

X-ray Study of *Cis-Trans* Isomerism in Some Pyridyl Antihistamines

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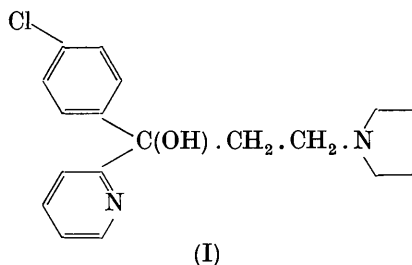
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(Received 31 May 1957 and in revised form 15 August 1957)

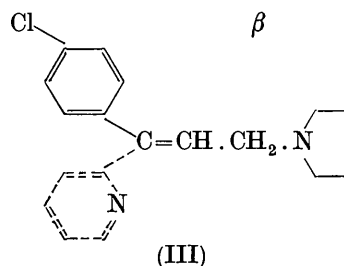
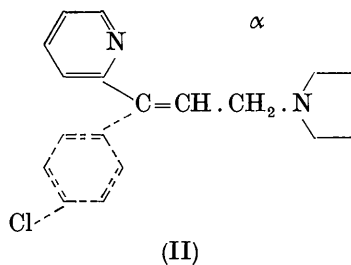
The problem of *cis-trans* isomerism in 1-(4-halogenophenyl)-1-(2-pyridyl)-3-pyrrolidinoprop-1-ene hydrohalogenides has been examined by X-ray crystal analysis. These compounds show antihistaminic activity, and the β -isomer, which is the less potent antihistamine, is shown to have a *cis* configuration (pyridine and pyrrolidino groups on the same side of the double bond), in support of previous suggestive chemical evidence. A projection of the structure of β -1-(4-chlorophenyl)-1-(2-pyridyl)-3-pyrrolidinoprop-1-ene hydrobromide has been refined by the least-squares method.

Introduction

By dehydration of 1-*p*-chlorophenyl-1- α -pyridyl-3-pyrrolidinopropan-1-ol (see I)



D. W. Adamson and his colleagues in the Wellcome Research Laboratories have prepared a pair of substituted prop-1-enes (Adamson & Billingham, 1950; Adamson *et al.*, 1951). Chemical evidence strongly indicates that these compounds, identified as α and β forms, are geometric isomers. The α -form is among the most powerful antihistamines known; the β -form is much less active. Ultra-violet absorption spectra of the isomers are distinctly different; that of the α -form is almost identical with that of α -pyridylethylene, while the spectrum of the β -isomer closely resembles that of *p*-chlorophenylethylene. Thus the indication is that in solution the pyridyl and ethylenic groups of the α -form are approximately coplanar, as in formula II; while in the case of the β -form in solution the *p*-chlorophenyl group is approximately in the plane of



the double bond, as in formula III. These formula (taken from Adamson *et al.* (1951)) have the approximately coplanar groups in solid lines.

The primary difference between these structures, however, is apparently that in one isomer the methylenepyrrolidino group is *cis* with respect to the pyridine ring, while in the other the configuration of these two groups is *trans*. Adamson and coworkers have subsequently obtained chemical evidence which strongly suggests that the β -form is the *cis*-isomer (Adamson, 1952). However, these investigators recognize that the chemical evidence for the assignment of *cis* or *trans* configuration is not unequivocal.

The same type of isomerism and differences in chemical and antihistaminic activity was observed for a series of related dehydrated α -pyridyl carbinols. Since, as Adamson *et al.* state (1951), 'this series of isomers ... provides an illustration of the selective influence of spatial configurations upon chemical and biological reactivity', it appeared worthwhile to have one pair of the structures examined by X-ray diffraction.

Crystals of a series of α - and β -1-(4-halogenophenyl)-1-(2-pyridyl)-3-pyrrolidinoprop-1-ene hydrohalogenides, $C_{18}N_{19}N_2X.HX'$, with X and X' chlorine or bromine atoms, were submitted to this laboratory by Dr. Adamson. All four α -compounds with $(X, X') = (Cl, Br)$, and two β -compounds with $X = Cl$ or Br and $X' = Br$, were provided. These had been crystallized from an alcohol and ethyl acetate mixture. This paper reports the results of an X-ray examination of these crystals.

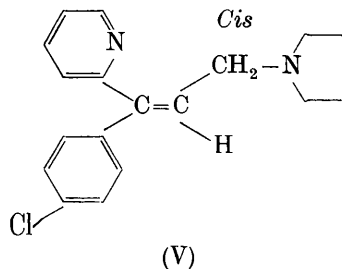
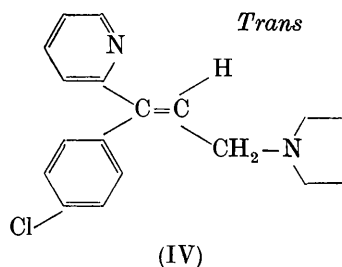
* Deceased.

Nature of the X-ray study

The purpose of the X-ray study was to establish, in conjunction with available chemical information, which of the two forms has the *cis* configuration for the methylenepyrrolidino and pyridine groups, and which the *trans*.

It is evident that the nitrogen in the pyrrolidino ring is involved in the ion formation, since at 25° C. the pK_B 's for N-methylpyrrolidine and pyridine are 3.8 (Craig & Hixon, 1931) and 8.7 (Hahn & Klockmann, 1930), respectively. Thus the major step in the X-ray study was the location of the halogen atoms X and X' with respect to the organic residue, and the direction of the ethylene bond. X must be attached to the phenyl group in the *para*-position, and X' closely associated with the pyrrolidino nitrogen. Once the position of X and the general location of the phenyl group are established, the critical problem is the direction of the ethylene bond.

It was not the purpose of the present investigation to establish either accurate atomic coordinates, bond distances, or inter-bond angles. The primary aim was to determine which isomer exists in the *cis* form (V) and which in the *trans* (IV). A more complete analysis, perhaps in three dimensions, will be required to establish which modification, II or III, represents each of these isomers. Since the point group is centro-symmetric, a three-dimensional analysis is quite feasible.

Preliminary X-ray examination of the α -isomer

Crystals of suitable size of the four derivatives of the α -isomer, with $(X, X') = (\text{Cl}, \text{Br})$, were obtained by recrystallization from ethyl acetate. Oscillation and equi-inclination Weissenberg photographs with $\text{Cu } K\alpha$ radiation showed that the space group for all four compounds is $P1$ or $P\bar{1}$, with 8 molecules in the unit cell. The cell dimensions of the four compounds do not

Table 1. Cell dimensions of β -isomers

	a (Å)	b (Å)	c (Å)	β (°)	ρ_o (g.cm. ⁻³)	ρ_c (g.cm. ⁻³)
Cl-phenyl.HBr	6.01	11.2	25.9	97.4	1.46	1.46
Br-phenyl.HBr	6.05	11.2	26.3	97.0	1.56	1.60

differ by more than a few per cent from one to another, and the compounds have quite similar melting points. It seems likely, consequently, that they are isomorphous. Since the structural problem with 4 or 8 non-equivalent molecules in the cell is an extremely complicated one, it seemed wisest to seek the answer to the isomerism problem via the structure of the β -form, or in some other α -isomer derivative.

X-ray examination of the β -isomer

Needle-shaped crystals of two derivatives of the β -isomer, with $X' = \text{Br}$ and $X = \text{Cl}$ or Br , were obtained by recrystallization from ethyl acetate. Optical measurements indicated that both crystals are biaxial.

Oscillation and equi-inclination Weissenberg pictures with $\text{Cu } K\alpha$ radiation showed that the two compounds are monoclinic and isomorphous, with the needle axis along a . Dimensions of the unit cells are given in Table 1, together with observed and calculated densities.

Extinction rules for both compounds are: $(h0l)$ present only for $h+l = 2n$, $(0k0)$ only for $k = 2n$. The space group for both compounds is thus $P2_1/n$, and the heavy atoms are in general (fourfold) positions. The extinctions establish the existence of a symmetry center. These facts indicated the probable usefulness of the isomorphous heavy-atom method.

Shortness of the a axis rendered study of the (100) projection advisable. A crystal of the Cl-phenyl hydrobromide ($\mu = 48 \text{ cm.}^{-1}$) with cross-section 0.10 mm. \times 0.25 mm., and one of the Br-phenyl hydrobromide ($\mu = 59 \text{ cm.}^{-1}$) with cross-section 0.25 mm. \times 0.25 mm., were selected for intensity measurements. Intensities on Weissenberg photographs, taken with $\text{Cu } K\alpha$, were visually estimated by comparison with intensity scales prepared by oscillating the crystals in various repetitions through one reflection, using a moving film. The intensities were corrected for Lorentz and polarization factors but not for absorption, and were brought to an approximately absolute scale by the Wilson method. Patterson projections from this data could be interpreted unequivocally in terms of the heavy-atom vectors, and permitted an approximate determination of the y and z coordinates of these atoms.

An electron-density projection on (100) was computed on X-RAC for the chlorophenyl compound, using phases determined solely from the Cl and Br positions, and employing Fourier coefficients with l indices only up to 20. Utilizing models based upon reasonable interatomic distances and bond angles, a molecule was fitted on to this projection. Despite the roughness of

Table 2. Final coordinates and temperature factors for the Cl-phenyl hydrobromide of β -pyridyl antihistamine

	<i>y</i>	<i>z</i>	$B \times 10^{16}$ (cm. ²)
C ₁	0.8536	0.0388	3.53
C ₂	0.8207	0.0536	4.46
C ₃	0.7854	0.0099	2.72
C ₄	0.2015	0.0402	3.04
C ₅	0.1604	0.0523	3.36
C ₆	0.1294	0.0138	3.17
C ₇	0.2274	0.0873	2.79
C ₈	0.1495	0.1260	4.36
C ₉	0.1602	0.1763	4.48
C ₁₀	0.2095	0.2400	3.91
C ₁₁	0.6699	0.2052	3.51
C ₁₂	0.5959	0.1874	5.00
C ₁₃	0.5872	0.2308	4.81
C ₁₄	0.3349	0.0858	5.50
C ₁₅	0.4399	0.0593	2.62
C ₁₆	0.5421	0.0604	3.65
C ₁₇	0.5368	0.0860	5.31
C ₁₈	0.4266	0.1172	3.75
N ₁₉	0.1178	0.2211	3.60
N ₂₀	0.3344	0.1150	2.51
Cl ₂₁	0.8863	0.0938	3.92
Br ₂₂	0.9100	0.2007	3.89

the approximation, an encouraging fit was obtained.

From the available chemical information, the rings could be unequivocally identified. The chlorine atom on the phenyl group established the identity of that ring, and the position of the pyrrolidino ring was deduced from its proximity to the Br atom, and by its distance from the phenyl in the elongated section of the molecule. The pyridine ring was properly near the phenyl group.

A series of successive Fourier projections were made, taking into account more and more peaks in the cell, and improving the Cl and Br coordinates. Fourier maps were accomplished on X-RAC, and structure factors were computed by means of numerical tables and Beever-Lipson strips. The general shape of the molecule emerged fairly clearly, but the disagreement did not decrease properly as the approximations progressed; cut-off of the Fourier series at $l_{\max} = 20$ is no doubt the chief reason for this and for the elongation of peaks in these Fourier maps.

The successive-approximation method on the Cl-phenyl derivative was abandoned at this point, and data were collected on the isomorphous β -Br-phenyl.HBr compound. Application of the isomorphous method caused the organic moieties to show up quite clearly in the projections, which were computed without any assumptions concerning the positions of C and N atoms. Structure factors were computed on S-FAC. After a number of successive approximations, still involving Fouriers with $l_{\max} = 20$, but adequate to refine the heavy-atom positions, the disagreement factor $R = \frac{\sum ||F_o| - |F_c||}{\sum |F_o|}$ for the β -Cl-phenyl.HBr compound dropped to 0.34, and that for the β -Br-phenyl.HBr to 0.27. With all non-observed structure factors omitted from the computation, the factors were 0.22 and 0.24 for the β -Cl and β -Br crystals, respectively.

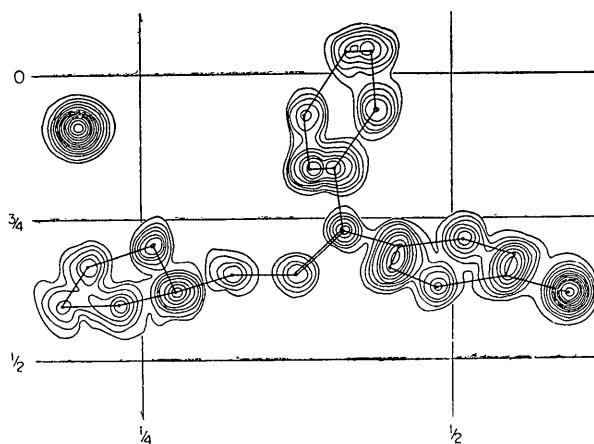


Fig. 1. Electron-density map of pyridyl antihistamine with all coefficients as computed on I.B.M. Contour intervals: 0.5 e.Å⁻² for light atoms, 1 e.Å⁻² for Cl, 2 e.Å⁻² for Br; lowest contour 3 e.Å⁻².

As a final step, all the observed data ($F_o \neq 0$) for the β -Cl-phenyl.HBr compound were used for a least-squares refinement accomplished on the IBM 704 computer. After six cycles, the R -factor dropped from 0.22 to 0.130 for $F_o \neq 0$, and from 0.34 to 0.194 when $F_o = 0$ were included. Final coordinates and temperature factors are shown in Table 2. Calculated and observed F_{ohl} are compared in Table 3.

The electron-density projection on (100) of the β -Cl-phenyl.HBr derivative is shown in Fig. 1, with a line drawing of the molecule superimposed. Fig. 2 indicates the chemical structure of the compound, with the atoms numbered to correspond to the list of atomic coordinates, and with the configuration of the structure corresponding to the (100) projection.

The Fourier map clearly reveals the position of the pyrrolidino ring with respect to the other groups and to the ethylene linkage. The β -isomer is thus established as the *cis*-form.

No conclusions as to the nature of the α -form can be made on the basis of the X-ray study; but chemical and physical evidence that the α -form must be *trans*

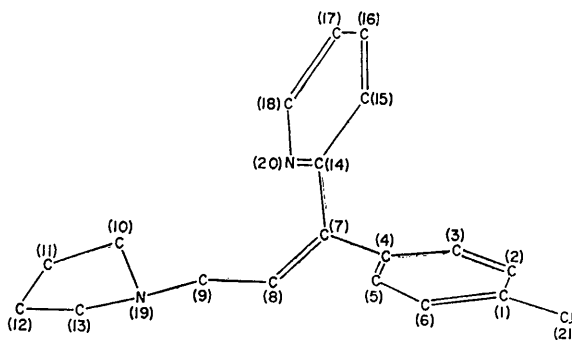


Fig. 2. Projection of structure of Cl-phenyl derivative of pyridyl antihistamine, with atoms numbered as in text.

Table 3. Comparison of calculated and observed F_{0kl} for the Cl-phenyl hydrobromide of β -pyridyl antihistamine

hkl	$ F_o $	F_c	hkl	$ F_o $	F_c	hkl	$ F_o $	F_c	hkl	$ F_o $	F_c
000	776.0	—	0,2,19	64.6	-59.4	0,4,23	14.2	-19.6	0,6,28	6.5	+13.2
002	29.6	-10.8	0,2,20	< 0.7	+11.8	0,4,24	5.8	-4.7	0,6,29	9.4	+10.0
004	44.5	+35.3	0,2,21	37.7	+40.2	0,4,25	6.5	+10.0	0,6,30	7.7	-14.0
006	89.2	-96.4	0,2,22	21.4	-17.7	0,4,26	4.8	+4.0			
008	105.2	-111.2	0,2,23	14.9	-18.8	0,4,27	< 0.7	+2.1	071	< 0.7	+5.9
0,0,10	133.6	+134.0	0,2,24	14.9	-9.7	0,4,28	8.9	+13.2	072	60.8	-51.9
0,0,12	68.7	-71.3	0,2,25	8.2	+5.9	0,4,29	5.8	-15.9	073	31.2	+23.6
0,0,14	< 0.7	+4.7	0,2,26	< 0.7	-2.2	0,4,30	4.1	-7.7	074	32.0	+28.6
0,0,16	< 0.7	+8.3	0,2,27	7.7	+8.7	0,4,31	< 0.7	+9.1	075	44.5	-39.6
0,0,18	23.6	-25.2	0,2,28	< 0.7	-7.2	0,4,32	< 0.7	+2.5	076	20.0	-15.5
0,0,20	52.6	+54.5	0,2,29	18.3	-19.4				077	28.6	+24.8
0,0,22	32.7	-4.5	0,2,30	7.0	+10.0	051	26.0	-23.4	078	35.6	+34.3
0,0,24	19.0	+20.0	0,2,31	4.8	+7.5	052	34.1	+31.7	079	22.4	-19.4
0,0,26	< 0.7	+11.5	0,2,32	0.7	+1.6	053	93.2	+78.8	0,7,10	< 0.7	+6.0
0,0,28	29.6	-33.1				054	40.6	-33.9	0,7,11	18.5	-20.0
0,0,30	< 0.7	-1.1	031	141.8	-134.1	055	40.6	-35.2	0,7,12	35.3	-38.0
0,0,32	< 0.7	-6.7	032	109.3	+109.6	056	15.8	+16.1	0,7,13	9.4	+12.1
			033	48.5	-43.0	057	71.0	+76.9	0,7,14	15.9	+17.3
011	48.5	+50.3	034	76.9	-68.0	058	10.8	-8.1	0,7,15	19.5	-23.4
012	7.0	-8.8	035	16.1	-15.6	059	52.6	-54.2	0,7,16	11.3	-8.6
013	48.5	-49.0	036	101.4	+100.7	0,5,10	7.7	+8.0	0,7,17	26.7	+30.0
014	68.7	-74.9	037	44.7	+36.4	0,5,11	48.5	-44.9	0,7,18	18.3	+18.8
015	101.2	+122.6	038	102.8	-103.2	0,5,12	7.0	+8.1	0,7,19	5.8	-4.9
016	81.0	+89.0	039	27.2	+27.1	0,5,13	23.1	+30.4	0,7,20	15.9	+11.9
017	44.7	-47.2	0,3,10	39.6	-35.9	0,5,14	8.9	-12.0	0,7,21	< 0.7	-6.1
018	36.8	-37.3	0,3,11	19.0	+15.9	0,5,15	30.3	-36.8	0,7,22	8.9	-11.7
019	44.7	+42.4	0,3,12	52.6	+52.9	0,5,16	16.1	+13.7	0,7,23	8.4	+10.6
0,1,10	25.5	-22.2	0,3,13	4.1	-1.8	0,5,17	60.8	+63.6	0,7,24	7.0	+9.3
0,1,11	30.8	+25.0	0,3,14	17.8	-23.5	0,5,18	19.5	+17.8	0,7,25	19.5	-21.3
0,1,12	44.7	+37.4	0,3,15	10.6	+10.4	0,5,19	17.1	-21.7	0,7,26	5.8	-11.8
0,1,13	44.5	-44.5	0,3,16	38.7	+44.6	0,5,20	7.0	+11.9	0,7,27	4.8	+6.2
0,1,14	22.6	-27.5	0,3,17	13.5	-6.2	0,5,21	< 0.7	-3.0	0,7,28	4.8	+7.8
0,1,15	26.0	+23.0	0,3,18	56.7	-55.8	0,5,22	< 0.7	+2.5	0,7,29	< 0.7	-6.9
0,1,16	56.7	+50.9	0,3,19	8.4	-4.5	0,5,23	< 0.7	+12.1			
0,1,17	64.6	-62.8	0,3,20	44.5	-40.0	0,5,24	< 0.7	-2.3	080	11.3	-12.8
0,1,18	44.5	-41.9	0,3,21	30.0	-21.8	0,5,25	< 0.7	-10.4	081	48.5	-44.0
0,1,19	18.3	+19.2	0,3,22	18.3	+18.6	0,5,26	< 0.7	+5.4	082	< 0.7	+5.6
0,1,20	< 0.7	-1.5	0,3,23	18.3	-13.2	0,5,27	17.1	+20.6	083	17.8	+12.2
0,1,21	29.6	+23.0	0,3,24	13.0	-22.1	0,5,28	4.8	+5.3	084	7.0	-7.8
0,1,22	23.1	+25.3	0,3,25	< 0.7	+6.9	0,5,29	< 0.7	-5.0	085	8.9	+9.0
0,1,23	11.3	-0.6	0,3,26	22.4	+27.0	0,5,30	< 0.7	+2.2	086	< 0.7	-4.2
0,1,24	5.8	-6.1	0,3,27	8.9	+13.3	0,5,31	8.9	-7.0	087	31.2	-27.7
0,1,25	9.6	+15.7	0,3,28	11.3	-20.8				088	14.9	+17.9
0,1,26	< 0.7	+11.5	0,3,29	5.8	+3.7	060	60.8	-51.3	089	48.5	+48.2
0,1,27	20.7	-22.9	0,3,30	8.9	-3.0	061	33.9	-28.3	0,8,10	20.7	+17.1
0,1,28	8.9	-16.8	0,3,31	< 0.7	-4.0	062	81.0	+71.8	0,8,11	36.0	-38.7
0,1,29	4.8	+7.6	0,3,32	< 0.7	+5.1	063	34.4	-30.5	0,8,12	21.9	+23.6
0,1,30	< 0.7	-1.1				064	33.2	-25.0	0,8,13	22.4	+21.0
0,1,31	6.5	+5.4	040	170.6	-173.5	065	23.1	-21.6	0,8,14	< 0.7	-1.7
0,1,32	8.2	+10.8	041	89.2	+87.1	066	8.9	-4.5	0,8,15	< 0.7	-8.4
0,1,33	4.1	-9.3	042	52.6	+57.7	067	18.5	+20.0	0,8,16	20.0	-24.3
			043	48.5	-46.0	068	37.5	+34.3	0,8,17	19.5	-18.9
020	4.8	-6.2	044	< 0.7	+1.0	069	40.4	+39.7	0,8,18	< 0.7	-7.7
021	40.6	+50.4	045	< 0.7	-4.9	0,6,10	68.7	-67.8	0,8,19	14.9	+16.5
022	60.8	-60.6	046	4.1	-1.4	0,6,11	< 0.7	+0.8	0,8,20	< 0.7	-4.8
023	93.2	+76.8	047	44.7	+38.4	0,6,12	17.8	+17.3	0,8,21	18.5	-29.5
024	24.3	-17.2	048	40.6	+36.5	0,6,13	19.0	-18.0	0,8,22	14.2	+14.5
025	< 0.7	-8.0	049	52.6	-50.5	0,6,14	25.0	-21.4	0,8,23	< 0.7	+4.2
026	9.6	-5.4	0,4,10	76.9	-79.8	0,6,15	5.8	-5.1	0,8,24	< 0.7	-1.7
027	25.5	-14.2	0,4,11	52.6	+53.4	0,6,16	< 0.7	-1.0	0,8,25	9.6	-13.0
028	48.5	-51.3	0,4,12	48.5	+49.6	0,6,17	8.2	+11.3	0,8,26	< 0.7	-5.6
029	105.2	-102.2	0,4,13	37.5	-33.1	0,6,18	26.7	+29.6	0,8,27	0.7	-2.2
0,2,10	35.6	+36.6	0,4,14	< 0.7	+2.8	0,6,19	52.6	+45.7			
0,2,11	85.1	+78.2	0,4,15	9.6	-8.7	0,6,20	25.5	-27.1	091	40.4	+40.4
0,2,12	24.8	-24.2	0,4,16	14.7	+9.8	0,6,21	< 0.7	+6.8	092	22.6	-18.8
0,2,13	< 0.7	-10.3	0,4,17	13.0	+13.3	0,6,22	12.5	+15.1	093	10.8	-13.3
0,2,14	23.1	+23.6	0,4,18	10.6	+13.9	0,6,23	< 0.7	+7.5	094	52.6	+49.8
0,2,15	4.8	+2.9	0,4,19	32.4	-38.1	0,6,24	7.7	+1.8	095	7.7	-8.8
0,2,16	13.0	+9.6	0,4,20	21.2	-23.9	0,6,25	< 0.7	-4.5	096	34.8	-35.0
0,2,17	< 0.7	+5.8	0,4,21	21.4	+25.3	0,6,26	< 0.7	-1.9	097	29.6	-30.5
0,2,18	6.5	-9.9	0,4,22	13.0	+4.0	0,6,27	< 0.7	+0.4	098	25.0	+21.2

Table 3 (cont.)

<i>hkl</i>	$ F_o $	F_c	<i>hkl</i>	$ F_o $	F_c	<i>hkl</i>	$ F_o $	F_c	<i>hkl</i>	$ F_o $	F_c
099	36.8	+34.7	0,10,9	14.2	+ 8.9	0,11,12	10.1	+10.1	0,12,17	<0.7	+ 2.8
0,9,10	7.0	- 4.2	0,10,10	26.7	+30.8	0,11,13	14.7	-14.7	0,12,18	<0.7	- 4.1
0,9,11	24.3	+21.3	0,10,11	8.9	-12.4	0,11,14	<0.7	+ 2.1			
0,9,12	14.2	-16.2	0,10,12	7.0	- 7.3	0,11,15	17.8	+20.4	0,13,1	<0.7	- 1.8
0,9,13	5.8	+ 3.9	0,10,13	13.5	+16.0	0,11,16	<0.7	- 2.7	0,13,2	10.6	+11.4
0,9,14	14.2	+20.5	0,10,14	5.8	+ 3.0	0,11,17	9.6	-10.1	0,13,3	4.1	- 2.5
0,9,15	< 0.7	+ 2.5	0,10,15	<0.7	+ 3.5	0,11,18	<0.7	+ 2.3	0,13,4	11.8	-13.6
0,9,16	26.0	-28.7	0,10,16	4.8	- 7.2	0,11,19	7.0	+ 9.9	0,13,5	7.0	+12.0
0,9,17	14.9	-17.5	0,10,17	4.8	- 8.9	0,11,20	<0.7	+ 2.8	0,13,6	18.3	+19.9
0,9,18	6.5	+ 3.9	0,10,18	10.6	-16.6	0,11,21	<0.7	+ 3.1	0,13,7	<0.7	- 3.0
0,9,19	6.5	+ 7.6	0,10,19	<0.7	- 1.5				0,13,8	9.4	-10.2
0,9,20	< 0.7	+ 7.2	0,10,20	9.6	+16.4	0,12,0	8.9	+12.7	0,13,9	7.7	- 8.6
0,9,21	7.0	+ 4.7	0,10,21	5.8	- 8.7	0,12,1	11.8	+11.0	0,13,10	<0.7	+ 1.0
0,9,22	< 0.7	-11.3	0,10,22	4.1	- 2.3	0,12,2	21.9	-24.3	0,13,11	<0.7	- 0.4
0,9,23	4.1	- 2.7	0,10,23	<0.7	+ 9.0	0,12,3	4.9	+ 2.0	0,13,12	<0.7	+ 2.6
0,9,24	< 0.7	+ 5.3	0,10,24	<0.7	+ 2.8	0,12,4	<0.7	- 2.4	0,13,13	<0.7	- 3.7
0,9,25	< 0.7	+ 4.1				0,12,5	<0.7	- 2.8	0,13,14	0.7	-10.0
0,9,26	< 0.7	-11.2	0,11,1	<0.7	+ 1.3	0,12,6	6.5	+ 8.8	0,13,15	3.9	+11.1
			0,11,2	19.5	+22.9	0,12,7	<0.7	- 4.4			
0,10,0	23.6	+24.5	0,11,3	16.6	-15.9	0,12,8	11.8	-15.5	0,14,0	<0.7	- 2.3
0,10,1	22.4	-21.7	0,11,4	14.7	+18.0	0,12,9	14.2	-15.4	0,14,1	9.4	+ 8.9
0,10,2	33.2	-30.3	0,11,5	17.8	+18.5	0,12,10	12.3	+13.4	0,14,2	<0.7	+ 3.1
0,10,3	< 0.7	+ 3.0	0,11,6	10.8	-18.2	0,12,11	<0.7	+ 5.9	0,14,3	8.4	- 9.6
0,10,4	20.0	+16.5	0,11,7	21.4	-24.5	0,12,12	17.8	-22.2	0,14,4	<0.7	+ 5.8
0,10,5	8.2	- 5.9	0,11,8	5.8	-10.6	0,12,13	<0.7	+ 3.2	0,14,5	<0.7	+ 0.2
0,10,6	7.0	+ 4.4	0,11,9	<0.7	- 8.4	0,12,14	<0.7	+ 1.6	0,14,6	<0.7	+ 6.5
0,10,7	< 0.7	- 4.6	0,11,10	8.9	-11.2	0,12,15	<0.7	+ 5.3	0,14,7	<0.7	+ 6.6
0,10,8	9.6	-10.4	0,11,11	4.8	+ 0.3	0,12,16	<0.7	+ 9.5	0,14,8	0.7	+ 6.2

if the β -form is *cis* has been obtained by Adamson (1952).

Discussion

Although the above X-ray analysis has been limited to a two-dimensional study, no acceptable model can be fitted to the Fourier map which does not have the ethylene linkage in the position indicated in Fig. 1 with the three rings positioned approximately as shown there; i.e. the molecule must be in the *cis* form. The further interesting question, concerning the precise spatial relations of the phenyl and pyridyl groups to the ethylene linkage, cannot be discussed without a complete three-dimensional study.

The authors express their gratitude to Dr D. W. Adamson, who suggested the problem and furnished the crystalline material; to the National Institutes of Health, which supported the X-ray study under Grant No. A-228; to the Office of Naval Research, which supported X-RAC and S-FAC computations

under Contract No. N6onr-269, T.O. 16; to the directors of the General Motors Research Staff for making the IBM 704 computer available to us; and to Prof. V. Vand of our laboratory, who carried out the IBM 704 computations, using a modification of the least-squares program kindly furnished by Dr David Sayre of the I.B.M. Data Processing Center in New York.

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