses if we assume that the anchoring force to the site of action is governed not only by non-specific *van der Waals'* force but also by charge-transfer bonding at a definite position with electron-rich moiety of the receptor, which may be supposed to be sulfhydryl ion, imidazol group or so. From this viewpoint the activity found in 8-methyl-1-naphthoic acid or 2,6-dimethyl-substituted benzoic acids³⁷), which is unable to undergo any replacement at C₈ or *ortho* position, may be well explained. Such an assumption seems to be reasonable, when the orientational property of charge-transfer force and the severe sterical condition at the site of action of growth

* All the benzoic acids calculated are presumed as of coplanar structure. It is well anticipated, however, that the conclusion is not affected significantly even if the indices of *diortho*-substituted benzoic acids are recalculated according to their carboxyl group twisted appreciably from the ring plane.

substance are considered. This may be also consistent with the view anticipated from the physico-chemical mechanism that "the function of the ring system implies a contribution to a reversible fixation of the growth substance at the receptor"¹¹, for the strength of charge-transfer bonding would be weak enough to dissociate reversibly.* Moreover, from that the charge-transfer occurs at a position neighboring to the carboxyl group, *i.e.*, 8-position in the naphthoic acids and *ortho* position in the benzoic acids, it could be expected that this force plays an important role in making the carboxyl group locate exactly in the right position.

In conclusion, we should like to propose that such a charge-transfer force is a very important factor required for the plant growth activity through participation in anchoring the molecule to the site of action, as Mulliken suggested that "charge-transfer forces may afford new possibilities for understanding intermolecular interactions in biological systems"⁵⁶. For definite conclusions, the correlation between reactivity indices and growth activities should be established further in other series of growth substances, and the experimental evidence should be required. It is also necessary to re-examine from this point of view the effect of substitution in the hydro-1-naphthoic acids discussed in Section 1.

Supplement : Simple Evaluation of the HL-balance

In the foregoing discussions, it is concluded that an appropriate HL-balance is required for plant growth activity, though in a qualitative way. Provided that the HL-balance is evaluated quantitatively, the discussions could be understood more accurately.

In the field of surface active agents, a numerical value of HL-balance, "HLB-value", is commonly used to estimate their emulsifying or solubilizing power⁵⁶⁻⁵⁸. It is devised by Oda⁵⁹ that the HLB-value can be calculated conveniently using the "organic conceptional diagramm" proposed by A. Fujita^{60,61}. According to this, the HLB-value is given by the ratio of two coordinates in the conceptional diagramm, namely, the ratio of the inorganic (hydrophilic) character to the organic (lipophilic) character, each of which is estimated by summing the numerical values characteristic to groups or atoms in a given molecule, the value being deduced from several physical properties, *viz.* boiling point, solubility and partition coefficient of a number of organic compounds.

Though the properties of surface active agents and the activity of plant growth substances are different in their appearance, both are to be discussed essentially on the same basis with regard to the HL-balance. In the organic conceptional diagramm, it is indicated that the physiologically active compounds must possess both inorganic (hydrophilic) and organic (lipophilic) characters

* The heat of formation of some aromatic molecular complex, which results from charge-transfer force and *London-van der Waals'* force (dipole-dipole interaction force, dispersion force *etc.*) is estimated to be several kilocalories per mole⁵³. The greatest strength of a bond which can readily dissociate at room temperature or body heat seems about 10 kcal/mole⁵⁴.

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at a ratio within a certain limit^(60, 61).

Numerical values of inorganic and organic characters of some common groups in the growth substances are selected from the table presented by A. Fujita and shown in Table 3. The HLB-value is given according to Oda, as inorganic character/organic character $\times 10$. In Tables 4-6, the values of the compounds discussed in the present paper are shown. Those of other common growth substances are also calculated (Tables 7-9).

 Table 3. Inorganic and organic characters of some common groups⁽⁶¹⁾.

Groups	Inorg. character	Org. character	Groups	Inorg. character	Org. character
-CH ₃ , =CH ₂ , } ≡CH, =C= }		20	-NO ₂	70	70
Anthryl- Phenanthryl- }	105	280	-Br	10	60
Naphthyl-	60	200	-Cl	10	40
-COOH	150	20	Aromatic single nucleus	15	
-CSSR	50	130	Non-aromatic single nucleus	10	
-CSOR	50	80	Double bond	2	
-OH	100		<i>iso</i> -, >-		-10
=N-	70		<i>tert</i> -, ≥-		-20
-O-	20				

Table 4.

	Inorg. character	Org. character	HLB
H ₂ -naphthoic	177	210	8.4
H ₄ -naphthoic	175	210	8.3
Cl-H ₂ -naphthoic	187	250	7.5
Br-H ₂ -naphthoic	187	270	6.9
CH ₃ -H ₂ -naphthoic	177	230	7.7
Cl-H ₄ -naphthoic	185	250	7.4
Br-H ₄ -naphthoic	185	270	6.9
CH ₃ -H ₄ -naphthoic	175	230	7.6

Table 5.

	Inorg. character	Org. character	HLB
CH ₃ -phenylacetic	165	170	9.7
C ₂ H ₅ -phenylacetic	165	190	8.7
C ₃ H ₇ -phenylacetic	165	210	7.9
C ₄ H ₉ -phenylacetic	165	230	7.2
C ₅ H ₁₁ -phenylacetic	165	250	6.6
Benzocyclobutenecarboxylic	175	170	10.3
Indancarboxylic	175	190	9.2
H ₄ -naphthoic	175	210	8.3
Benzocycloheptenecarboxylic	175	230	7.6
Benzocycloöctenecarboxylic	175	250	7.0

Table 6.

	Inorg. character	Org. character	HLB
Naphthoic	210	220	9.5
Cl-naphthoic	220	260	8.5
Br-naphthoic	220	280	7.9
CH ₃ -naphthoic	210	240	8.8
NO ₂ -naphthoic	280	290	9.7

From these tables, it is conceivable that the HL-balance required for growth activity possesses its value between 6.5 and 10.5 with a maximum at about 8.5 as shown in hydro-1-naphthoic acids, naphthaleneacetic acid, and 2,4-dichlorophenoxyacetic acid. This seems to correspond very well with the result obtained by Veldstra that the lipophilic part of the active growth substances has a "aliphatic lipophily equivalent" of C₅-C₈ with a maximum at C₇, which is estimated by comparing the effect on the oleate coacervate of *n*-fatty acids with that of growth substances^{1,32,42,62}. The synthetic carboxylic acids possessing the value above 10.5, *i.e.*, benzoic, phenoxyacetic and dimethoxybenzoic acids⁴⁶ or some hydroxy-acids and dicarboxylic acids⁸, and those possessing the value below 6.5, *i.e.*, dihydroanthroic⁸, diphenylacetic⁶³ and pentachlorobenzoic acids⁴⁶, are generally inactive or very weakly active. By this procedure, the HLB-values of positional isomers cannot be distinguished from one another, but the positional effect of substituents or carboxyl group on the activity would be determined by some other factors. When any compounds, in spite of their HLB-value in the optimum, are inactive, the origin must be required in other conditions, *viz.* molecular size, anchoring force of the ring and/or steric circumstance of the carboxyl group.

As is seen in Table 4, the HLB-values of the hydro-1-naphthoic acids are consistent with the discussions in Section 1. That the abrupt drop of activity of the α -alkylphenylacetic and 1,2-benzocyclohexene-3-carboxylic acids are affected by the molecular form rather than HL-balance seems comprehensible from Table 5 as suggested in Section 2. Though the HLB-values of the substituted 1-naphthoic acids seem to quantify not so apparently the presumption in Section 3, their activities are not determined only by HL-balance (Table 6). The mode of variation of the HLB-value in naphthaleneacetic acid series and phenoxyacetic acid series corresponds very well with those estimated from the action on the oleate coacervate by Veldstra⁴² (Tables 7, 8). The effect of HL-

Table 7.

	Inorg. character	Org. character	HLB
Phenylacetic	165	160	10.3
Naphthaleneacetic	210	240	8.8
H ₄ -naphthaleneacetic	175	240	7.3
Naphthalenebutyric	210	280	7.5
H ₁₀ -naphthaleneacetic	170	240	7.1

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Table 8.

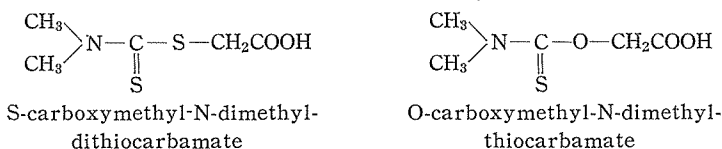
	Inorg. character	Org. character	HLB
Phenoxyacetic	185	160	11.6
Cl-phenoxyacetic	195	200	9.8
Cl ₂ -phenoxyacetic	205	240	8.5
Cl ₃ -phenoxyacetic	215	280	7.7

Table 9.

	Inorg. character	Org. character	HLB
Benzoic	165	140	11.8
Cl-benzoic	175	180	9.7
Cl ₂ -benzoic	185	220	8.4
Cl ₃ -benzoic	195	260	7.5
Phenylacetic	165	160	10.3
Cl-phenylacetic	175	200	8.8
Cl ₂ -phenylacetic	185	240	7.7
Cl ₃ -phenylacetic	195	280	7.0
Cinnamic	167	180	9.3
Cl-cinnamic	177	220	8.1
Indoleacetic	250	200	12.5
Cl-indoleacetic	260	240	10.8

balance in benzoic, phenylacetic and cinnamic acid series may be also understandable from Table 9.

The HL-balance of natural growth substance, indole-3-acetic acid, possesses the value 12.5, far above the optimum and those of non-ring structured growth substances, S-carboxymethyl-N-dimethyldithiocarbamate and its analogs⁶⁴⁾, are evaluated to be above 12.9.



The enhanced activity of the chloro-substituted indole-3-acetic acids⁶⁵⁾ may be caused by that the lipophilic character is not yet optimum in indole-3-acetic acid as suggested by Veldstra from the oleate coacervate test^{1, 42)}. The high hydrophilic character of the compounds, however, may indicate that a somewhat different mode of action is operative. The facts that indole-3-acetic acid is different in the mode of competition with some anti-auxins from the synthetic growth substances⁶⁰⁾, and that exceptionally the thiocarbamates are more active in the avena straight-growth test than in pea curvature test²⁷⁾ would support this view.

Thus, this procedure, though too simple, seems to suffice for evaluation of

the HL-balance of the plant growth substances as well as the measurements of the colloid chemical property.

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