3.36 g. of lithium aluminum hydride in 120 ml. of ether. After the addition was completed, the reaction mixture was stirred for 4 hours, and the excess hydride was then destroyed by the addition of wet ether, followed by dilute hydrochloric acid to dissolve the aluminum salts. The organic layer was separated, the aqueous layer extracted with ether and the combined fractions treated in the usual manner. Upon concentration of the ethereal solution there was obtained 7.20 g. (72%) of an oil, b.p. 94–98° (0.15 mm.), which showed infrared absorption at 3.0 and 5.98 $\mu$. Possibly this oil was 8-hydroxy-1-keto-4-methyl-1,2,3,4,5,6,7,8-octahydronaphthalene, but no attempt was made to purify it or determine the structure.

To 7.2 g. of the above oil in a 25-ml. Claisen flask was added 50 mg. of palladium-on-charcoal[15] and the mixture heated to 220–230° for 3 hours. The reaction mixture was then distilled *in vacuo* to yield 4.73 g. (82%) of 1-methylnaphthalene, b.p. 112–114° (14 mm.), which formed a picrate,[16] m.p. 141.5–142.0°, which was undepressed on mixing with an authentic sample.

**4-Methyl-5,6,7,8-tetrahydro-1-naphthol (VII).**—A mixture of 0.44 g. of VI, 1.3 g. potassium hydroxide, 3 g. of 85% hydrazine monohydrate and 35 ml. of redistilled diethylene glycol was heated. The distillate was removed until the solution temperature reached 196°. The solution was refluxed until the nitrogen evolution had decreased sharply (about 4 hours). The warm reaction mixture was poured on to 50 ml. of ice and 33 ml. of 6 *N* hydrochloric acid. The mixture was then extracted with ether–benzene and the combined organic extracts treated in the usual manner. Concentration of the organic solution yielded 0.369 g. of the tetralol. Recrystallization from petroleum ether (b.p. 30–60°) gave 0.328 g. (81%) of colorless crystals of VII, m.p. 87.5–88.5°.

The X-ray powder diffraction photograph of VII was identical to that of authentic material.[7]

**4,8-Dimethyl-8-hydroxy-1-keto-1,2,3,4,5,6,7,8-octahydronaphthalene (VIII).**—A solution of 9.4 g. of III in 75 ml. of dry ether was added dropwise with stirring during one hour to 200 ml. of approximately 1.25 *M* methylmagnesium iodide. The reaction mixture was refluxed with stirring for 2 hours, cooled, and then poured onto an ice–hydrochloric acid mixture. The mixture was extracted with ether–benzene and the combined organic fractions treated in the usual manner. Distillation afforded 9.3 g. (89%) of an oil, b.p. 104–105° (1 mm.), which yielded a red 2,4-dinitrophenylhydrazone, m.p. 243–245° dec. For this reason the oil is assumed to have structure VIII with the double bond conjugated to the carbonyl group. However, since no ultraviolet absorption spectral measurements were made, we cannot be sure that in the hydroxy ketone, the double bond was not conjugated.

*Anal.* Calcd. for $C_{18}H_{22}N_4O_5$: C, 56.5; H, 5.8; N, 16.3. Found: C, 56.7; H, 5.7; N, 16.3.

**1,4-Dimethylnaphthalene.**—A mixture of 9.2 g. of VIII and 50 mg. of palladium-on-charcoal[16] was heated to 220–230° for 4 hours. The reaction mixture was distilled to yield 3.18 g. (43%) of 1,4-dimethylnaphthalene, b.p. 107–110° (1 mm.), which formed a 1,3,5-trinitrobenzene addition compound, m.p. 165–166°, and a picrate, m.p. 143.5–144°, alone and mixed with authentic material.[17]

(15) The catalyst was supplied by Baker Catalyst Co., Newark, N. J.

(16) G. Darzens, *Compt. rend.*, **183**, 748 (1926), reports a m.p. of 141–142° for the picrate of 1-methylnaphthalene.

(17) M. C. Kloetzel, THIS JOURNAL, **62**, 1708 (1940), reports m.p. 143–144° for the picrate of 1,4-dimethylnaphthalene and m.p. 165–166° for the TNB derivative.

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[CONTRIBUTION FROM THE DEPARTMENT OF AGRICULTURAL CHEMISTRY, KYOTO UNIVERSITY, KYOTO, JAPAN]

# Electronic Structure and Plant Growth Activity of Substituted 1-Naphthoic Acid Derivatives[1,2]

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The relationship between plant growth activity of the substituted 1-naphthoic acid derivatives reported in the preceding paper[2] and the reactivity indices of these acids calculated by a molecular orbital method has been discussed. The ability of substituted 1-naphthoic acids to form a molecular complex of a charge-transfer type at the 8-position with plant substrates appears to be a very important factor determining the plant growth activity.

## Introduction

The prominent plant growth activity found in certain halogeno-benzoic acids,[3,4] has stimulated many studies of the relationship between chemical structure and growth activity of substituted benzoic acid derivatives.[5–11] Substituted 1-naphthoic acid derivatives have however not been studied so extensively. Studies on substituted naphthoic acids may contribute to an understanding of the structural requirement for growth promoting activity, since these two series, in which a carboxyl group is bound directly to the aromatic ring, seem to be similar in their modes of action.

In the study reported in the preceding paper,[2] 1-naphthoic acid derivatives substituted with a chlorine, bromine, methyl or nitro group in various positions were prepared and their growth activities were measured. The growth activity was intensified by 2- or 8-halo- and 8-methyl substitution, while it was reduced in the other acids, some of them being inactive.

Veldstra and his co-workers[12–15] have affirmed that the action of the growth substance is of physico-chemical nature, the function of the nuclear ring system being considered to be an adsorption to the cellular interface caused by several weak bonds,

(1) Published as Part XIV of Studies on the Plant Growth Substances. Presented before the monthly meeting of Kansai Branch of the Agricultural Chemical Society of Japan, Kyoto, Sept., 1959.

(2) Part XIII in series: K. Koshimizu, T. Fujita, T. Mitsui and J. Kato, *Bull. Agr. Chem. Soc. Japan*, in press.

(3) P. W. Zimmerman and A. E. Hitchkock, *Contrib. Boyce Thompson Inst.*, **12**, 321, 491, 497 (1942).

(4) J. A. Bentley, *Nature*, **165**, 449 (1950).

(5) K. V. Thimann, *Plant Physiol.*, **27**, 392 (1952).

(6) H. Veldstra, *Rec. trav. chim. Pays-Bas*, **71**, 15 (1952).

(7) H. Veldstra and C. van de Westeringh, *ibid.*, **71**, 318 (1952).

(8) H. Veldstra, "The Chemistry and Mode of Action of Plant Growth Substances," Butterworths Scientific Publications, London, 1955, p. 117.

(9) R. M. Muir and C. Hansch, *Plant Physiol.*, **26**, 369 (1951).

(10) C. Hansch, R. M. Muir and R. L. Metzenberg, *ibid.*, **26**, 812 (1951).

(11) R. M. Muir and C. Hansch, *ibid.*, **28**, 218 (1953).

(12) H. Veldstra, *Enzymol.*, **11**, 97, 137 (1944).

(13) H. Veldstra, *Biochim. Biophys. Acta*, **1**, 364 (1947).

(14) H. Veldstra and H. L. Booij, *ibid.*, **3**, 278 (1949).

(15) H. Veldstra, *Ann. Rev. Plant Physiol.*, **4**, 151 (1953).

perhaps by non-specific London–van der Waals attraction forces, by means which the carboxyl group—more functional with regard to the mode of action—plays its role in a very definite spatial position, and that an essential requirement for activity is a three dimensional amphipatic structure of the molecule. From this viewpoint they have stated[6-8] that the activities of substituted benzoic acids are dependent on a non-planar configuration caused by the *ortho* substitutent, and have considered on the same basis that the weak activity of 1-naphthoic acid is attributable to a structure in which the carboxyl group is hindered slightly by the methine group in the *peri* position, and that on enhanced activities of the 2-chloro-, 8-halogeno- (chloro-, bromo- and iodo-) and 8-methyl acids result from the carboxyl group twisted more strongly by these substituents.

Our results[2] on the activities of 2-chloro-, 8-halo- and 8-methyl acids are in good agreement with those of Veldstra[6,8] in spite of the different test methods. It is, however, difficult to explain by his hypothesis alone what determines the order of activities of the 3-, 4-, 5- and 6-substituted acids which seem to have the carboxyl group in a spatial relation to the ring system similar to 1-naphthoic acid.

On the other hand, Muir and Hansch[9-11] have suggested a definite chemical reaction between the auxin molecule and a cellular proteinous material. According to this hypothesis, at least one of the positions on the aromatic ring *ortho* to the carboxyl group must be capable of reacting with an electron-rich plant substrate. Therefore, the *ortho* position must have a proper electron density and the group or atom at this position must be prone to be displaced under the conditions of reaction. Recently, Fukui and his associates[16-19] have developed the frontier electron theory, and found a distinct parallelism between the reactivity indices derived from this theory and the experimental chemical reactivity of a number of $\pi$-electron systems. They have applied this theory to various benzoic acid derivatives,[20] and concluded that the chemical reactivity of benzoic acid derivatives at the *ortho* position with a nucleophilic group of the plant substrate is the most important factor determining plant growth activity.

Thus, it is expected that the order of activity of the substituted 1-naphthoic acids may be determined by the order of chemical reactivity at a definite position in the naphthalene ring. In order to estimate the reactivity indices, however, it is necessary to determine the molecular structures of these acids, since when the carboxyl group is twisted from the plane of the naphthalene ring by the steric effects of the neighboring substituents, the reactivity would be different from that of the coplanar structure.

Recently, we have studied the molecular structures of these 1-naphthoic acids by measuring their dipole moments[21] and ultraviolet[21] and infrared spectra,[22] and concluded that 1-naphthoic acid and its 3-, 4-, 5- and 6-substituted derivatives are equilibrium mixtures of two coplanar (or almost coplanar) rotational isomers in which the direction of the carboxyl group is different, and that the 2- and 8-substituted compounds are non-coplanar with the carboxyl group twisted considerably from the plane of the ring, the angle of twist being estimated to be around 60°, though affected by the nature and position of the neighboring substituent.

In this paper, the reactivity indices of these 1-naphthoic acids are calculated, according to the frontier electron theory, taking into consideration the steric configuration, and a good correlation is found between the indices at the 8-position and plant growth activities.

**Theoretical Index for Activity.**—It has been shown that in the frontier electron theory, "Superdelocalizability ($S_r$)" is a good index for expressing the effect of aromatic substitutions intermolecularly.[18,19] However, it has been emphasized that the "Approximate Superdelocalizability ($S_r'$)", the contribution of the frontier electrons to $S_r$, is a better index than $S_r$ in some *in vivo* reactions.[20,23] This approximate superdelocalizability is defined as [20,23]

(a) for an electrophilic reaction

$$S_r'^{(E)} = 2\frac{C_r^{(m)2}}{\lambda_m}$$

(b) for a radical reaction

$$S_r'^{(R)} = \frac{C_r^{(m)2}}{\lambda_m} + \frac{C_r^{(m+1)2}}{-\lambda_{m+1}}$$

(c) for a nucleophilic reaction

$$S_r'^{(N)} = 2\frac{C_r^{(m+1)2}}{-\lambda_{m+1}}$$

where $C_r^{(m)}$ or $C_r^{(m+1)}$ is the coefficient of the $r$-th atomic $\pi$-orbital in the following molecular orbitals: the highest occupied denoted by $m$ and the lowest unoccupied by $m+1$, and $\lambda_m$ or $\lambda_{m+1}$ is the coefficient of the resonance integral when the energy of a molecular orbital is expressed in the form $\alpha+\lambda\beta$.

Recently, it has been indicated[24] that the reactivity index $S_r'$ at a definite position of aromatic compound is, depending on the nature of reacting groups, not only an index of reactivity of substitution reaction, but also that of total stabilization energy in the formation of charge-transfer complex bonding with another molecule or ion at that position. Therefore, even if a good parallelism between $S_r'$ and physiological activity should be established in an *in vivo* reaction, it does not allow

(16) K. Fukui, T. Yonezawa and H. Shingu, *J. Chem. Phys.*, **20**, 722 (1952).

(17) K. Fukui, T. Yonezawa, C. Nagata and H. Shingu, *ibid.*, **22**, 1433 (1954).

(18) K. Fukui, T. Yonezawa and C. Nagata, *Bull. Chem. Soc. Japan*, **27**, 423 (1954).

(19) K. Fukui, T. Yonezawa and C. Nagata, *J. Chem. Phys.*, **26**, 831 (1957).

(20) K. Fukui, C. Nagata and T. Yonezawa, THIS JOURNAL **80**, 2267 (1958).

(21) T. Fujita, K. Koshimizu and T. Mitsui, unpublished.

(22) T. Fujita, Z. Kumazawa and K. Koshimizu, unpublished.

(23) C. Nagata, K. Fukui, T. Yonezawa and Y. Tagashira, *Cancer Research*, **15**, 233 (1955).

(24) F. Fukui, T. Yonezawa and A. Imamura, Abstract of the Symposium on the Electronic Structure of Molecule (Chemical Society of Japan, 1959), p. 71; *cf.* R. S. Mulliken, THIS JOURNAL, **74**, 811 (1952).

one to decide whether the physiological action was due to a substitution reaction or to molecular complex formation, since one is not yet equipped with an unequivocal knowledge of the type or the nature of the reacting group on the substrate molecule in the living cell.

**Calculation.**—The calculation of $S_r'$ is carried out by using the simple LCAO–MO treatment, solving the secular equation. The parameters used in the calculation are the same as those by Fukui and his co-workers[20] as shown in Table I. The coulomb integral of the substituent X, that of the C atom attached to X, and the resonance integral of the C–X bond, are written as $\alpha+a_x\beta$, $\alpha+a_r\beta$ and $l\beta$, respectively. The coulomb integral of the two O atoms in the carboxyl group is taken to be equal with their value $\alpha+2\beta$ in order to simplify the calculation. As the resonance integral between the carboxyl-C and $C_1$, $0.5\beta$[25] is used in the 2- and 8-substituted acids, while $\beta$ is used in the other cases. In the 8-nitro acid, in which both carboxyl and nitro groups are twisted from the plane, the resonance integral of the C–N bond is also taken as $0.5\beta$.

TABLE I

PARAMETERS USED IN THE CALCULATION

| X | $a_x$ | $a_r$ | |
|---|---|---|---|
| Cl | 2 | 0.5 | 0.8 |
| Br | 1.8 | .4 | .7 |
| $CH_3$ | 2 | 0 | 1 |
| $NO_2$ | $\alpha_N = 1$, $\alpha_O = 1$ | 0.2 | 1 |

## Result and Discussion

It was found as shown in Table II that the growth activities show good parallelism with the values of $S_r'^{(N)}$ or $S_r'^{(R)}$ at the 8-position, the parallelism with $S_r'^{(R)}$ being a little better than that with $S_r'^{(N)}$ while $S_r'^{(E)}$ does not show any parallelism. No correlation exists at the other positions, including the 2-position which corresponds to the *ortho* position of the benzoic acid derivatives. As to the benzoic acid derivatives, Fukui and his co-workers[20] concluded a parallelism only with $S_r'^{(N)}$ at the *ortho* position, but the growth activity varies also with $S_r'^{(R)}$ somewhat more poorly than with $S_r'^{(N)}$. With these MO-treatments alone, therefore, one is not yet in the position to decide on which of the two types of group, nucleophilic or radical group of the plant substrate, is more apt to be involved in the interaction. Moreover, it is quite inconsistent to postulate a true chemical reaction, such as a nucleophilic substitution, between the growth substance and the plant substrate, because the 8-methyl acid, which is unable to undergo any substitution at the 8-position, is highly active. Therefore it is reasonable to consider that the ability of 1-naphthoic acid derivatives to form a molecular complex at the 8-position with the plant substrate is a very important factor determining their growth activity.

Thus, the hypothesis of Muir and Hansch appears to need revision as follows; the interaction between the growth substance and the plant substrate are not a true chemical reaction but presumably molecular complex formation, and the position at which the interaction occurs varies depending on the nature of the series of compounds, that is, it is not always the *ortho* position to the carboxyl group.[26] From the viewpoint of molecular complex formation, the activity of some 2,6-dimethyl substituted benzoic acid derivatives[7,8] may be well explained.

The Veldstra hypothesis is also to be modified so that the absorptive bonding between the growth substance and the plant substrate is determined not only by non-specific London–van der Waals attraction forces but also by charge-transfer force at a definite position and the high growth activity is caused by a strong molecular complex-forming ability as well as a non-planar configuration.

Thus, from the above discussions, a combination of the Veldstra and Muir–Hansch hypotheses seems to be required. The concept of the molecular complex formation is consistent with the reversibility in the earlier stage of the growth substance action.[27]

There are, of course, some other important factors, for example, dissociation constant or *HL*-

TABLE II

RELATION BETWEEN REACTIVITY INDICES AND PLANT GROWTH ACTIVITY OF 1-NAPHTHOIC ACID DERIVATIVES

| | $S_r'^{(R)}$ | $S_r'^{(N)}$ at 8-position | $S_r'^{(E)}$ | Pea straight growth[a] | Callus formation[a] |
|---|---|---|---|---|---|
| 5-$NO_2$– | 0.9058 | 1.3843 | 0.4273 | ± | Inactive |
| 4-$NO_2$– | .6460 | 0.6994 | .5926 | + | ± |
| 2-Cl– | .4542 | .3305 | .5778 | +++ | +++ |
| 8-Cl– | .4538 | .3592 | .5484 | +++ | +++ |
| 8-Br– | .4519 | .3454 | .5584 | +++ | +++ |
| 2-$CH_3$– | .4336 | .2543 | .6129 | + | + |
| 8-$CH_3$– | .4305 | .2128 | .6482 | +++ | ++ |
| 5-Br– | .4286 | .2793 | .5780 | Inactive | Inactive |
| 5-Cl– | .4187 | .2778 | .5597 | Inactive | Inactive |
| 4-Cl– | .4113 | .2441 | .5785 | + | ± |
| 1-Naphthoic | .4081 | .2108 | .6054 | ++ | + |
| 4-Br– | .4036 | .2342 | .5729 | + | ± |
| 6-Cl– | .4015 | .2156 | .5873 | + | + |
| 3-Cl– | .4013 | .2121 | .5904 | Inactive | Inactive |
| 6-Br– | .3990 | .2144 | .5837 | ± | + |
| 3-Br– | .3977 | .2117 | .5836 | Inactive | Inactive |
| 8-$NO_2$– | .3639 | .2171 | .5108 | ± | ± |
| 6-$NO_2$– | .3618 | .1393 | .5842 | Inactive | ..... |
| 3-$NO_2$– | .3584 | .1097 | .6071 | Inactive | Inactive |
| 6-$CH_3$– | .3402 | .2014 | .4790 | Inactive | Inactive |
| 4-$CH_3$– | .3325 | .1475 | .5174 | Inactive | Inactive |
| 3-$CH_3$– | .3196 | .2065 | .4328 | Inactive | Inactive |
| 2-Naphthoic[b] | .8467 | 1.2657 | .4276 | Inactive[c] | ..... |

[a] Order of activity: +++, ++, +, ±; see Part XIII.[2] [b] In this acid there are two non-equivalent *ortho* positions with respect to the carboxyl group. The $S_r'$ at 1-position greater than that at 3-position is shown. [c] Ref. 30.

(25) The resonance integral is given approximately as $\beta \cos\theta$, when the angle of twist of the carboxyl group is $\theta$; *cf.* C. A. Coulson, "Steric Effects in Conjugated Systems," Butterworths Scientific Publications, London, 1958, p. 10.

(26) In the phenoxyacetic and S-phenylthioglycolic acid derivatives, Fukui, *et al.*, suggested an interaction at the *meta* position; K. Fukui, C. Nagata and T. Yonezawa, Abstract of the Symposium on π-Electrons (Chemical Society of Japan, 1956), p. 24.

(27) R. J. Foster, D. H. McRae and J. Bonner, *Plant Physiol.*, **30**, 323 (1955).

balance which seems to affect solubility, permeability and diffusibility into the tissues and cells. The steric circumstance of the molecule should also be considered.

The last may possibly explain the fact that the 5-substituted and some of the 4-substituted compounds are inactive or weakly active in spite of their relatively large indices; there would be a severe restriction to the length of the molecule in the transverse direction in order for the 1-naphthoic acid derivatives to reach the site of action or to fill the gap which has been proposed to exist[28] in the plant substrate (receptor protein). This hypothesis seems to explain satisfactorily why the correlation between the growth activity and the theoretical index is close at the 8-position only, though these acids *in vitro* should be attacked by a reagent at the 2- or 4-position far more easily than at the 8-position.

In the benzoic acid derivatives, Veldstra[8] found that all 4-substituents larger than fluorine are incompatible with activity, and Fukui and his associates[20] showed that some of the *p*-chlorobenzoic acids have large theoretical indices at the *ortho* position in spite of their inactivity. Although the molecular geometry of the benzoic acid derivatives is different from that of the 1-naphthoic acid derivatives, the situation *in vivo* may be similar. The same basis may explain the inactivity of 2-naphthoic acid.[29,30]

The above suggestion that an interaction with the plant substrate occurs at the 8-position next to the carboxyl group leads to the suggestion that the role of the molecular complex formation is to facilitate the approach of the molecule to the substrate so that the carboxyl group may easily be subjected to an interaction with another site of the plant substrate.

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(28) H. Linser, "The Chemistry and Mode of Action of Plant Growth Substance," Butterworths Scientific Publications, London, 1955, p. 141.

(29) T. Mitsui and A. Tamura, *J. Agr. Chem. Soc. Japan*, **25**, 17 (1951).

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# Studies on Compounds Related to Pyrazine. II. The Reaction of 3-Substituted-2-hydrazinoquinoxalines with Carbonyl Compounds

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The reactions of 3-substituted-2-hydrazinoquinoxalines (I) and carbonyl compounds can be summarized as: (1) with carboxylic acids, *s*-triazoloquinoxaline are produced; (2) with ketones or aldehydes, hydrazones are formed which upon pyrolysis give *s*-triazoloquinoxalines; (3) with α-ketonic acids hydrazones are also produced which upon pyrolysis or boiling with organic acids give *s*-triazoloquinoxalines; (4) with β-ketonic esters, either an *s*-triazoloquinoxaline or a pyrazolone derivative is obtained; and (5) the reaction with diketones gives *s*-triazoloquinoxalines, pyrazoles or a pyridazine derivative.

Several purine, alloxazine and pterin derivatives have been shown to be potent agents in cancer chemotherapy; for example, 2,6-diaminopurine which Hitchings[1] prepared as a possible adenine inhibitor and Burchenal[2] tested for activity against leukemia. Roblin[3] and Kidder[4] synthesized a purine inhibitor, 8-azaguanine, which they used with some success in mouse leukemia.[5] Of these compounds 6-mercaptopurine and 8-azaguanine are the most promising anti-cancer agents.

In a previous paper[6] we reported the synthesis of oxazolo[b]quinoxaline which we hoped would inhibit the metabolism of micrö-organisms. With the same aim in mind, we have now prepared some 3-substituted 2-hydrazinoquinoxalines (I) and studied their reactions with carbonyl compounds.

(1) G. H. Hitchings, G. B. Elion, H. V. Werff and A. A. Falco, *J. Biol. Chem.*, **174**, 765 (1948).

(2) J. H. Burchenal, J. R. Burchenal, M. N. Kusihida, S. F. Johnston and B. S. Williams, *Cancer*, **2**, 113 (1949).

(3) R. O. Roblin, Jr., J. O. Lampen, J. P. English, Q. P. Cole and J. R. Vaughan, Jr., THIS JOURNAL, **67**, 290 (1945).

(4) G. W. Kidder and V. C. Dewey, *J. Biol. Chem.*, **179**, 181 (1949).

(5) G. W. Kidder, V. C. Dewey, R. E. Parks, Jr., and G. L. Woodside, *Science*, **109**, 511 (1949).

(6) D. Shiho and S. Tagami, *Pharm. Bull. (Tokyo)*, **5**, 45 (1957).

The starting material, 2-hydrazino-3-R-quinoxaline (I) (R = H, $CH_3$ $C_6H_5$, $CH(CH_3)C_2H_5$), was prepared as shown in Scheme 1. Condensation of *o*-phenylenediamine with an α-ketonic acid[7] or its ester[8] afforded 2-hydroxy-3-R-quinoxaline which was converted to 2-chloro-3-R-quinoxaline. Treatment of this chloro compound with hydrazine hydrate yielded 2-hydrazino-3-R-quinoxaline.[9]

**(1) Reaction of I with Carboxylic Acids and Related Compounds.**—According to the literature, a heterocyclic compound such as I, which has a hydrazino group *ortho* to a ring nitrogen, should react with an organic acid, acid chloride or acid anhydride to give the desired *s*-triazoloquinoxaline; in some cases, however, only the acylated intermediate is obtained, depending on the nature of the heterocyclic compound.[10] 2-Hydrazino-3-R-quinoxaline (I) reacted with acid chlorides or

(7) O. Hinsberg, *Ann.*, **292**, 245 (1896); H. Burton and C. W. Schopee, *J. Chem. Soc.*, 546 (1937).

(8) A. H. Cowenlock and G. T. Newbold, *ibid.*, 622 (1945).

(9) D. Shiho and S. Tagami, paper presented at the 4th Hokuriku Local Meeting of the Pharmaceutical Society of Japan, June 15, 1957.

(10) D. Shiho and S. Tagami, *Yakugaku Zasshi*, **76**, 804 (1956).