observing the chemical shifts of $H_a$ and $H_b$[15] in the *P*-methoxy and *P*-phenyl derivatives compared to model compounds, *i.e.*, IIc and IId. When methoxy is the P substituent (IIb), a deshielding of $H_a$ occurs, which is in line with an axial positioning. Moreover, the presumably axial phenyl in IIa *shields* both $H_a$ and $H_b$, but $H_a$(axial) is shielded substantially more than $H_b$. In fact, the shielding influence of the phenyl group is so strong that the normal order (axial at lower field) of the chemical shifts for the 4,6 proton is reversed in *cis*-Ia.[16]

Finally, compelling evidence for the above conclusions was obtained by a nuclear Overhauser effect (NOE) experiment with IIc. Irradiation of the *P*-methyl signal gave substantial enhancement (*ca.* 7%) of the axial $C_4$ protons. Such enhancement indicates a close proximity between the methyl and the axial protons which is possible only if the methyl group is axial.

The evidence presented here extends the scope of the preference for axiality of phosphorus substituents in six-membered rings. Such a phenomenon is probably largely a consequence of axial–axial van der Waals attractive interactions (a function of the long P–X bonds and flattening of the X–P–X portion of the ring) rather than polar bond or adjacent lone-pair interactions,[3b] since the axial preference still exists in the absence of adjacent heteroatoms.[4] A complete discussion of this and additional related work will appear at a later date.

**Acknowledgment.** We wish to express our gratitude to Mrs. Carol Folk (University of Pennsylvania) for the 100-MHz proton and $^{31}P$ nmr spectra and to Davis W. Lamson (Johnson Foundation) for obtaining 220-MHz pmr spectra. We also thank Dr. Ernest Eliel for helpful discussion and suggestions and M. Gail Hutchins for low-temperature nmr spectra.

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[15] The assignment of the axial and equatorial methylene protons in IIa–d was based on a comparison with *cis*-Ia (and *cis*-Ib) and was confirmed by double-irradiation experiments ($Me_{ax}$ decoupled from $H_a$).

[16] It was observed that the axial $C_4$,$C_6$ protons in *cis*-2-phenyl-5-*tert*-butyl-2-phospha-1,3-dioxacyclohexane (the most stable isomer) resonated at higher field relative to the equatorial protons, a reversal of the usual order in these systems. This anomaly was attributed to shielding caused by the benzene ring current and was presented as evidence for the preferred axial position of the *P*-phenyl.[2]

**Robert O. Hutchins,* Bruce E. Maryanoff**
*Department of Chemistry, Drexel University*
*Philadelphia, Pennsylvania 19104*

*Received January 3, 1972*

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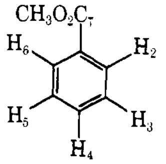
## Proton Magnetic Resonance Spectrum of Methyl Benzoate-*carboxyl*-$^{13}C$

*Sir:*

A limited number of long-range $^{13}C$–H coupling constants[1] have been successfully determined from natural abundance carbon-13 spectra[2a] and from the carbon-13 satellite regions of proton spectra.[2b] The former method entails the inherently difficult task of obtaining high-resolution nmr from the weak cmr spectra while the latter method involves deciphering tightly spaced carbon-13 satellites from an intense proton center band.[3] As a continuation of our nmr studies of carbon-13 enriched compounds,[4] we have determined long-range $J_{^{13}C-H}$ values of methyl benzoate-*carboxyl*-$^{13}C$ by a detailed pmr study. In this study it was also possible to determine the relative signs of these $J_{^{13}C-H}$ values.[5]

The pmr spectrum of methyl benzoate-*carboxyl*-$^{13}C$ was much different from the pmr spectrum of the natural abundance compound, reflecting the extensive coupling between the C-7 carbon and the various protons. Both of these spectra were analyzed by the LAOCOON-III program[6] to give the parameters listed in Table I. In this LAOCOON analysis, various combina-

**Table I.** Proton Magnetic Resonance Parameters for Natural and Labeled Methyl Benzoate-*carboxyl*-$^{13}C^a$



| Chemical shift, δ | Natural | Labeled |
|---|---|---|
| $H_2$, $H_6$ | 8.03$^b$ | 8.03 |
| $H_3$, $H_5$ | 7.40$^b$ | 7.40 |
| $H_6$ | 7.51$^b$ | 7.52 |
| Coupling constants, Hz | | |
| $J_{23}$, $J_{56}$ | +7.86$^b$ | +7.87 |
| $J_{24}$, $J_{46}$ | +1.30$^b$ | +1.33 |
| $J_{25}$, $J_{36}$ | +0.65$^b$ | +0.61 |
| $J_{26}$ | +1.86$^b$ | +1.85 |
| $J_{34}$, $J_{45}$ | +7.45$^b$ | +7.50 |
| $J_{35}$ | +1.35$^b$ | +1.33 |
| $J_{C_7-H_2}$, $J_{C_7-H_6}$ | | (+) 4.08 |
| $J_{C_7-H_3}$, $J_{C_7-H_5}$ | | (+) 1.11 |
| $J_{C_7-H_4}$ | | (+) 0.48 |
| $J_{C_7-OCH}$ | | 3.73$^c$ |

[a] Samples run in $CDCl_3$ with a concentration of 100 mg of solute/0.5 ml of solvent with 3% TMS as an internal standard, on a JEOL PS-100 nmr spectrometer. [b] The pmr parameters for methyl benzoate have been previously determined (neat with 10% TMS) to be (K. Hayamizu and O. Yamamoto, *J. Mol. Spectrosc.*, **25**, 422 (1968)), respectively: δ 8.05, 7.35, 7.45 ($J$ = 7.88, 1.31, 0.61, 1.85, 7.52, 1.33 Hz). [c] Observed and measured directly from the methyl pmr region.

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[1] For references to long-range $^{13}C$–H spin–spin coupling, see: (a) J. Feeney and P. J. S. Panwels, *Mol. Phys.*, **14**, 209 (1968); (b) F. J. Weigert and J. D. Roberts, *J. Amer. Chem. Soc.*, **89**, 2967 (1967); (c) S. Porcic and J. D. Roberts, *ibid.*, 87, 1056 (1965); (d) E. A. Hill and J. D. Roberts, *ibid.*, 89, 2047 (1967); (e) A. B. Harmon and K. M. Harmon, *ibid.*, 88, 4093 (1966); (f) A. R. Tarpley, Jr., and J. H. Goldstein, *ibid.*, **93**, 3573 (1971); (g) G. J. Karabatsos, J. D. Graham, and F. M. Vane, *ibid.*, 83, 2778 (1961); (h) G. J. Karabatsos, J. D. Graham, and F. M. Vane, *ibid.*, 84, 37 (1962); (i) G. J. Karabatsos, *ibid.*, 83, 1230 (1961); (j) G. Miyazima, Y. Utsumi, and K. Takahashi, *J. Phys. Chem.*, 73, 1370 (1969); (k) K. M. Crecely, R. W. Crecely, and J. H. Goldstein, *ibid.*, 74, 2680 (1970); (l) H. Dreeskamp and E. Sackmann, *Z. Phys. Chem.*, 34, 273 (1962); (m) G. Govil, *J. Chem. Soc. A*, 1420 (1967); (n) E. Sackmann and H Dreeskamp, *Spectrochim. Acta*, 21, 2005 (1965); (o) A. R. Tarpley, Jr., and J. H. Goldstein, *J. Mol. Spectrosc.*, 37, 432 (1971); (p) J. M. Read, Jr., R. E. Mayo, and J. H. Goldstein, *ibid.*, 22, 419 (1967); (q) R. Freeman, *J. Chem. Phys.*, 43, 3087 (1965); (r) H. Dreeskamp, K. Hildenbrand, and G. Pfisterer, *Mol. Phys.*, 17, 429 (1969).

[2] For references to long-range $^{13}C$–H spin–spin coupling in aromatic systems, (a) see ref 1b; (b) see ref 1o and 1p.

[3] Some success has been experienced in suppressing the center band so that weak satellites can be observed.[1m,1q]

[4] A. M. Ihrig and J. L. Marshall, *J. Amer. Chem. Soc.*, **94**, 1756 (1972).

[5] For examples of $J_{^{13}C-H}$ sign determinations, see ref 1b, 1k, 1o, and 1r.

[6] A. A. Bothner-By and S. M. Castellano, "Computer Programs for Chemistry," Vol. 1, D. F. DeTar, Ed., W. A. Benjamin, New York, N. Y., 1968, p 10.

tions of the signs of $J_{C-H}$ were tried.[7] Of the four possible relative sign combinations for $J_{C_7-H_2}$, $J_{C_7-H_3}$, and $J_{C_7-H_4}$—[+++], [−++], [+−+], and [++−][8]—it quickly became apparent from the simulated spectra that the last two cases could be ruled out. Of the remaining two possibilities, the relative sign combination [+++] was favored because a smaller root-mean-square error could be obtained (0.039 Hz for [+++] *vs.* 0.08 Hz for [−++]). This tentative conclusion was substantiated by a close look at weak combination lines. The region between 785 and 795 Hz included four signals which by the LAOCOON study were shown to be particularly sensitive to the relative signs of the $J_{C-H}$ values. Comparison of these observed frequencies with those frequencies predicted by the various relative sign combinations indicated the [+++] combination to be the best.[9] Figure 1 compares observed and simulated spectra for methyl benzoate-*carboxyl*-$^{13}C$ using the [+++] combination.

To confirm the [+++] relative spin combination, spin-tickling experiments were conducted.[10] Three different frequencies were irradiated and in each case collapse of various signals unequivocally showed the relative sign combination (+++) to be correct and the relative sign combination (−++) to be incorrect.[11]

Although it was not possible in the LAOCOON study to decide between the absolute sign combinations [+++] and [−−−], it was hoped that the spin-tickling experiment would do this. Disappointingly, virtually identical collapsing patterns were predicted to result from both absolute sign combinations [+++] and [−−−]. However, in one instance a choice could be made, and the results clearly favored [+++]. This conclusion, albeit tentative, is consistent with previous absolute $J_{C-H}$ sign determinations; the sign of $^3J_{C-H}$ is positive in acetone,[1r] and the sign of $^3J_{C-H}$ is positive (but that for $^4J_{C-H}$ is negative ) in benzene[1b] and in dihalobenzenes.[10] Furthermore, if one attempts to relate the $J_{C-H}$ values in this present study to the $J_{H-H}$ values in the model compound[12] benzene, the correspondence is quite good,[13] lending substantiation to the contention that the $J_{C-H}$ signs in the benzoate system **1** are all positive as for the $J_{H-H}$ signs in the geometrically equivalent benzene molecule **2**.

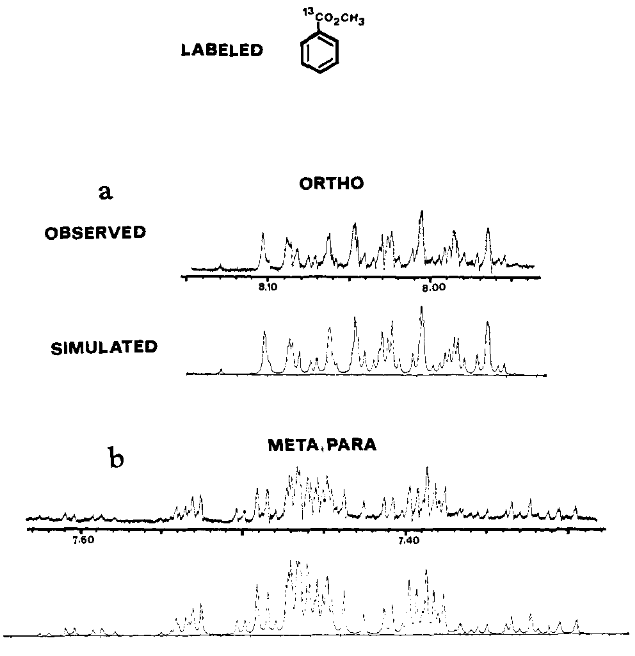
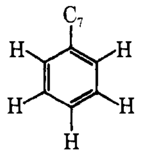
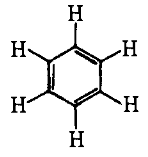


Figure 1. Observed and simulated pmr patterns for methyl benzoate-*carboxyl*-$^{13}C$: (a) ortho region; (b) meta, para region.



**1**



**2**

**Acknowledgment.** We should like to acknowledge support for this work by the Robert A. Welch Foundation, Grant No. B-325, and by the North Texas State University Faculty Research.

[14] Robert A. Welch Postdoctoral Fellow, 1970–1972.

**Arthur M. Ihrig,[14] James L. Marshall***
*Department of Chemistry, North Texas State University*
*Denton, Texas 76203*

*Received October 12, 1971*

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[7] The $J_{H-H}$ signs were all held positive [J. M. Emsley, J. Feeney, and L. H. Sutcliffe, "High Resolution Nuclear Magnetic Resonance Spectroscopy," Vol. II, Pergamon Press, Elmsford, N. Y., 1966, pp 682, 771].

[8] In this LAOCOON study it was not possible to differentiate between the absolute sign combinations, *e.g.*, the predicted spectrum for the sign combination [+++] was identical with that for the combination [−−−].

[9] The experimental values of these low-intensity frequencies and those predicted by the various sign combinations were

| Rel sign combination, $J_{C_7-H_o}$, $J_{C_7-H_m}$, $J_{C_7-H_p}$ | Transition frequencies, Hz | | | | Av error |
|---|---|---|---|---|---|
| Exptl | 787.87 | 790.13 | 792.37 | 794.67 | |
| (+++) | 787.83 | 790.17 | 792.32 | 794.70 | 0.04 |
| (+−+) | 788.60 | 791.07 | 791.48 | 793.85 | 0.84 |
| (++−) | 787.43 | 789.78 | 792.65 | 795.11 | 0.38 |
| (−++) | 788.19 | 790.63 | 791.86 | 794.27 | 0.43 |

[10] S. M. Castellano and A. A. Bothner-By, *J. Chem. Phys.*, 47, 5443 (1967).

[11] These spin-tickling experiments also confirmed that the previously discarded relative sign combinations [+−+] and [++−] were incorrect.

[12] For an example of relating $J_{H-H}$ values in model compounds to $J_{C-H}$ values in geometrically equivalent systems, see ref 1b.

[13] The $^3J_{H-H}$, $^4J_{H-H}$, and $^5J_{H-H}$ values of benzene, respectively, 7.7, 1.4, and 0.6 Hz [S. Castellano and C. Sun, *J. Amer. Chem. Soc.*, 88, 4741 (1966)], compare with benzoate $^3J_{C-H}$, $^4J_{C-H}$, and $^5J_{C-H}$ values, respectively, 4.1, 1.1, and 0.5 Hz.

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## Structure of Thermorubin A, the Major Orange-Red Antibiotic of *Thermoactinomyces antibioticus*

*Sir:*

Growth of *Thermoactinomyces antibioticus*,[1] a thermophilic actinomycete, in submerged culture produces a mixture of orange-red antibiotics which are highly active against both Gram-positive and Gram-negative bacteria; the major component is thermorubin A.[2] Structure I deduced (*vide infra*) for this antibiotic is unique by virtue of the presence, within the same molecular framework, of xanthone and anthracene moieties which presumably arise from the same polyketide precursor.

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[1] R. Craveri, C. Coronelli, H. Pagani, and P. Sensi, *Clin. Med.*, **71**, 511 (1964).

[2] Thermorubin A is identical with the antibiotic BT 3-3 described by M. Terao, K. Furuya, and R. Enokita, *Sankyo Kenkyusho Nempo*, 17, 110 (1965).