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Key words: $tRNA^{Phe}$; Tertiary structure; Hydrogen bond; Bond index; Non-Watson-Crick pairs.

ABSTRACT

The rigidity and stability of the tertiary structure of yeast $tRNA^{Phe}$ is related to a bond index employed in an IEHT calculation. The index permits a quantitative estimate of the electronic cloud along the hydrogen bond, having thus an appealing physical meaning. The results indicate that Hoogsteen-type bonds have, as expected, greater electronic population than Watson-Crick type ones. Other non-Watson-Crick pairings, the wobble pair and G_{15}-C_{48}, exhibit high values of the index for the NH...O bond. In the triples, the electronic density of the hydrogen bridges does not weaken, comparing it with the one of the pairs involved. Contour density maps are shown and dipolar moments of pairs and triples are qualitatively discussed.

Key words: $tRNA^{Phe}$; Tertiary structure; Hydrogen bond; Bond index; Non-Watson-Crick pairs.

INTRODUCTION

The three-dimensional crystalline structure of yeast phenylanine tRNA has been thoroughly studied in recent years [1,2]. Much work has also been devoted to tRNA structure by NMR spectroscopy [3,4] and different theoretical approaches have been proposed to explain this structure [5,6]. The non-Watson-Crick pairing found by Hoogsteen [7] has open the way to numerous quantum-mechanical studies [8], including theoretical contributions to the interpretation of NMR results [9]. Among the different complex factors responsible for the stability and rigidity of the yeast $tRNA^{Phe}$ tertiary structure, base pairing plays an important part, through the hydrogen bonds in pairs and triples [2].

Since the first theoretical works about the hydrogen bond [10] considerable effort has been devoted to this kind of bonding [11]. In the particular case of nucleic acids, a copious literature exists [12].

In the present paper, we restrict ourselves to the discussion of bond indices of some base pairings appearing in yeast $tRNA^{Phe}$; this index [13] (used in the IEHT approximation) involves a quantitative estimate of the electronic cloud along the bridge and has lended itself to a simple physical interpretation in the Watson-Crick case [14].

We wish to explore, through this simple approach, the meaning of a non-Watson-Crick pairing as regards the tertiary structure; for example, whether the electronic population along a non-Watson-Crick hydrogen bond (as Hoogsteen's) differs from a Watson-Crick one.

Let us remember that the use of the IEHT method is satisfactory enough for our purposes [14]. Non-empirical methods are economically prohibitive for such large systems, and both EHT and IEHT are being improved at present with a view to extend their applications [15].

The present study includes more than fifteen pairs of bases (some of which are not reported here) and two triples, considered as supermolecules [16,17]†.

The consideration of different geometries for some pairs have led us to the conclusion that, as bond indices are fairly insensitive to geometry, we may safely disregard geometry optimization. We shall see that bond indices have aspects rather topological more than geometrical.

The variety of hydrogen bonds appearing in the nonhelical regions of yeast $tRNA^{Phe}$ has drawn the attention of workers in this area. The fact that experimental data published hitherto are far from conclusive [18,19] makes worthwhile further theoretical contributions to the understanding of its molecular features.

HYDROGEN BOND INDICES

A bond index formulation [13] has been found appropriate for the IEHT analysis of Watson-Crick hydrogen bonded nucleic acids [14]. Let us briefly remind the definition. Bond index $I_{\mu\nu}$ between atoms μ and ν is [13].

$$I_{\mu\nu} = \sum_{i,j} \sum_{k_\mu, r_\nu} n_i \, x_{ik_\mu} \, y_{ir_\nu} \, n_j \, x_{jr_\nu} \, y_{jk_\mu} \qquad (1)$$

†The calculation involves matrices of order ranging from 81 (A-U or A*-U*) up to 135 (G-G-C) and around 18 CPU hours from a 378/158 IBM computer; see [14].

where x_{ik_μ} is the LCAO coeefficient of the k_μ-th atomic orbital belonging to the i-th MO and

$$y_{ir_\nu} = \sum_{p_\sigma} S_{p_\sigma r_\nu} x_{ip_\sigma} \qquad (2)$$

being S the overlap matrix. $I_{\mu\nu}$, which is rotationally invariant, may be interpreted as the active charge [13,20] distributed along both effective and formal bonds between atom μ and all the other atoms.

Table I shows the $I_{\mu\nu}$ values for the atoms involved in the XH...Y bonds appearing in the different base pairs and triples. Let us recall that in the calculation of the associations as supermolecules the only expressive intermolecular $I_{\mu\nu}$ values are those corresponding to the hydrogen bonds [14]; this fact, which our present results ratify, strongly reinforces the physical sence attached to this magnitude. Again, as has been suggested in an early study [10] and obtained as a result in [14], they are of σ nature.

The table reports the pairings appeating in some tRNAs (in particular yeast $tRNA^{Phe}$). The C_1-C_2 dimer has been included for the sake of comparison with an experimental contour density map (see next section). The labelling (Fig.1) corresponds to the known sequence given for example by Robertus et al. [2], who studied the X-ray structure of yeast $tRNA^{Phe}$ through the isomorphous replacement method with a resolution of 3 Å.

The familiar picture which we reproduce in Fig. 2, is most fitting to our discussion. The bases interactions conferring stability and rigidity to its tertiary structure use to be non

-Watson-Crick type. As we mentioned in the introduction, we want to see whether this intriguing fact evidences itself in some way through the information which the I_{XY}s supply; that is, whether the electronic densities along H bonds in non-Watson-Crick pairings are or not different from the Watson-Crick ones.

Let us remind that in the Watson-Crick pairing (Fig.3), I_{NN} is constant (0,054) [14], while I_{NO} (in NH...O) increases noticeably from A-T and A-U ($\sim$0.026) to G-C (0.039). It has already been remarked the need to distinguish the H-donor ability of the different XY groups, since the points relative to OH, NH and CH fall within well separated regions of the $\Delta\nu_{XH}$ diagrams [21]. But this constancy of the NH...N bond, compared with the NH...O one seems to be unexpected.

Now, the Hoogsteen pairings (Fig.4) exhibit an appreciably higher I_{NN} value ($\sim$37% higher) for the direct (cis) and reversed (trans) conformations, in agreement with calculated stabilities [8]. The invariant A_{14}-U_8 pair is of the reversed kind, which apparently is preferred in Nature to the direct one. Sundaralingham [22] argues that the construction of the cis conformation "would necessitate flipping the adenine base from the preferred anti to the less favoured syn conformation". As our preliminary calculations threw the same I_{XY} values for Watson-Crick A-T and A-U, we have not calculated the trans Hoogsteen pair T_{54}-A_{58}.

The pair G_{15}-C_{48} (Fig.5), which is also invariant, plays an important part in the tertiary structure, for it links loop D with the variable loop, beeing an apparently unfavorable pairing with only two hydrogen bonds. However, comparing it with the three-bonded G-C pair, I_{NO} is greater in 66%, I_{NN} keeping equal. The

G_{15}-C_{48} resonance at the high-field end of the NMR spectrum could correspond to a bonding less dishielding than normal Watson-Crick one [23]. An exception to the constancy of the G_{15}-C_{48} pair is the A-C pair found for glycine tRNA [2]; for A-C, the two I_{NN} values are quite close to the I_{NN} and I_{NO} values of the G_{15}-C_{48} pair.

The Crick wobble pair (Fig.6) [24] appearing in the acceptor stem is the only non-Watson-Crick pair in the double helical stems [25]. From the I_{XY} point of view, there is no objection to the wobble.Let us compare with the G-U* pair, which is the pairing predicted usually for U under enol form [26]. On the one hand, G-U* has three H-bonds with one O-O bond (the only one appearing in the present study) with a relatively high I_{OO} value. On the other hand, both I_{NO} of G_4-U_{69} are larger than the corresponding one in G-U* (∿25%). The NO bonds involving pyrrole-type nitrogens tend to higher I_{XY} values than those with amino-type nitrogens.

In order to roughly explore the influence of neighbourhood upon the bond index, we have calculated a pair similar to the wobble one, placing artificially an oxygen in uracil's position 6 instead of it being in 4 (a 180º rotation about the axis through C_2 and C_5). We obtain the surprising result of lowering, not only the upper bridge from I_{NO}= 0.052 to 0.041, but also the lower one from I_{NO}= 0.054 to 0.033. The bond index value is thus related with the pairing positions in a much more intricate fashion than we perceive.

The pair G_{46}-G_{22} (Fig.7), entering one of the triples, has equal (and hence favorable) I_{XY} values to the A-U Hoogsteen

pair. Let us name Hoogsteen type pairing the seven-sided one and Watson-Crick type pairing, in an extended sense, the six-sided one. Each type of pairing exhibits a constant I_{NN} value except for A-A. The A-A we have reported, which is not A_9-A_{23}, is found in some initiator tRNAs and seems to be the one observed in the crystal structure of 9-MeAde [8]. Despite being seven-sided, its I_{NN}s look as extremes for the six-sided typical values. In turn, A_9-A_{23} eight sided pair belonging to the triple (Fig.9) shows the lowest values. It seems thus as if seven-sided pairs maximize I_{NN}.

Dimer C_1-C_2 (fig.8), which appears in crystalline cytosine monohydrate [27], displays an unusually high I_{NO}, surpassed only by G_{15}-C_{48} (see next section), which in turn is equal to I_{ON} in A*-U*; this last pair possesses the only OH...N bond here reported. Experimental results for dimer formation enthalpies indicate a stronger hydrogen bonding for C-C than A-U or A-T [28], which could be related with our high I_{NO} value.

The only classical Watson-Crick pair contributing to the tertiary structure of yeast $tRNA^{Phe}$ is G_{19}-C_{56}. If a classical Watson-Crick pair should appear in this structure, we expect it to be G-C instead of A-T or A-U for, besides owning three hydrogen bonds, it has higher I_{NO} values. Still, it has recently been suggested that conformational changes of yeast $tRNA^{Phe}$ induced by various intercalators may entail a weakening of the D-loop-T-loop interaction [29]. In such a weakening the G_{19}-C_{56} pair would be involved; it is thus possible that this only tertiary structure Watson-Crick pair is slightly distorted, and seems to bear a peculiar lability. We shall see immediately that

when the Watson-Crick G-C pair enters the G-G-C triple its indices change, while the Watson-Crick A-U pair maintains its values in A-A-U.

When analyzing the behaviour of triples (Fig.9) compared to the pairs they include, the first conclusion could be that their formation does not involve any loss or dissipation in the hydrogen bond electronic density. The A-A pair appearing in A-A-U being eight-sided instead of the seven-sided one shown in the first part of the table, its I_{NN} values are lower in about 15%. Nevertheless, let us remark that G-C in the triple compared with the pair strengthens its I_{NO} for the second NH...O bond in 50%. It is not obvious that the electron density does not weaken under triple formation; this may be a factor of triple stability, which in turn could be related to the significative contribution of the triples to the three-dimensional tRNA structure. Unlike what is expected [10], both of the two hydrogen bonds involving the same oxygen atom in the triple have values close to each other.

From Figs.1 and 2, the known rigidity of the $tRNA^{Phe}$ molecule in the D-loop region [30] seems to be due to the combined effect of the triples and the G_{19}-C_{56} pair. It has been pointed out [22] that most of the tertiary base-pairing interaction obey the anti pairing scheme , and suggested that quantum calculations could account energetically for this. We can say nothing about this question; there is no evident relation between the electronic density along the hydrogen bond and chain direction of the glycosyl configuration. Besides, the claimed relative energetic stability [22] is beyond the scope of our esti-

mations, due to the known IEHT limitations regarding energy.

We had noticed [14] that the fraction of an electron lost by the NH bond of the separate bases when forming a Watson-Crick pair goes virtually entirely to the bridge. This, in line with our present results, appears as a characteristic of the NH bond, not being verified for OH. Accordingly, when this happens (i.e. for nitrogen as an X atom) hydrogen has the same total charge as in the separate bases, for what is lost by I_{XH} goes to I_{HY}. Formation of the hydrogen bond affects instead, although not much, the total X and Y charges. In this sense, G-C in the triple behaves abnormally; for the I_{NH} weaken, relative to the separate bases, appreciably more than the I_{HY} increase.

It has long since been recognized that hydrogen bond lengthens the XH distance; also, the relation between the infrared band due to the XH stretching vibration and the inverse dependence of the XY distance as a function of the bond strenght [10]. In the separate bases, our I_{NH} keeps within the range = 0.968-0.980 [14] and I_{OH} in U* is 0.936; we see from Table I that in pairs I_{XH} spans form 0.854 (OH in G-U*) upto 0.940 (NH in Watson-Crick A-T and A-U). Actually, the mean I_{XH} value of Table I is 0.90, clearly lower than that of the separate bases. This trend is in satisfactory agreement with the mentioned experimental evidence.

The values of Table I suggest a proportionality between I_{XY} and I_{HY}. We have found

$$I_{HN} = (1.44 \pm 0.01)\ I_{NN}; \quad I_{HO} = (1.31 \pm 0.01)\ I_{NO}$$

There is only one I_{ON} and one I_{OO}. For them, $I_{HN} = 1.40\ I_{ON}$ and $I_{HO} = 1.40\ I_{OO}$ respectively.

ELECTRON-DENSITY DIAGRAMS

Since density diagrams are heavily time-consuming, we have chosen to center our attention to a few significant diagrams and to leave aside, for the moment, electron density difference maps [31]. We display in Fig.10 the reversed Hoogsteen A-U pair and through Fig.11 the comparison between cytosine and its dimer. The dimer adopted obeys the model proposed for an experimental result for a cytosine derivative [27]. In table II Watson-Crick A-U values are taken from ref. [14]; the addition of the Watson--Crick G-C diagram is unnecessary to the comprehension of the table, which reports the conjugation curves ρ together with the I_{XY} values. The conjugation curves for the reversed Hoogsteen A-U pair are higher than those of the Watson-Crick A-U pair, in agreement with the I_{XY} values.

Our C_1-C_2 dimer diagram does not reproduce the detailed experimental structure, but its rather delocalized aspect is better visualized in Fig. 11a than in an ab-initio diagram of cytosine [32]. Fig. 11b shows that under association the 0.030 outer contour merely splits into the 0.025 and the 0.035 conjugation curves in the hydrogen bonding region, thus rounding off the picture obtained upon considering only this region in the other diagrams.

Refinement analysis of X-ray diffraction data at 2.5 $\mathring{A}$ resolution leads to electron density maps of the pairings appearing in yeast $tRNA^{Phe}$; previous results were obtained with lower resolution and, as refinement proceeded, the hydrogen bonding regions became clearer [25], With the mentioned 2.5 $\mathring{A}$ resolu-

tion, however, the electron density maps show clusters of atoms rather than atoms, so that the conjugation curves appear clearly quite seldom. It is hence difficult to compare our Fig.10 with the experimental A_{14}-U_8 map including the sugar phosphate backbone, which is beyond our possibilities. Instead, the conjugation curve corresponding to our enhanced I_{NO} value of G_{15}-C_{48} is distinctly beheld. In the experimental diagrams for pairs and tripples, the contours for any single base look different depending on which association they enter. Nevertheless, as they are undoubtedly concerned by the sugar-phosphate backbone, we cannot separate the effect of the backbone from that of association.

Table II suggests a rough proportionality between ρ and I_{XY}; anyhow, we have found that in an unusual G-5FU pairing the NH...F bond has a lower I_{XY} and a slightly higher conjugation curve than the OH...O one [33].

Table III shows the origin of HOMO and LUMO in the pairs and triples of the present calculation. In ref. [14] we have drawn the HOMOs of the Watson-Crick A-U pair, and those of U and A separately. It is clearly depicted there that HOMO is almost wholly U; more, it arises fundamentally from uracil's O_4. The table manifests that this kind of behaviour is quite a general feature. Association merely changes the orientation of the bulkily contributing HOMO's lone pair.

It could have been expected the HOMOs to be hybrid lone-pair orbitals, but they are decidedly p orbitals. Recently, through an ab-initio calculation, Fukui et al. [34] have met a similar trait for the delocalization interaction orbitals of ammonia and methylamine, and suggested that the p nature must be enhanced in

order to create a new bond. This is consistent with our results for uracil. HOMO is $2p_{\sigma}$ for O_4, the position where it tends to enolize. Only when the O_4 position is already enolized, the HOMO becomes a 2p belonging to O_2, which in turn is thus ready to receive a proton. This behaviour is independent from pairing, for hydrogen bond is usually a too weak interaction as to influence the HOMO nature, at least within the limits of an IEHT calculation.

Thus, wherever an oxygen is present, HOMO is always a $2p_{\sigma}$ oxygen orbital, with coefficient higher than 0.8. This holds both for pairs and triples. LUMOs are all π, and hence delocalized.

Although more frequently HOMO and LUMO originate from different single bases, as has been mentioned for a π semiempirical selfconsistent calculation of the G-C pair [35], this is not always the case; in particular our result is not so for the Watson-Crick G-C base pair. This does not depend on the hydrogen bond. Sometimes the HOMO's oxygen is involved in it, sometimes not.

The A-A dimer, which is the only pair considered not containing oxygen, exhibits a disparate HOMO; it is also σ, but a delocalized one (Fig. 12). Both adenines have diagrams similar to that of the separate base [14]. It is seen that the left base contributes somewhat more than the right one; N_1 enters in the 0.0001 delocalization curve in the first and does not in the second one.

Each of the two triples behave differently. In A_9-A_{23}-U_{12}, HOMO is uracil's, and LUMO is built from both adenines. In G_{46}-G_{22}-C_{13}, G_{22} does not take part neither in HOMO nor in LUMO.

In the separate bases too our HOMO is σ and LUMO is π. Some other calculations differ regarding this prediction [36].Recently, theoretical studies and analysis of experimental data have testified to the presence of n-π* transitions in the first absorption bands of the bases [37].

HYBRIDIZATION AND DIPOLE MOMENTS

Table IV reproduces the range of hybridization ratios sp^{α}. In the bases, parameter α is < 2 for the pyrrole of amino-type N, and > 2 for pyridine-type ones. Under enolization, uracil's oxygen decreases appreciably its p-character at that position. It has been found [10] that the experimental trend of the energy is reproduced only if the s-character of the orbital associated to atom Y increases as the bond becomes stronger.The range of variation of the results reported in table IV is too small as to relate them to such a strength.

Oxygen keeps the same α value under association, be it in a X or in a Y role. For the pyridine-type nitrogens (Y atoms) the same occurs, but when they are pyrrole – or amino-type (X atoms) their α value is increased by entering hydrogen bonds.Guanine's oxygen α (2.23) suffers a slight alteration (2.21) under association (G-C, G_{15}-C_{48}, G_4-U_{69}, G-U*), with the only exception of the G-G pair and the corresponding triple, where it becomes 2.17.

Pullman [38] compares hybridizations in different all-valence electron calculations of A, U, G and C, and she obtains a hybridization of the carbonyl's oxygens with a nearly $(2p)^2$ orbital in direction perpendicular to the CO bond. This result, verified here, is insensitive to association (Fig.10).We find values less far from the classical representation both for NH or NH_2-type

($\underline{s}^{1.2}\underline{p}^{2.3}$) and for pyridine-type nitrogens ($\underline{s}^{1.3}\underline{p}^{2.8}$).

Table V presents the calculated dipole moments. It has been shown [39] that both semiempirical and ab-initio methods lead to reasonably consistent predictions for dipole moments of the DNA bases. The difficulties in determining experimental dipole moments are well known; they use to be measured in dilute solutions of some non-polar solvent such as benzene or dioxane, and extrapolation to gaseous μ is by no means straightforward. Corrections through empirical formulae change dipole moment in pyridine, for example, from two solution values 2.21 D and 2.26D, to 2.37 and 2.42 D for the gaseous ones [40]. The experimental data of table V are in solution. Let us examine the results for the pairs and triples. Although we cannot ensure quantitative conclusions, the qualitative comparison certainly makes sense.

Watson-Crick A-U and A-T should be much more soluble in water than G-C (as they are) if the only moment were the pair one. Of course, account must be taken of the sugar-phosphorous backbone presence. Actually, all the pairs and the triple involving G have higher dipole moments than the other associations, suggesting thus a possible source of difference in aggregation state, solubility or other properties related to μ. The strikingly high μ values of the G_{15}-C_{48} pair and of the G-G-C triple may play a role in delucidating the tertiary structure through the enhancement of the dipole-monopole, dipole-multipole interactions.These interactions have been extensively analyzed [12,39,41].

The direct and reversed A-U pairs lead to similar μ values; so do both pairing schemes for G-U, the wobble and G-U*. The A-A-U triple is not at all equivalent, from the μ viewpoint, to the other one including G.

The contribution of $\mu_{orbital}$ is much lower than that of $\mu_{charges}$, as it should. Nevertheless in A-T, Watson-Crick A-U and C-C they show similar values. It has been claimed [31] that retention of atomic moment is advantageous, for charge moments are usually in poor agreement with experiment and atomic moments generally correct them in the proper direction. It could be argued that in our approximation, as point charges give enough agreement with experiment, the correction would be unnecessary. However, taking account the above mentioned uncertainties in the experimental data and that anyway they are too few as to allow such a conclusion, we have chosen to report both values. If it is true that the correction is in the proper direction, then it always increases the charge moment (except for Watson-Crick A-U, where it decreases) and more, they approximately add, for the orientation of both vectors turns to be similar in most cases.

CONCLUSIONS

- The electronic density along a NH...N bond shows two distinct constant values depending on whether it appears in a Watson-Crick pairing or in a Hoogsteen pairing: 0.08 of an electron in H...N in the first one and 0.11 in the second one. In a NH...O bond, it suffers a large variation, from 0.03 upto 0.08 of an electron in H...O, not being related to the kind of pairing.
- I_{NO} exhibits unusually high magnitude for two of the $tRNA^{Phe}$ pairings, the Crick wobble and G_{15}-C_{48}. In the wobble, the I_{NO} values are strongly dependent on the pairing positions. For G_{15}-C_{48}, the magnified I_{NO} evidences itself through one of the few conjugation curves met in the experimental electronic densi

ty maps.

- Under triple formation, the I_{XY} corresponding to the hydrogen bonds of the pairs do not weaken, thus contributing to the rigidity of the core region.
- Both for pairs and triples, if an oxygen is present the HOMO is always practically a $2p\sigma$ oxygen orbital, with coefficient higher than 0.8. LUMO is always π. There is tendency for HOMO and LUMO of pairs to originate from different bases.
- All the associations involving guanine have dipole moments significantly higher than the other associations.

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BIBLIOGRAPHY

[1] F.L. Suddath, G.J. Quigley, A. McPherson, D. Sneden, J.J. Kim, S.H. Kim and A. Rich, Nature 248, 20(1974).

[2] J.D. Robertus, J.E. Ladner, J.T. Finch, D. Rhodes, R.S.Brown, B.F.C. Clark and A. Klug, Nature 250, 546(1974).

[3] D.R. Kearns, Ann. Rev. Biophys. Bioeng. 6, 477(1977).

[4] P.D. Johnston and A.G. Redfield, Biochem. 20, 1147(1981).

[5] D. Perahia, B. Pullman, D. Vasilescu, R. Cornillon and H. Broch, Biochim. Biophys. Acta 478, 244(1977).

[6] K. Kim and M.S. John, Biochim. Biophys. Acta 565, 131(1979).

[7] K. Hoogsteen, Acta Cryst. 12, 822(1959).

[8] B. Pullman, P. Claverie and J. Caillet, Proc. Nat. Acad. Sci. USA 55, 904(1966).

[9] B. Pullman, Int. J. Quantum Chem., Quantum Biol. Symp. 4, 3(1977).

[10] L. Paoloni, J. Chem. Phys. 30, 1045(1959).

[11] M.D. Joesten and L.J. Schaad, Hydrogen Bonding, (Marcel Dekker Inc., N. York,1974), p. 114.

[12] J. Langlet, P. Claverie, F. Caron and J.C. Boeuve, Int. J. Quantum Chem. 19,299(1981).

[13] M. Giambiagi, M.S. de Giambiagi, D.R. Grempel and C.D. Heyman, J. Chim. Phys. 72, 15(1975).

[14] M. Giambiagi, M.S. de Giambiagi and W. Barroso Filho , Chem. Phys. Lett. 78, 541(1981); program from P. Dibout, QCPE 10, 256(1973) to which we added the subroutine for bond indices.

[15] A.K. Mukhopadhyay and N.G. Muderjee, Int. J. Quantum Chem. 19, 515(1981); S. Beran, Z. Slanina and D.C. Zidarov, Int. J. Quantum Chem. 19, 585(1981).

[16] E. Clementi, J. Mehl and W. von Niessen, J. Chem. Phys. 54, 508(1971).

[17] S. Scheiner and C.W. Kern, J. Am. Chem. Soc. 101, 4081(1979).

[18] J.N. Spencer, J.E. Gleim, C.H. Blevins, R.C. Garrett, F.J. Mayer, J.E. Merkle, S.L. Smith and M.L. Hackman, J. Phys. Chem. 83, 2615(1979).

[19] V. Sánchez, A.G. Redfield, P.D. Johnston and J. Tropp, Proc. Nat. Acad. Sci. USA 77, 5659(1980).

[20] C.A. Trindle, J.Am. Chem. Soc. 91, 219(1969).

[21] L. Paoloni, A. Patti and F. Mangano, J. Mol. Structure 27, 123(1975).

[22] M. Sundaralingham, Int. J. Quantum Chem., Quantum Biol. Symp. 4, 11(1977).

[23] B.R. Reid and R.E. Hurd, Acc. Chem. Res. 10, 396(1977).

[24] F.H.C. Crick, J. Mol. Biol. 19, 548(1966).

[25] G.J. Quigley and A. Rich, Science 194, 796(1976).

[26] S. Abdulnur, J. Theor. Biol. 58, 165(1976).

[27] G.A. Jeffrey and Y. Kinoshita, Acta Cryst. 16, 20(1963).

[28] I.K. Yanson, A.B. Teplitsky and L.F. Sukhodub, Biopolymers 18, 1149(1979).

[29] P.E. Nielsen, Biochim. Biophys. Acta 655, 89(1981).

[30] M.A. Reuben, P.R. Ainpour, H.L. Hester, V.L. Neveln and E. Wickstrom, Biochim. Biophys. Acta 654, 11(1981).

[31] D.B. Boyd, J. Am. Chem. Soc. 94, 64(1972).

[32] A. Pullman, M. Dreyfus and B. Mély, Theor. Chim. Acta 16, 85(1970).

[33] M.S. de Giambiagi, M. Giambiagi and D.M.S. Esquivel, Z. Naturforsch. 37a,292 (1982).

[34] K. Fukui, N. Koga and H. Fujimoto, J. Am. Chem. Soc. 103,196(1981).

[35] R. Rein and J. Ladik, J. Chem. Phys. 40, 2466(1969).

[36] B. Mély and B. Pullman, Theor. Chim. Acta 13, 278(1969).

[37] V.I. Danilov, V.I. Pechenaya and N.V. Zheltovsky, Int. J. Quantum Chem. 17,307(1980).

[38] A. Pullman, Int. J. Quantum Chem. IIs, 187(1968).

[39] M.N. Stamatadiou, T.J. Swissler, J.R. Rabinowitz and R. Rein, Biopolymers 11, 1217(1972).

[40] M.S. de Giambiagi, M. Giambiagi and R. Ferreira, J. Chim. Phys. 61, 697(1964).

[41] B. Pullman and J. Caillet, Theor. Chim. Acta 8, 223(1967).

FIGURE CAPTIONS

Fig. 1 - Sequences of yeast $tRNA^{Phe}$.

Fig. 2 - Orientation of bases in tRNA molecule. Taken from S.H. Kim, in Transfer RNA, S. Altman, ed., (MIT press, Cambridge, Massachussetts, 1978), p.248.

Fig. 3 - Watson-Crick pairings.

Fig. 4 - Direct and reverse Hoogsteen pairings.

Fig.10 - Contour density diagram of the H-bond region in reversed Hoogsteen A-U, in the molecular plane. Units are $\underline{e}$ au^{-3}.

Fig.11 - Comparison between contour density diagrams of cytosine (a) and its dimer (b), in the molecular plane. The contours are respectively, from outside, 0.030, 0.1, 0.2 and 1.0 $\underline{e}$ au^{-3}. The 0.030 contour splits into 0.025 and 0.035 in the H-bond region.

Fig.12 - HOMO of the A-A pair, in the molecular plane. Contours are respectively, from outside, 0.001, 0.005 and 0.01 $\underline{e}$ au^{-3}.

TABLE I - Bond indices in XH...Y bonds, (i) Pairs, (ii) Triples

(i)

Pair	Fig.	X	Y	I_{XY}	I_{XH}	I_{HY}
A-U	(3a)	N	O	0.026	0.941	0.033
		N	N	0.054	0.897	0.076
		N	O	0.039	0.923	0.051
G-C	(3b)			0.032	0.932	0.042
		N	N	0.053	0.889	0.077
A-U	(4a)	N	O	0.038	0.932	0.048
		N	N	0.073	0.868	0.107
A_{14}-U_8	(4b)	N	O	0.037	0.933	0.047
		N	N	0.073	0.868	0.107
G_{15}-C_{48}	(5a)	N	O	0.058	0.890	0.081
		N	N	0.052	0.900	0.073
A-C	(5b)	N	N	0.053	0.901	0.074
				0.054	0.901	0.075
G_4-U_{69}	(6a)	N	O	0.052	0.901	0.072
				0.054	0.889	0.077
		O	O	0.065	0.854	0.091
G-U*	(6b)	N	N	0.055	0.885	0.079
		N	O	0.044	0.915	0.059
G_{46}-G_{22}	(7a)	N	N	0.076	0.859	0.114
		N	O	0.036	0.929	0.046
A-A	(7b)	N	N	0.056	0.901	0.077
				0.049	0.910	0.068
C_1-C_2	(8a)	N	N	0.051	0.901	0.074
		N	O	0.056	0.899	0.075
A*-U*	(8b)	O	N	0.058	0.877	0.081
		N	N	0.054	0.893	0.078

TABLE I - (cont.)

Triple	Fig.	X	Y	I_{XY}	I_{XH}	I_{HY}
$A_9-A_{23}-U_{12}$	A_9-A_{23} (9a)	N	N	0.047	0.911	0.066
				0.043	0.911	0.068
	$A_{23}-U_{12}$	N	O	0.026	0.940	0.033
		N	N	0.054	0.896	0.076
$G_{46}-G_{22}-C_{13}$	$G_{46}-G_{22}$ (9b)	N	O	0.036	0.929	0.045
		N	N	0.076	0.859	0.114
	$G_{22}-C_{13}$	N	O	0.032	0.918	0.044
				0.048	0.889	0.067
		N	N	0.052	0.885	0.073

TABLE II - Conjugation curves (ρ) and I_{XY} values

base pair	X	Y	ρ(e au^{-3})	I_{XY}
Watson-Crick A-U [14]	N	O	0.015	0.026
	N	N	0.025	0.054
Hoogsteen A_{14}-U_8	N	O	0.020	0.037
	N	N	0.040	0.073
Watson-Crick G-C	N	O	0.015	0.039
	N	N	0.025	0.053
	N	O	0.015	0.032
C-C dimer	N	N	0.025	0.051
	N	O	0.035	0.056

TABLE III - HOMO and LUMO of pairs and triples

	Fig.	HOMO(σ)	LUMO(π)
A-U	(3a)	U (O_4)	A
G-C	(3b)	C (O)	C
A-U	(4a)	U (O_4)	A
A_{14}-U_8	(4b)	U (O_4)	A
G_{15}-C_{48}	(5a)	G (O)	C
A-C	(5b)	C (O)	C
G_4-U_{69}	(6a)	G (O)	U
G-U*	(6b)	U (O_2)	U
G_{46}-G_{22}	(7a)	G_{46} (O)	G_{22}
A-A	(7b)	A + A	A + A
C_1-C_2	(8a)	C_2 (O)	C_1
A*-U*	(8b)	U (O_2)	U
A_9-A_{23}-U_{12}	(9a)	U (O_4)	A_9+A_{23}
G_{46}-G_{22}-C_{13}	(9b)	G_{46} (O)	C_{13}

TABLE IV - Hybridization ratios $\underline{sp}^{\alpha}$.α values

Separate bases	
Pyrrole- or amino- type N	1.85 - 1.89
Pyridine- type N	2.13 - 2.23
Carbonyl- O	2.22 - 2.24
Enol - O	2.06

Pairs and triples (in XH...Y)

	X	Y
N	1.90 - 1.97	2.11 - 2-21
O	2.07 - 2.09	2.20 - 2.23

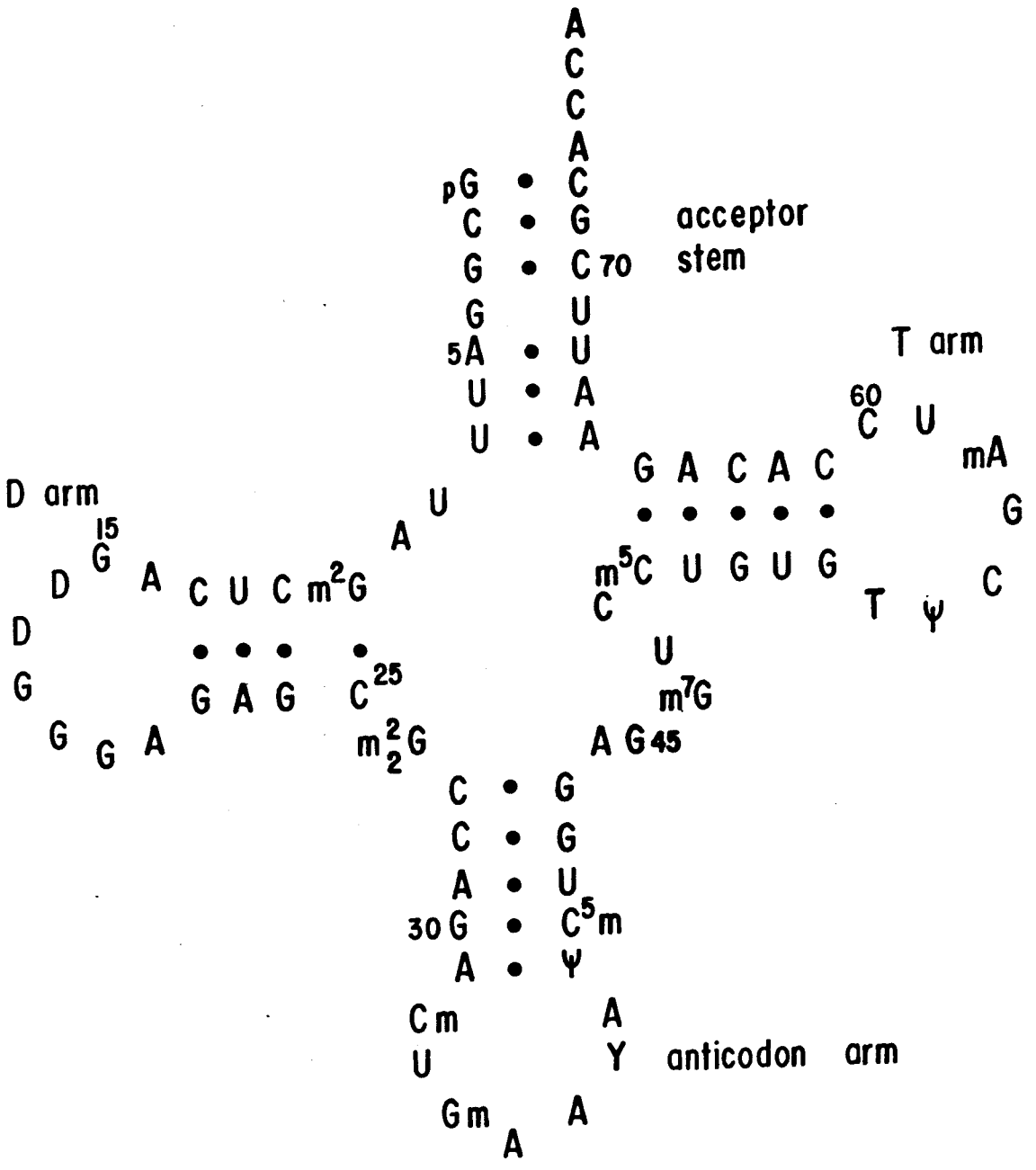
TABLE V - Dipole moments μ in Debyes

	Fig.	$\mu_{tot.}$	$\mu_{charges}$	$\mu_{orb.}$	μ_{exp}
A(A*)		3.40(5.86)	2.50(4.59)	1.39(1.34)	3.0[a]
U(U*)		5.04(11.47)	4.01(7.41)	1.16(4.24)	4.16[b]
T		7.18	5.10	2.59	4.13[b]
G		8.85	6.02	2.84	
C		9.06	6.63	2.56	7.0[c]
A-T		3.37	2.64	2.32	
A-U	(3a)	1.13	1.81	1.18	
G-C	(3b)	9.42	6.69	2.96	
A-U	(4a)	7.48	5.64	2.18	
A_{14}-U_8	(4b)	6.30	5.25	1.06	
G_{15}-C_{48}	(5a)	18.84	14.51	4.34	
A-C	(5b)	6.11	4.22	1.91	
G_4-U_{69}	(6a)	10.77	7.40	3.54	
G-U*	(6b)	9.78	6.98	3.31	
G_{46}-G_{22}	(7a)	14.83	11.22	3.77	
A-A	(7b)	6.03	5.04	1.06	
C_1-C_2	(8a)	4.96	2.55	2.41	
A*-U*	(8b)	3.46	2.88	0.98	
A_9-A_{23}-U_{12}	(9a)	4.43	3.38	1.31	
G_{46}-G_{22}-U_{12}	(9b)	18.54	13.75	4.82	

a) De Voe, H. and Tinoco Jr., I. (1962) J. Mol. Biol. 4, 500 - 517

b) Kulakowska, I., Geller, M., Lesing, B and Wierzchowski, K.L. (1975) Biochim. Biophys. Acta 361, 119-130

c) Kulakowska, I., Geller, M., Lesyng, Bolewska, K. and Wierzchowski, K.L. (1975) Biochim. Biophys. Acta 407, 420-429.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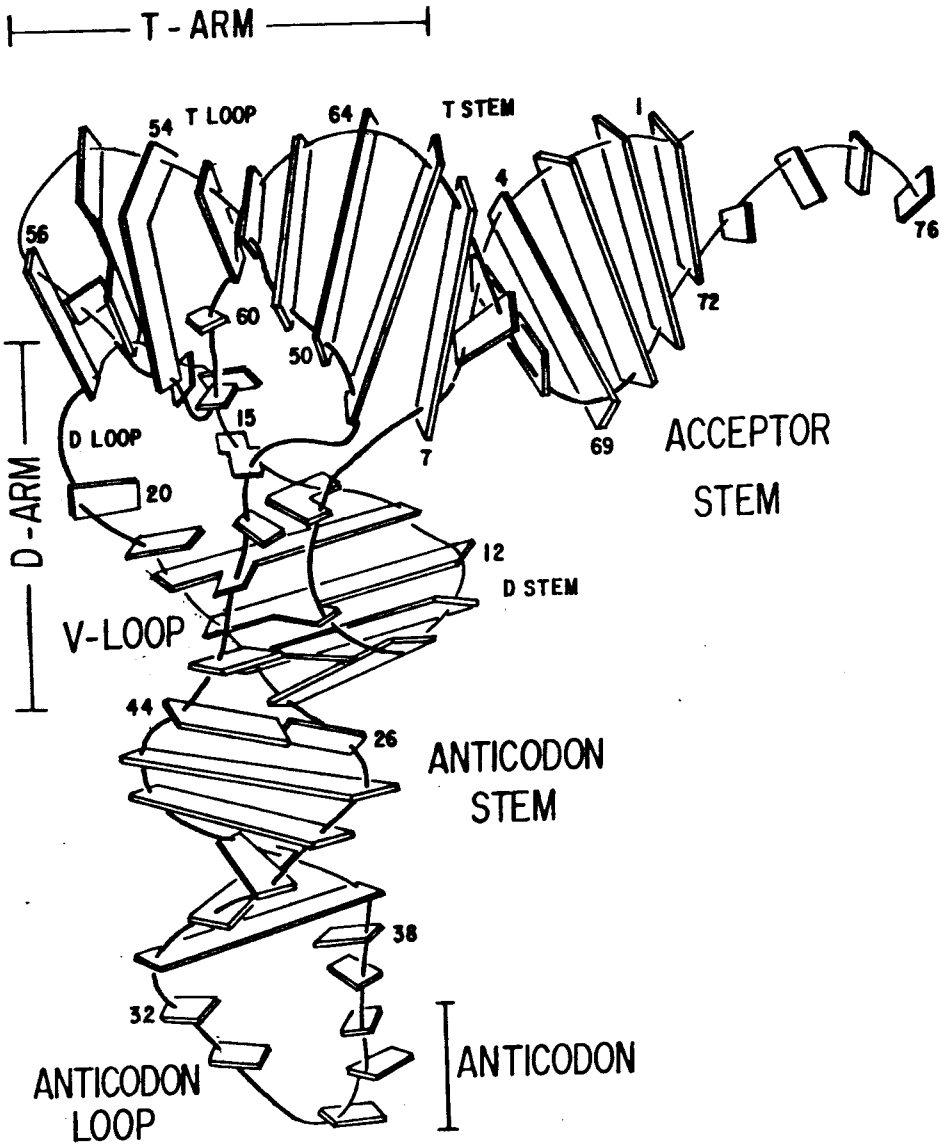
C
C
A
pG • C
C • G
G • C 70
G U
5A • U
U • A
U • A
acceptor
stem
T arm
60
C U
mA
G A C A C
G
m5C U G U G
C
T ψ
C
U
m7G
A G 45
D arm
15
G
D G A C U C m2G
D
G G A
G A G C25
m22G
C • G
C • G
A • U
30 G • C5m
A • ψ
Cm
U
A
Y anticodon arm
Gm A
A

FIG. 1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50
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D LOOP
7
69
ACCEPTOR
STEM
D-ARM
20
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V-LOOP
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26
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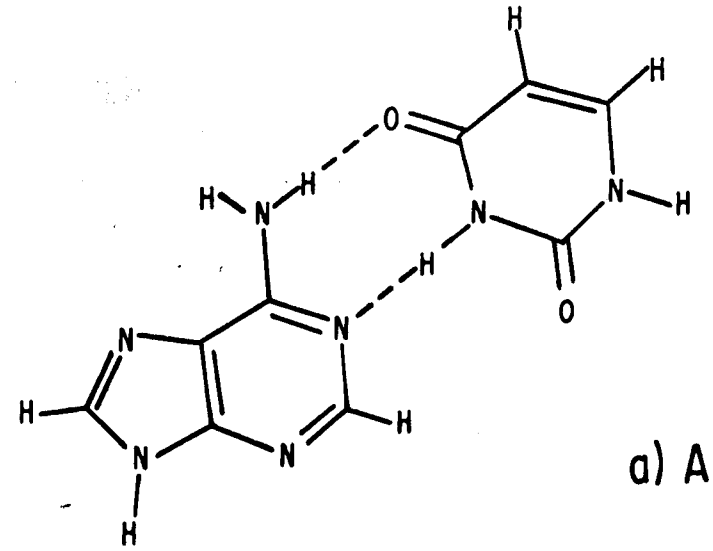
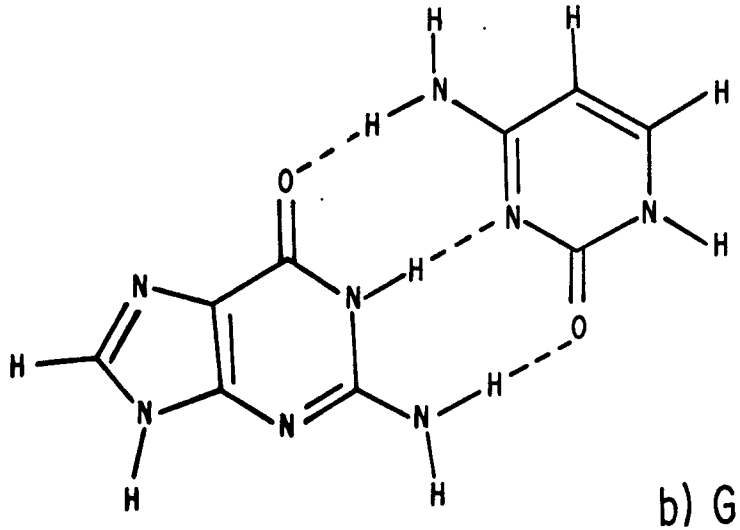
38
32
ANTICODON
LOOP
ANTICODON

FIG. 2

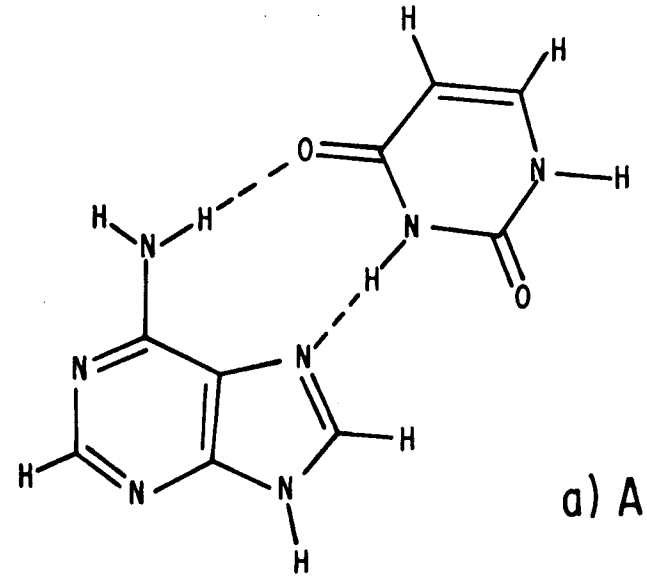


a) A - U

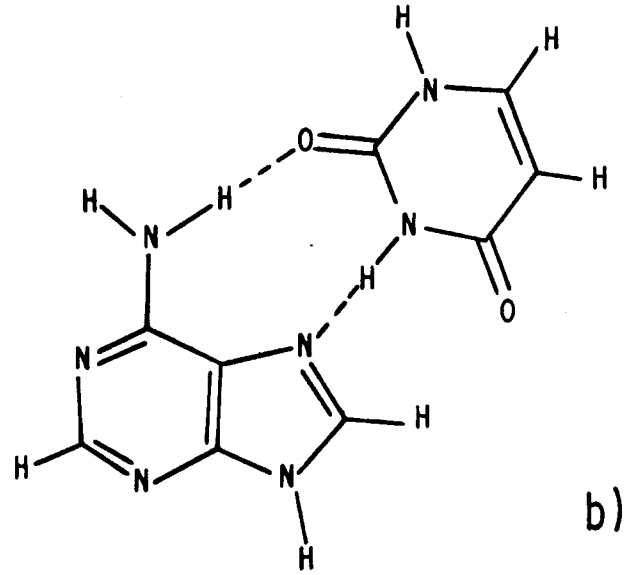


b) G - C

FIG. 3



a) A - U



b) $A_{14} - U_8$

FIG. 4

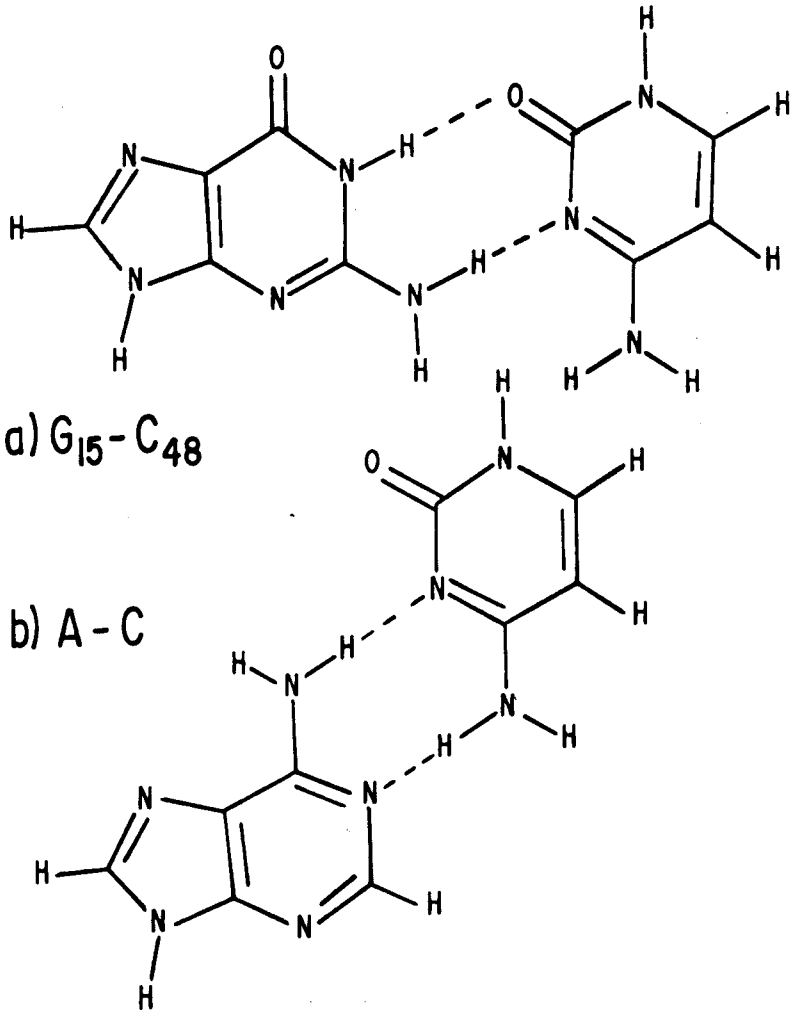
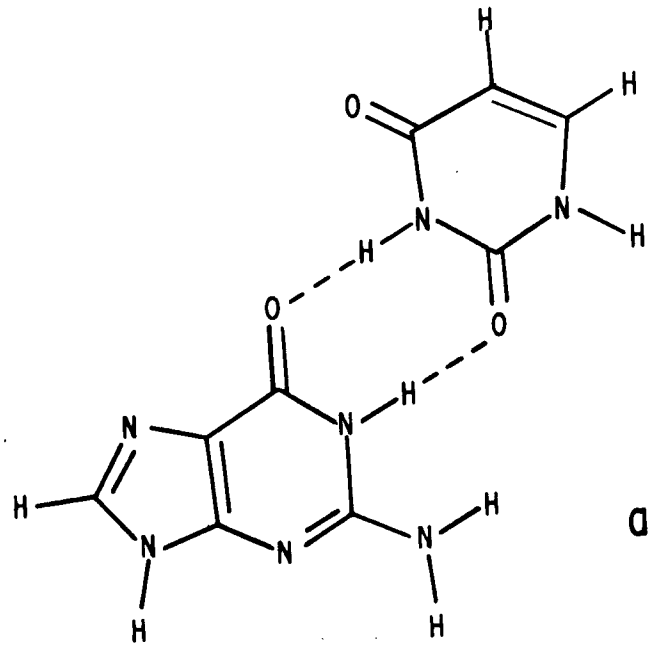
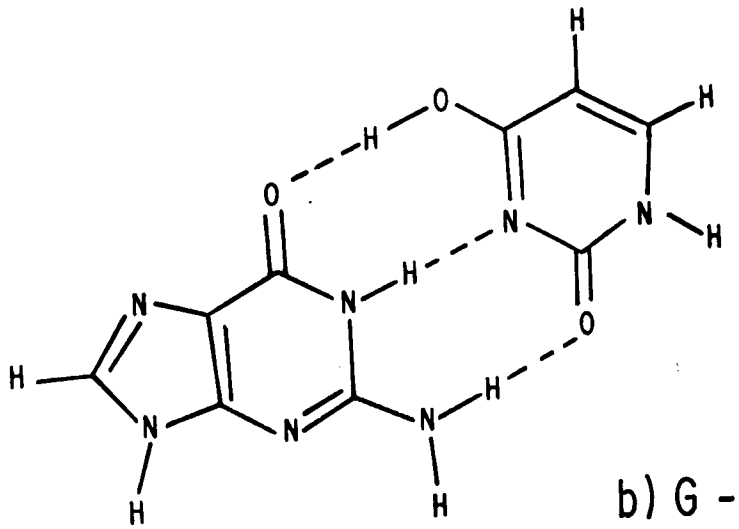


FIG. 5

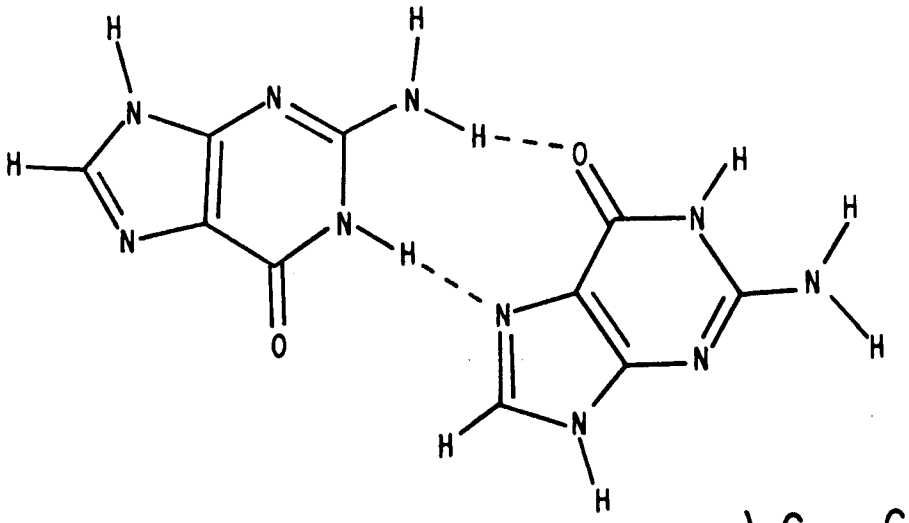


a) $G_4 - U_{69}$

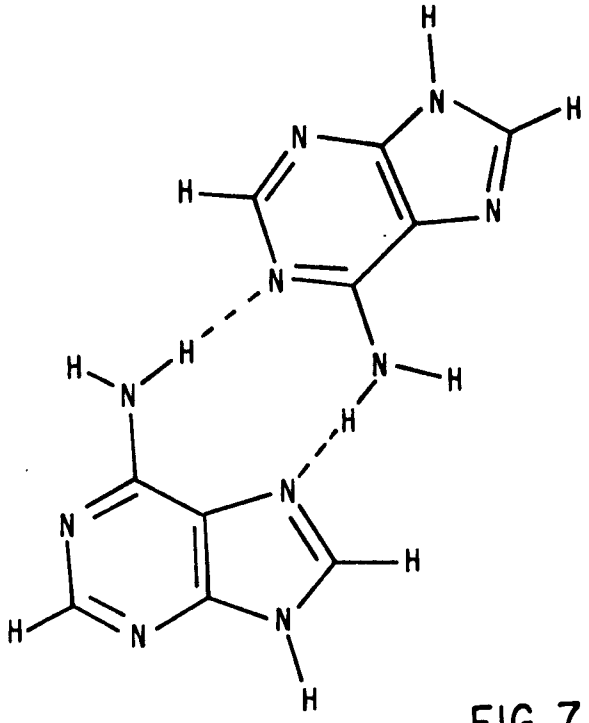


b) G - U*

FIG. 6

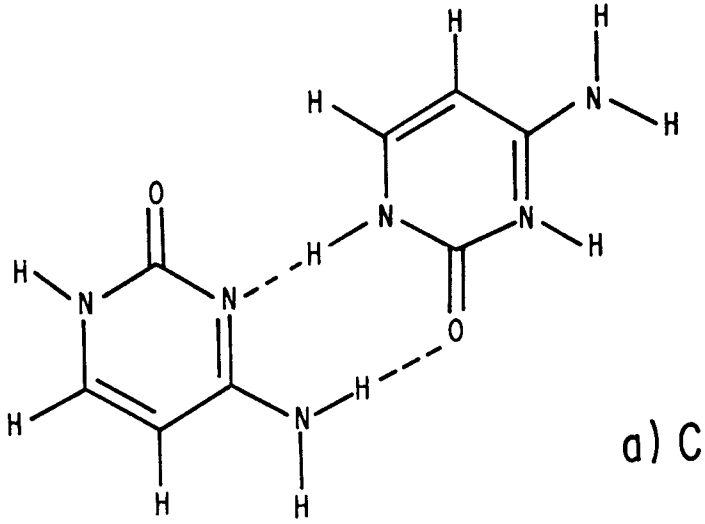


a) G_{46}-G_{22}

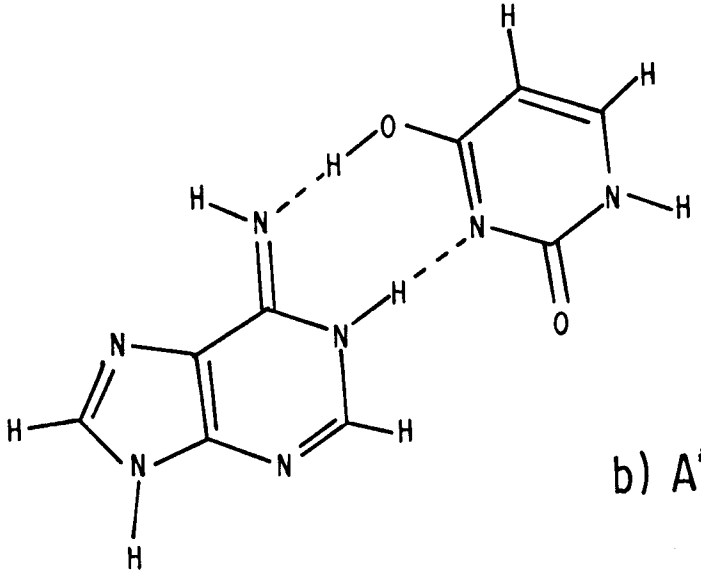


b) A-A

FIG. 7

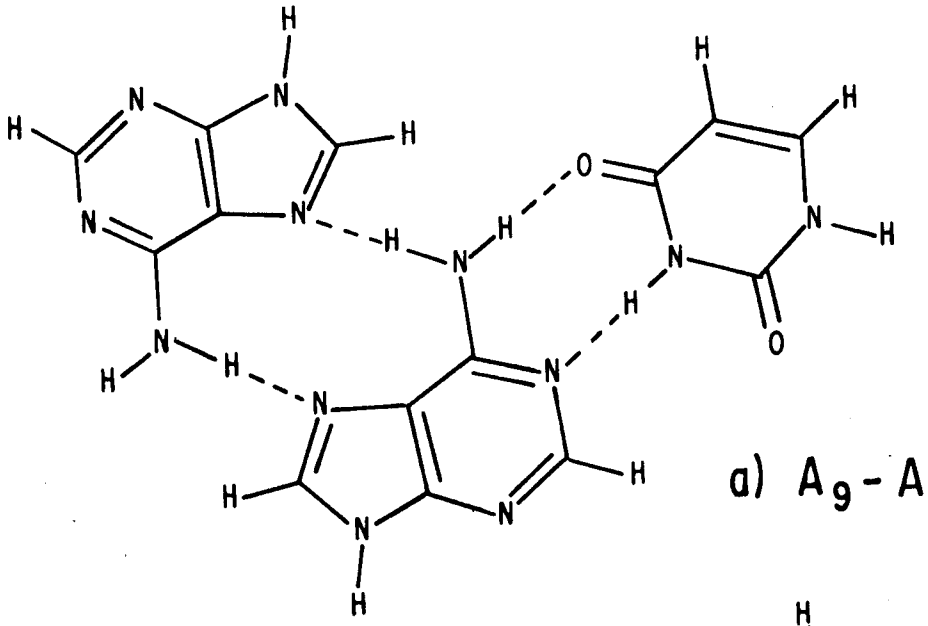


a) $C_1 - C_2$

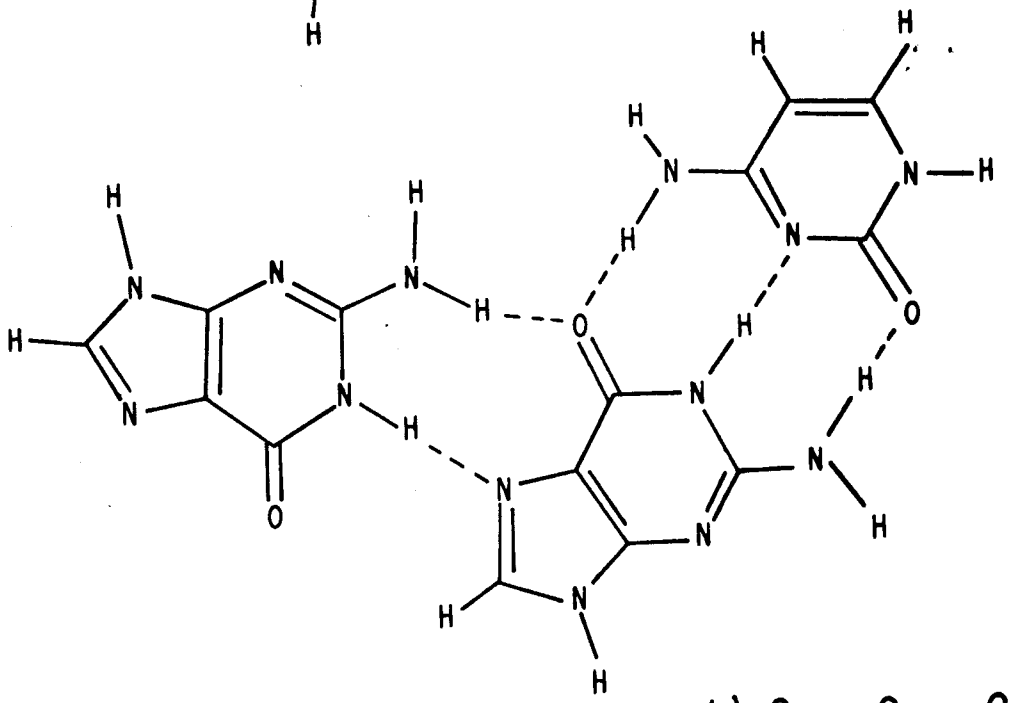


b) $A^* - U^*$

FIG. 8

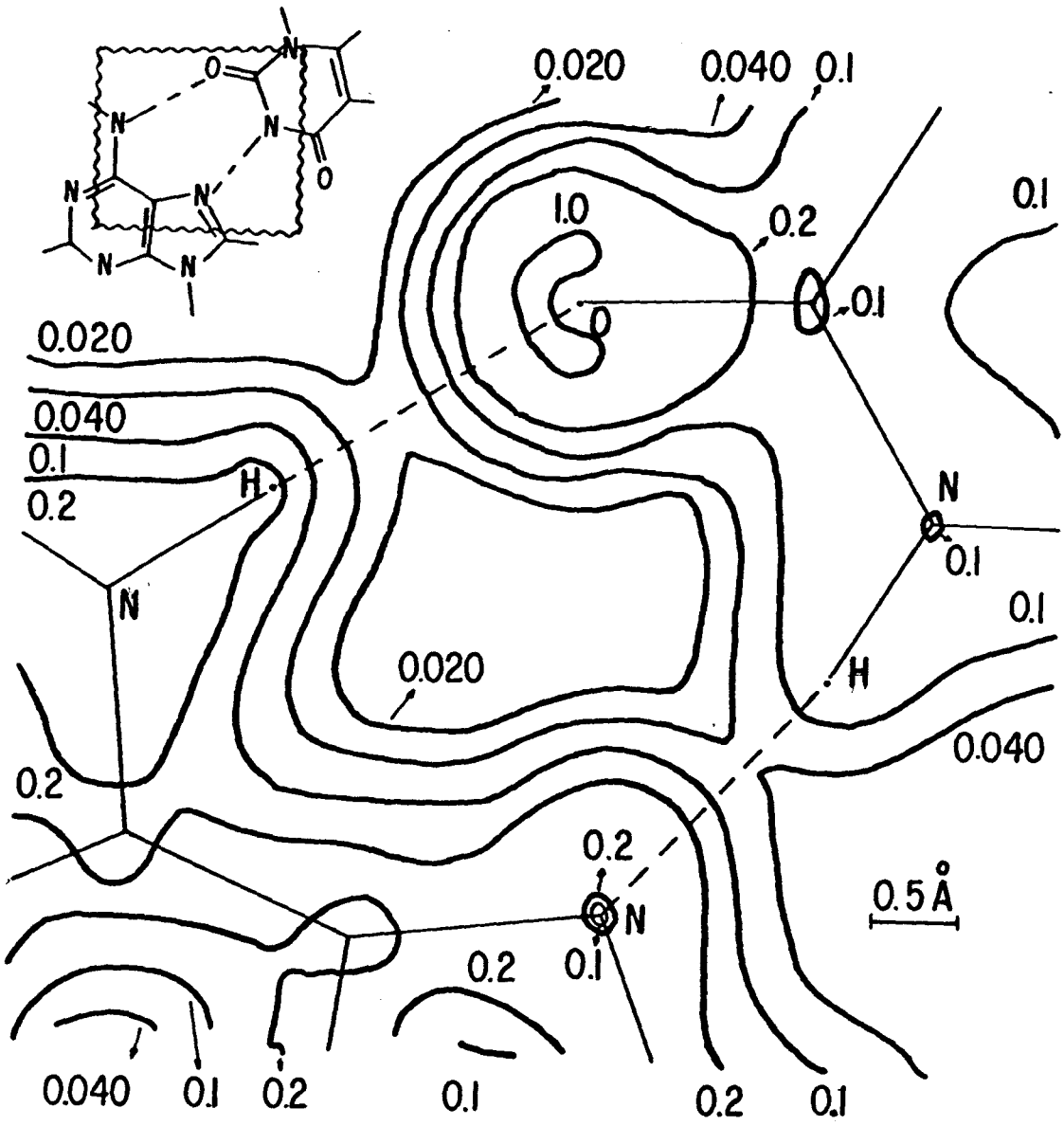


a) $A_9 - A_{23} - U_{12}$



b) $G_{46} - G_{22} - C_{13}$

FIG. 9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0.1

FIG. 10

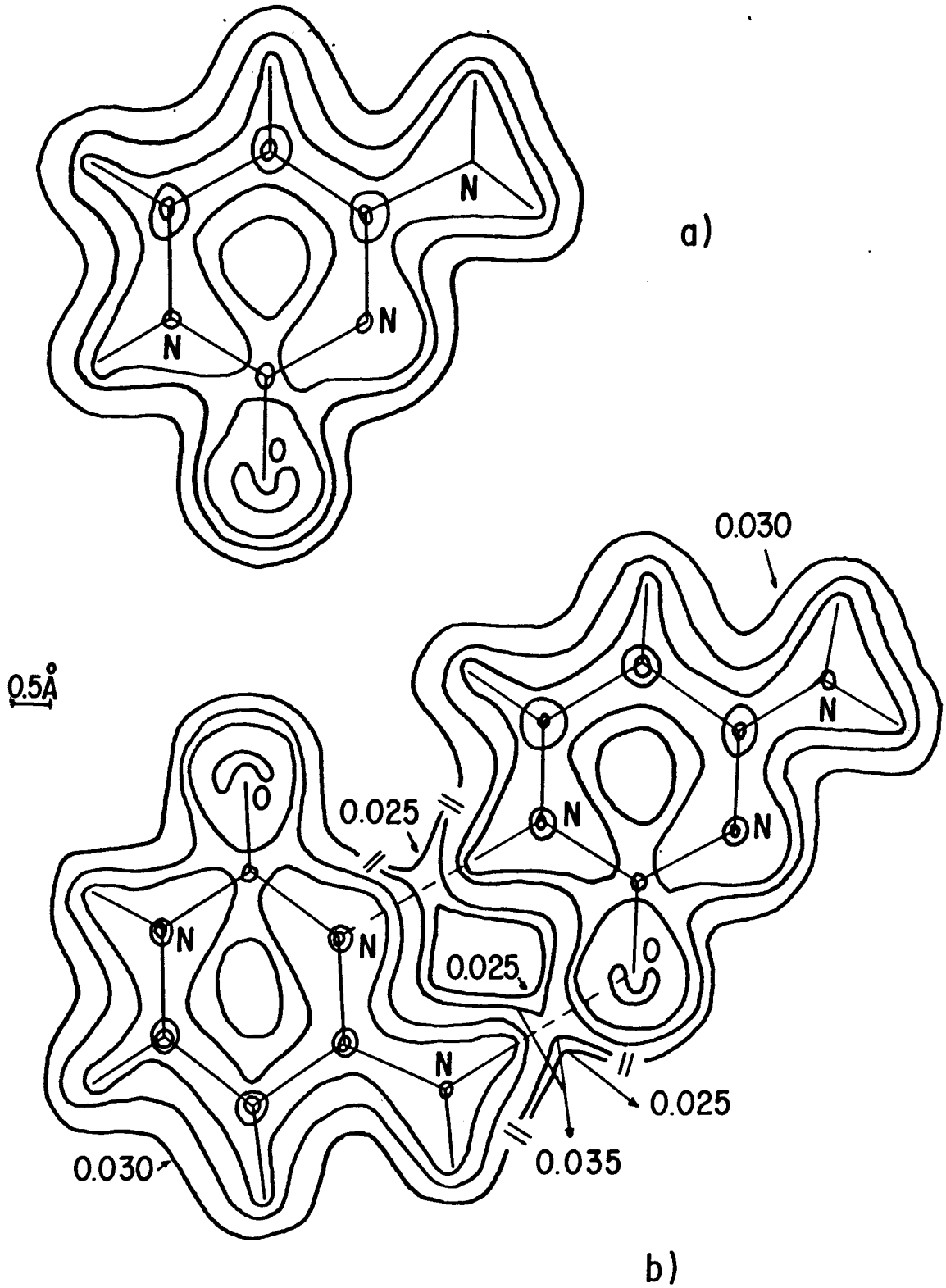

FIG.II

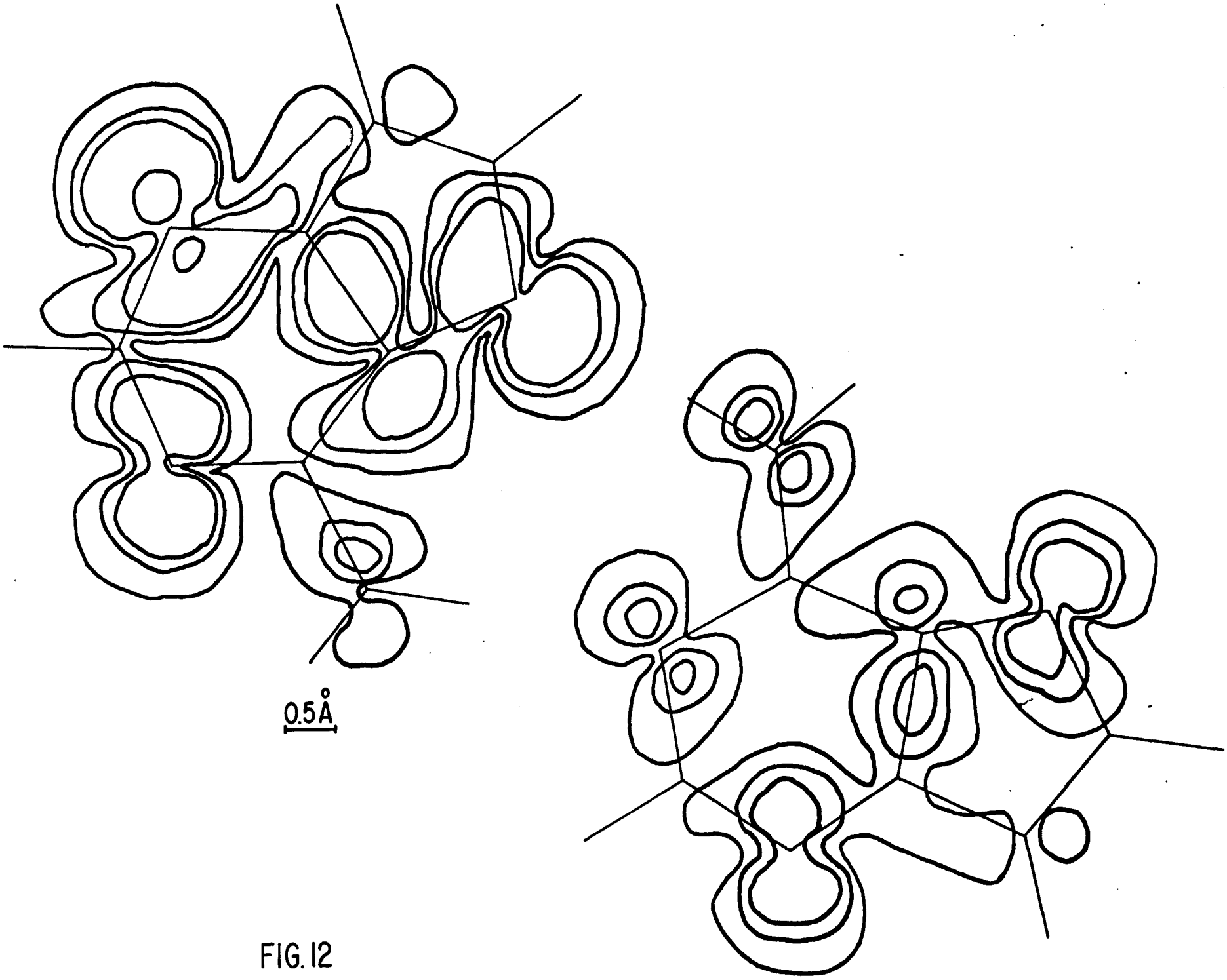

FIG. 12