spectral change induced by carbon monoxide in the presence of aminopyrine is presented in Fig. 3. The sharp absorption maximum at 450 nm is reminiscent of the spectrum of the carbon monoxide complex of reduced cytochrome P-450.

Failure to respond to ethanol would also be expected if the cytochrome P-450 were in the oxidized state. However, when the cytochrome was reduced by addition of 0.5 m*M* aminopyrine in the presence of carbon monoxide, no effect on the redox state of cytochrome P-450 could be observed when 80 m*M* ethanol was subsequently added.

Using these experimental conditions and livers from noninduced animals, we determined the accumulation rate of 4-amino-1,5-dimethyl-2-phenyl-3-pyrazolone, which in isolated microsomes accounts for only one-third of the metabolic products of aminopyrine (and probably much less in the intact liver). Expressed per gram of liver, this rate was 7.6 ± 0.84 nmole/min (mean ± standard error of the mean) and was reduced 18 percent in the presence of 8 percent carbon monoxide. The rate of ethanol oxidation per gram of liver was 1.36 ± 0.13 μmole/min at a substrate concentration of 80 m*M*, and was not affected by 8 percent carbon monoxide. Higher concentration of carbon monoxide cannot be used in studying intact tissue, because the mixed function oxidase system is sensitive to metabolic changes not directly related to it, for instance, changes in the nutritional or redox status of the liver (*18*). Thus, monitoring of the redox state of cytochrome P-450 in the intact liver seems to be a more sensitive method for detecting interactions with the mixed function oxidase system than is the inhibition of substrate conversions by carbon monoxide. Also, a partial inhibition of cytochrome oxidase and an accompanying change in the cellular redox state would completely mask the direct action of effective concentrations of carbon monoxide on microsomal electron transport.

Our results do not lend support to the view that a close similarity exists between MEOS and the oxygenase system that metabolizes drugs in intact tissue. The results are also in accordance with the data of Thurman *et al.* (*19*) on the role of catalase in the ethanol oxidation by microsomes in vitro. Our results were obtained under conditions when turnover of cytochrome P-450 was high, in contrast with the anaerobic in vitro experiments with added carbon monoxide. Because of this, our results also have a bearing on the physiological significance of the cooperative interaction of NADH and NADPH in microsomal electron transport reactions (*20*).

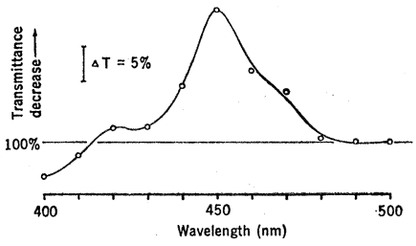

Fig. 3. The spectral change induced by carbon monoxide during aminopyrine demethylation in the isolated perfused liver of a rat treated with phenobarbital. A dual wavelength spectrophotometer was used to measure the transmittance changes in one liver at the wavelengths indicated; 500 nm was the reference wavelength. Five-minute pulses of carbon monoxide were given at intervals of 10 minutes, and recordings for one wavelength were made during each pulse. Other conditions are the same as in Fig. 1. The initial aminopyrine concentration was 0.5 m*M*. Oxygen consumption was kept constant by a continuous infusion of aminopyrine into the perfusion medium at 60 μmole/hour.

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Wiswesser Line Notation: Simplified Techniques for Converting Chemical Structures to WLN

Abstract. *Techniques have been developed for the generation of Wiswesser Line Notations (WLN), which require knowledge neither of rules for manual conversion of structures to line notations nor of computer programming. The desired WLN are obtained simply by drawing the structures of the compounds of interest on a tablet, which is linked to an appropriately programmed computer.*

As more and more scientific data are handled by computer techniques (*1*), there is an increasing tendency to use line notations to encode chemical structures (*2*), since such notations may be filed within a data bank and subjected to computer search. Of the various line notations that have been described, Wiswesser Line Notation (WLN) (*3*) seems to have received more general acceptance than any other. The manual conversion of WLN to structure is straightforward with a symbol key, and the reverse process is, for commonly encountered structures, not overly difficult.

Several schemes (*4*) have been proposed for converting structure diagrams to WLN descriptions, in addition to manual translation. In the scheme described here the input is the drawing of the diagram at a writing tablet. This scheme was tested in the course of preparation of a second edition of the handbook *Psychotropic Drugs and Related Compounds* (*5*). It was necessary that the chemical structures be filed in line notation form, both to allow the con-

tents of the handbook to be updated routinely and to allow computer searching for any desired compound through structure delineation. Other nonmanual techniques for the generation of WLN or similar easily searched computer records depend on either the input of some kind of connection tables (*6*), which are very difficult to generate (*7*), or, for complex ring systems, the input of arbitrarily assigned connections between all the ring atoms (*8*), an exhaustive process which requires large amounts of computer time.

The general features of the National Institutes of Health program for obtaining WLN from structures drawn on a tablet (linked to a Digital Equipment Corporation PDP-10 computer) have been discussed (*9*). For even moderately complex structures, computations require less than 1 second. Essentially, the user draws a diagram of the structure of the compound on a Rand Tablet; this is a graphical input device, consisting of a 25-cm square hard surface with an underlying grid of 1024 by 1024 wires and a pen-like stylus with a movable tip containing a microswitch, which is actuated when the stylus is pressed down and then lifted from the surface. The operator's trace of the stylus is sensed electronically and simultaneously displayed on a cathode-ray tube while it is input into the computer program.

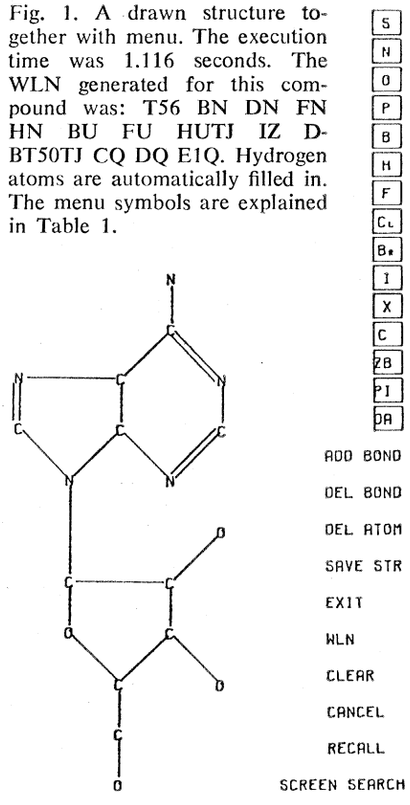

Fig. 1. A drawn structure together with menu. The execution time was 1.116 seconds. The WLN generated for this compound was: T56 BN DN FN HN BU FU HUTJ IZ D-BT50TJ CQ DQ E1Q. Hydrogen atoms are automatically filled in. The menu symbols are explained in Table 1.

Figure 1 is a photograph of the screen, including the selection-limiting "menu." Table 1 lists each of the menu actions of the "easy input" program written by Feldmann *et al.* (*10*). With the latest refinements in the program, well-spaced diagrams are obtained merely by drawing closed loops and lines on the tablet; closed loops generate six-membered rings, and lines generate chains of C atoms with the chain lengths proportional to the line lengths. The menu (Fig. 1) is then used to complete the structure. For example, placing the stylus on *DEL ATOM* and then on a C atom of a C_6 ring will delete that atom and change the starting C_6 ring to a C_5 ring; or placing the stylus on *N* and then on a ring C atom will change a C_6 ring to a C_5N ring. As the structure is drawn, an atom-by-atom connection table is generated internally. When the user has finished drawing a structure, he touches the WLN command and within a few seconds sees the computer-generated WLN under his displayed drawing and on the adjacent teletypewriter. Before doing this, he has the option of saving the structure (*SAVE STR*); later such a saved structure—for example a tricyclic phenothiazine parent compound—may be brought back and modified to process many of its derivatives with a minimum of composing effort.

Figure 1 shows a compound as drawn on a Rand Tablet, together with the generated WLN and the execution time. Additional examples are given in (*9*). To save composing time, the normal valences of the menu elements have been stored in the program so that H atoms are filled in automatically; thus, a chain C with only two drawn bonds will have its two H atoms attached automatically in the final connection table, while a C_6 ring C (assumed to be in a benzene ring) will have one H in the connection table.

An editing feature exists for indicating an atom with less than the normal number of bonds. The program currently can handle compounds as complex as a chain of two polycyclic fused-ring systems or perifused systems. It currently does not handle the topologically distinct bridged or spiro rings. If the program cannot produce the correct WLN for a compound, it outputs a "fail-safe" message indicating the condition that exceeded its limitations.

Wiswesser Line Notation entries for about one-third of the 1500 compounds to be included in *Psychotropic Drugs and Related Compounds* (*5*) were found in the *Common Data Base* (*11*), a collection of some 20,000 compounds of interest to the Food and Drug Administration and the National Library of Medicine. The task of processing the remaining 1000 compounds was as-

Table 1. Menu actions in WLN generation program.

Box symbol or editing command	Significance
S	Sulfur atom
N	Nitrogen atom
O	Oxygen atom
P	Phosphorus atom
B	Boron atom
H	Hydrogen atom
F	Fluorine atom
CL	Chlorine atom
BR	Bromine atom
I	Iodine atom
X	Any of 103 elements (selected from separate menu)
C	Carbon atom
ZB	Zero bond (used for ions)
PI	Pi bond (used for metallocene structures)
DA	Dative or chelate bond
ADD BOND	Addition of double (or triple) bond
DEL BOND	Deletion of undesired bond
DEL ATOM	Deletion of atom from structure
SAVE STR	Save on computer disk connection table for structure now on screen
EXIT	Exit from program
WLN	Initiates WLN generation program
CLEAR	Clears screen
CANCEL	Cancels last command and brings structure back to state before that command
RECALL	Recalls any structure saved on disk
SCREEN SEARCH	Initiates WLN bit-screen generation and substructure search program

signed to a third-year pharmacy student working during the summer in COSTEP (Commissioned Officer Student Training and Extern Program of the Public Health Service). She spent 1 to 2 hours a day for 3 weeks learning the system and encoding compounds. By the time she finished, she was processing more than 50 compounds an hour. Structures were obtained for about 90 percent of the compounds; "reject" messages were received for the remainder, since they were too complex for the current program and had to be manually encoded.

Currently, the WLN-composing program is being expanded to cover more complex molecular structures; it is written in Fortran IV and is being developed on a time-sharing computer, the PDP-10. While at present this method of encoding might not be more economical than manual encoding, by which one can also handle about 50 compounds an hour, there is the assurance that once such a computer program is debugged, only correct notation will be produced.

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Pollinators in High-Elevation Ecosystems: Relative Effectiveness of Birds and Bees

Abstract. *During the rainy season bird-flowered plants at high elevations are more effectively pollinated than closely related bee-flowered plants. With good flight conditions the effectiveness of birds and bees is essentially equal. Thus, the higher incidence of bird flowers at higher elevations is attributable in part to the competitive advantage gained through greater reproductive success.*

Observations in mountain Mexico (*1*) suggest that plants with hummingbird flowers are more numerous in terms of both species and numbers at elevations above 2300 m than in mid-elevational regions (1000 to 2300 m). This observation is in part substantiated by data in Blake (*2*), where nearly twice as many species of hummingbirds are reported in high-elevation communities as in mid-elevation communities. It is doubtful that the correlation is fortuitous.

This report is addressed to three questions: (i) Why is the frequency of bird-flowered plants greater at higher elevations? (ii) Are birds or bees more efficient pollinators? (iii) Can a conceptual model be constructed for predicting the relative abundance of bird-flowered plants in particular habitats?

Two areas were selected for study because they included sites which, on the basis of daily cloud formation, were classed as having good, medium, or poor flight conditions for bees. This judgment was made prior to the collection of data. In Chiapas, the study area, about 14 km southeast of San Cristóbal de las Casas, included a ridge top (altitude about 2750 m), a ridge side (2350 to 2600 m), and the adjacent valley (about 2250 m). These sites were classified as poor, medium, and good, respectively (Table 1). From 30 August to 3 September 1971 the ridge top was subject to daily rains and cloudiness from before dawn to as late as 1100 hours, which limited flight times to 0 to 3½ hours a day. These conditions spread to the sides of the ridge and the valley floor later in the day. In the state of Mexico data were collected at Tlamacas (below Popocatépetl), on the road to Tlamacas, and southwest of Toluca. At Tlamacas good flight conditions for bees extended into the late afternoon, as Tlamacas remained above the clouds most of the day. Here, poor flight conditions occurred earlier at lower elevations.

In both Chiapas and Mexico the fecundity [percentage of pollination times percentage of seed set (*3*)] of bee-flowered plants is lower in areas with poor flight conditions, whereas the fecundity or pollination, or both, of bird-flowered plants is relatively high (Table 1). The same trend is noted with respect to pollination and seed set in various mints (Labiatae) collected in Oaxaca, Chiapas, Mexico, and Durango (Table 2).

Table 1. Pollination, seed set, and fecundity in bee and bird flowers from about 12 km southeast of San Crisóbal de las Casas, Chiapas, and from Tlamacas and southwest of Toluca, Mexico. Localities were selected for good (G), medium (M), and poor (P) flight conditions for bees.

Species	Flower type	Flowers (*N*)	Pollination (%)	Seed set (%)	Fecundity (%)	Flight condition
		Chiapas				
Salvia cacaliaefolia	Bee	53	77	60	45	P
Salvia lavanduloides	Bee	205	93	66	61	M
Lepechinia schiedeana	Bee	54	96	86	83	G
Stachys coccinea	Bird	130	89	98	87	M
Salvia chiapensis	Bird	200	88	81	71	M
		Tlamacas, altitude 3940 to 4000 m				
Lupinus montanus	Bee	2106	94	92	87	G
Penstemon gentianoides	Bee	514	91			G
Stachys eriantha	Bee	150	95	90	86	G
		Road to Tlamacas, altitude 3330 m				
Lupinus montanus	Bee	1553	88	81	71	M
Penstemon gentianoides	Bee	408	95			M
		Ruta 130, southwest of Toluca, altitude 3030 m				
Lupinus cf. *persistens*	Bee	561	66	78	52	P
Penstemon kunthii	Bird	515	93			P
Salvia cardinalis	Bird	120	98	72	71	P