Figure 1. Electron density in the villalstonine molecule, contoured at 2, 4, 6, ... e. Å.$^{-3}$, and a schematic structural formula.

of villalstonine and confirms the recently revised[6] empirical formula as $C_{41}H_{48}O_4N_4$.

Crystals of villalstonine from methanol solution are monoclinic and belong to space group P2₁. The unit cell of dimensions $a = 13.756$ Å., $b = 13.645$ Å., $c = 10.045$ Å., and $\beta = 101° 41'$ contains two molecules of the alkaloid and two molecules of methanol. The Patterson function was calculated using 3337 observed, independent X-ray intensities, densitometrically evaluated from integrated oscillation photographs. The solution of the structure made use of the known presence in the molecule of a rigid group of 11 atoms in known configuration, namely an indole group and two adjacent carbon atoms. Rotational and translational searches[7] of the Patterson function yielded several plausible positions for the two symmetry-related (2₁) rigid groups in the unit cell. A vector-space refinement procedure was employed in making a choice among these possibilities. This procedure, programmed for the IBM 7090, refines the atomic coordinates of a partially known crystal structure by optimizing the fit of the interatomic vectors to the stored, three-dimensional Patterson function. The best-fitting set of refined atom coordinates was then used as the basis for a 22-fold Patterson superposition, which yielded the positions of most of the remaining atoms. Difference Fourier syntheses and least-squares refinement ultimately established the complete structure, with $R = 0.059$ for the observed reflections.

The structure and relative configuration of villalstonine are shown in Figure 1. The lower part of the figure matches the structure of pleiocarpamine,[8] confirming the observation[9] that the latter alkaloid is a product of the acid-catalyzed fission of villalstonine.

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(7) C. E. Nordman and K. Nakatsu, J. Am. Chem. Soc., 85, 353 (1963).
(8) M. Hesse, W. von Philipsborn, D. Schumann, G. Spiteller, M. Spiteller-Friedmann, W. I. Taylor, H. Schmid, and P. Karrer, Helv. Chim. Acta, 47, 878 (1964).
(9) B. S. Joshi and W. I. Taylor, unpublished; M. F. Bartlett, R. Sklar, A. F. Smith, and W. I. Taylor, J. Org. Chem., 28, 2197 (1963).

The other half of the villalstonine molecule does not appear to correspond to any alkaloid whose structure is known at the present time. However, the skeleton of this half is closely related to that of Alkaloid C,[2,7] an oxindole alkaloid from the same source, A. muelleriana.

The absolute configuration of villalstonine is probably that of Figure 1, which is based on the probable absolute configuration of pleiocarpamine,[8] which in turn is based on the rule of uniform absolute stereochemistry at C-15 of yohimbinoid alkaloids.[10] In this connection it should be noted that the previously published configuration[7] for Alkaloid C, which was supposed to have conformed to the C-15 rule,[10] was in actual fact the mirror image of what had been intended.

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C. E. Nordman, S. K. Kumra
Department of Chemistry, University of Michigan
Ann Arbor, Michigan

## Nuclear Magnetic Resonance Spectra (200 Mc.p.s.) of the Aromatic Protons of Alkylbenzenes and Biphenyl

Sir:

Despite extensive investigation of the effect of a variety of substituents on the n.m.r. spectral parameters of benzene ring protons,[1-13] very little is known concerning the effect of alkyl groups alone. Monosubstituted benzenes give complex aromatic spectra arising from five strongly coupled spins; in alkylbenzene spectra this difficulty is aggravated by the very small chemical shift differences among these protons. Despite their forbidding appearance, however, the 60 Mc.p.s spectra of certain alkylbenzenes suggested that analyzable spectra might be obtained at frequencies of the order of 200 Mc.p.s. This communication describes the results of such a study.

The spectrometer was an experimental instrument developed by Varian Associates and described by Nelson and Weaver.[14] It employs a 47 kgauss superconducting solenoid, corresponding to a 200 Mc.p.s. radiofrequency field for protons. Resolution was 1.0–1.2 c.p.s. Sensitivity being somewhat below that of present commercial instruments, neat liquids or 25% (v./v.) solutions in $CCl_4$ were used.[15] Spectra

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(2) P. L. Corio and B. P. Dailey, ibid., 78, 3043 (1956).
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(10) P. F. Cox, J. Am. Chem. Soc., 85, 380 (1963).
(11) J. Martin and B. P. Dailey, J. Chem. Phys., 37, 2594 (1962).
(12) J. Martin and B. P. Dailey, ibid., 39, 1722 (1963).
(13) T. K. Wu and B. P. Dailey, ibid., 41, 2796 (1964).
(14) F. A. Nelson and H. E. Weaver, Science, 146, 223 (1964).
(15) Isotactic polystyrene, included in Figure 1 and Table I for comparison, was run in tetrachloroethylene solution at 128° using a Varian DP-60 instrument. Because of unusual shielding effects, the 60 Mc.p.s. spectrum was analyzable.

were obtained at *ca.* 25°. Chemical shifts reported in Figure 1 refer to CCl₄ solutions. Coupling constants are given in Table I. The spectra were analyzed

Table I. Coupling Constants for Alkylbenzenes and Biphenyl

| Compound | $J_{AB}$ | $J_{BC}$ | $J_{AC}{}^a$ | $J_{AB'}$ |
|---|---|---|---|---|
| Benzene | 6.0 | 6.0 | 2.0 | 1.0 |
| Toluene | 7.0 | 8.5 | 0.5 | 0.5 |
| Ethylbenzene | 7.0 | 7.0 | 1.0 | 0.5 |
| Cumene | 6.5 | 6.5 | 1.0 | 0.5 |
| *t*-Butylbenzene | 7.8 | 7.8 | 1.5 | 1.3 |
| *meso*-2,4-Diphenylpentane | 7.0 | 7.0 | 2.0 | 1.0 |
| *rac*-2,4-Diphenylpentane | 7.0 | 7.0 | 2.0 | 1.0 |
| Polystyrene | 6.5 | 6.5 | 2.0 | 1.0 |
| Biphenyl | 8.5 | 7.0 | 1.3 | 0.5 |
| *m*-Xylene[b] | 1.8 | 7.8 | 1.0 | 1.8 |

[a] $J_{AA'}$ and $J_{BB'}$ are assumed equal to $J_{AC}$ for calculation of spectra. [b] The methyl group spectrum is a binomial quartet with broadened peaks, resulting from equal couplings of 0.6 c.p.s. to A, B, and B' and a smaller coupling (probably less than 0.2 c.p.s.) to C; *cf.* H. Rottendorf and S. Sternhell, *Australian J. Chem.*, **17**, 1315 (1964).

as AA'BB'C systems (except *m*-xylene, which was treated as ABB'C) using a computer program devised by L. C. Snyder and R. L. Kornegay (Bell Telephone Laboratories). The spectra of *t*-butylbenzene and biphenyl exhibit chemical shift differences large enough to permit use of 60 Mc.p.s. spectra to refine the parameters obtained at 200 Mc.p.s. For most of the other compounds, the 60 Mc.p.s. spectrum appears as a single peak with weak indications of multiplicity near its base. The 200 Mc.p.s. spectrum, in contrast, shows in all cases a number of well-resolved resonances, that of *t*-butylbenzene being nearly first order in appearance.

Chemical shifts are probably accurate to ±0.01 p.p.m., *J*(*ortho*) to ±0.1–0.2 c.p.s.; *J*(*meta*) and *J*(*para*) are somewhat less certain, in view of the *ca.* 1 c.p.s. resolution. The values assigned are those which give calculated spectra best matching the observed, due regard being given to the somewhat more reliable values of *J*(*meta*) and *J*(*para*) determined for polystyrene[16] and benzene.[17] $J_{AA'}$ and $J_{BB'}$ were arbitrarily assumed to equal $J_{AC}$, the coupling of *ortho* to *para* protons.

For all previously analyzed substituted benzene spectra, *J*(*ortho*) is 7.7–9.0 c.p.s.,[3,5,10–12] tending to be larger for *para*-disubstituted than for *ortho*- and *meta*-disubstituted compounds. *J*(*meta*) is generally 2–3 c.p.s. and *J*(*para*) *ca.* 0.5–1.0 c.p.s. For many of the compounds reported here, *J*(*meta*) and *J*(*para*) are within the usual range, but *J*(*ortho*) *is unusually small*, 6.0–7.0 c.p.s., tending to increase with multiple substitution (*m*-xylene)[18] and with increase in chemical shift differences (*t*-butylbenzene, biphenyl).

The chemical shift trends can be at best only partially rationalized. For benzene, toluene, ethylbenzene, and cumene the results are roughly in accord with

(16) F. A. Bovey, F. P. Hood, E. W. Anderson, and L. C. Snyder, *J. Chem. Phys.*, in press.

(17) Couplings reported for benzene in Table I were obtained from analysis of benzene liquid crystal spectra by Snyder and Anderson (*J. Am. Chem. Soc.*, **86**, 5023 (1964)). They are in good agreement with values derived from analysis of C¹³ satellites (*cf.* ref. 8) in a study which we shall report later.

(18) *o*- and *p*-xylene did not yield analyzable spectra, but the C¹³ satellites of *p*-xylene showed *J*(*ortho*) to be 8.00 ± 0.05 c.p.s.
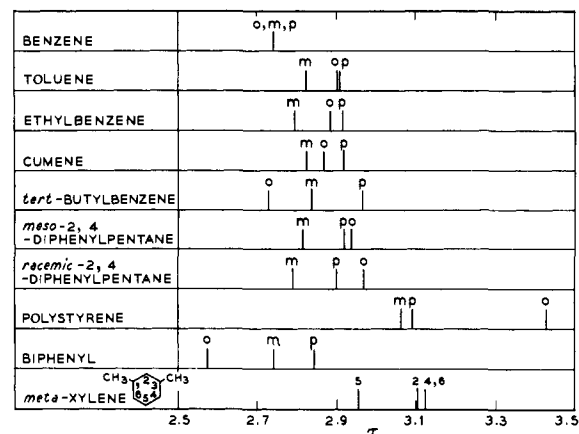


Figure 1. Chemical shifts of aromatic protons of alkylbenzenes and biphenyl; 25 vol. % solutions in CCl₄, *ca.* 25°.

the expected inductive effects of the alkyl groups, *ortho* and *para* protons being more shielded than *meta*.[12] Hyperconjugative influences appear to be weak or absent. The *ortho* protons exhibit the largest excursions in chemical shift. In polystyrene and biphenyl,[19] they experience extremes of shielding and deshielding, respectively, arising from neighboring phenyl group anisotropy. The very marked deshielding of the *ortho* protons of *t*-butylbenzene has been reported also for benzene rings multiply substituted by *t*-butyl groups.[20] It is puzzling, for one would expect *increased* shielding from the magnetic anisotropy of the alkyl group's carbon–carbon bonds, such as is observed for the *cis*-vinyl proton in the series propene, butene-1, 3-methylbutene-1.[21] Such deshielding has been attributed to intramolecular van der Waals forces, reflecting crowding of bulky groups.[20,22] In contrast, Friedel and Retcofsky[23] have observed that the resonance of the *para* C¹³ nucleus moves markedly downfield with increased branching of the alkyl groups in the series toluene, ethylbenzene, cumene, *t*-butylbenzene, whereas the *ortho* (and *meta*) carbons are little affected. Thus, in these systems, quite different influences appear to be at work on the ring carbon atoms and their associated protons, although aromatic C¹³ and H¹ chemical shifts usually show a strong parallelism.[7] It is clear that further experimental and theoretical work is necessary before the n.m.r. parameters of benzene rings can be properly interpreted.

These results will be described in full, together with observed and calculated spectra, in a later publication.

(19) R. A. Hoffman, P.-O. Kinell, and G. Bergstrom, *Arkiv Kemi*, **15**, 532 (1960); these authors attempted a moment analysis of the biphenyl spectrum but did not reach a definite conclusion. Our results agree with these reported by Kurland and Wise (*J. Am. Chem. Soc.*, **86**, 1877 (1964)) for biphenyl-4,4'-d₂.

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**F. A. Bovey, F. P. Hood, III**
*Bell Telephone Laboratories, Inc.*
*Murray Hill, New Jersey*

**Eugene Pier, H. E. Weaver**
*Varian Associates*
*Palo Alto, California*

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