Table I. Hyperfine Splitting Constants

Radical	Method of Preparation	Ref	Hyperfine splitting a_1^H	Hyperfine splitting a_2^H	Hyperfine splitting a_9^H	Line width[a]
Anthracene$^+$	$SbCl_5$–CH_2Cl_2	*b*	3.079	1.379	6.505	0.055
Anthracene$^+$	$SbCl_5$–CH_2Cl_2	*c*	3.08	1.38	6.49	
Anthracene$^+$	H_2SO_4	*d*	3.061	1.379	6.533	
(Anthracene)$_2^+$	$SbCl_5$–CH_2Cl_2	*b*	1.422	0.710	3.253	0.120
			(2.844)[e]	(1.420)[e]	(6.506)[e]	
Anthracene$^-$	Na–DME	*d*	2.740	1.509	5.337	
(Naphthalene)$_2^+$	$SbCl_5$–CH_2Cl_2	*b*	2.756	1.032		0.110
			(5.512)[e]	(2.064)[e]		
(Naphthalene)$_2^+$	$SbCl_5$–CH_2Cl_2	*c*	2.77	1.03		
			(5.54)[e]	(2.06)[e]		
Naphthalene$^-$	Na–DME	*f*	4.940	1.825		
(2,3,6,7-Tetramethylnaphthalene)$_2^+$	$SbCl_5$–CH_2Cl_2	*b*	2.785	1.144[g]		0.050
			(5.570)[e]	(2.288)[e,g]		
2,3,6,7-Tetramethylnaphthalene$^-$	Na–DME	*h*	4.62	1.62[g]		

[a] The line width is given as the separation in gauss between the extrema of the first derivative spectrum. [b] Data obtained in the present work. Except for the anthracene dimer, the radicals were made with an excess of $SbCl_5$ such that further addition of $SbCl_5$ had no effect on the reaction product. The anthracene dimer was made with an excess of anthracene. [c] From the work cited in ref 2. [d] From the work cited in ref 5. [e] Twice the observed splitting, for comparison with monomer results. [f] R. G. Lawler, J. R. Bolton, M. Karplus, and G. K. Fraenkel, to be published. [g] Methyl proton splitting. [h] J. R. Bolton, Thesis, Cambridge University, 1963.

state radical concentration is obtained because the solid redissolves.

The hyperfine splittings are presented, along with other data for comparison, in Table I. Our results were obtained at approximately $-85°$ and have standard deviations of about ± 0.002 gauss. Although to a first approximation the pairing theorem holds and corresponding splittings in the positive ion and negative ion radicals of the same hydrocarbon[3,4] are the same, there are in fact significant deviations, and at most of the positions the splittings are larger in the postive ion than in the corresponding negative ion. This trend has been studied by Colpa and Bolton,[5,6] who propose that the splittings at a position with spin density ρ and charge ϵ should be given by the relation $|a^H| = |\rho|(A + B\epsilon)$. Our results for the ring proton splittings at position 1 fit this relation reasonably well if we make the assumption, justified by the anthracene results, that dimerization does not cause a significant change of relative spin densities at the ring positions. A similar but larger charge dependence for the methyl proton splittings is in accord with the results found for some methyl-substituted anthracene anions and cations.[7] It is of interest that although most of the data for the ring proton splittings at position 2 in hydrocarbon ions are in poor accord with the Colpa–Bolton relation, the results for naphthalene are in reasonable agreement.

These results imply that no major molecular distortion or redistribution of π-electrons occurs on dimerization, and it therefore seems likely that the two hydrocarbon moieties lie in parallel planes. The interaction between two neutral hydrocarbon molecules in parallel planes and with parallel long axes has been studied by Forster and Kasper[8] to explain excimer spectra and by Ron and Schnepp[9] in an investigation of paracyclophanes. It is possible to explain the bonding of the dimers in terms of a simple resonance-integral type of interaction between the 2p orbitals in the two halves, but a similar stabilization is also predicted by a first-order theory for the anion dimers. We have attempted unsuccessfully to produce a negative monoanion dimer of naphthalene by treating a small amount of metallic potassium with an excess of naphthalene in dimethoxyethane; only the usual (but broadened) monomer spectrum was obtained. We are at present attempting to determine whether the tetrachloroantimonate anion plays a significant role in the dimerization.

Oliver W. Howarth, George K. Fraenkel
Department of Chemistry, Columbia University
New York, New York 10027
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(4) A. Carrington, F. Dravnieks, and M. C. R. Symons, *J. Chem. Soc.*, 947 (1959). Note that the naphthalene positive ion has not in fact been observed, as implied by an improper listing in a table in this paper.
(5) J. P. Colpa and J. R. Bolton, *Mol. Phys.*, **6**, 273 (1963).
(6) J. R. Bolton, *J. Chem. Phys.*, **43**, 309 (1965).
(7) J. R. Bolton, A. Carrington, and A. D. MacLachlan, *Mol. Phys.*, **5**, 31 (1962).
(8) T. Forster and K. Kasper, *Z. Phys. Chem.*, **1**, 19 (1954).
(9) A. Ron and O. Schnepp, *J. Chem. Phys.*, **44**, 19 (1966).

The Use of ^{13}C-Labeled Acetate in Biosynthetic Studies[1]

Sir:

The use of ^{14}C-labeled substrates to test and verify proposed biosynthetic pathways has led to the rapid advance of knowledge in this field. The initial concept that the head-to-tail linkage of acetic acid units accounts for the biogenesis of phenolic materials was advanced by Collie,[2] and the idea was further extended and biochemically tested by Birch.[3]

The radioactive tracer technique employing ^{14}C-labeled acetate was employed by Birch in the study of the biogenesis of fungal metabolites derived *via* the polyacetate route with significant results. The degradative reactions necessary for removing the radioactive ^{14}C label from the metabolites included the Kuhn–Roth oxidation for isolating C–CH_3 groups as acetic acid. Labeled carbon atoms in phenolic rings

(1) Acknowledgment is made for support of this work by Public Health Service Research Grant No. 5 SO1-FR-05522-04.
(2) (a) J. N. Collie, *J. Chem. Soc.*, **63**, 329 (1893); (b) *ibid.*, **91**, 1806 (1907).
(3) (a) A. J. Birch and F. W. Donovan, *Australian J. Chem.*, **6**, 360 (1953); (b) A. J. Birch, R. A. Massy-Westropp, and C. J. Moye, *ibid.*, **8**, 539 (1955); (c) for reviews see A. J. Birch, *Fortschr. Chem. Org. Naturstoffe*, **14**, 186 (1957); J. H. Richards and J. B. Hendrickson, "The Biosynthesis of Steroids, Terpenes, and Acetogenins," W. A. Benjamin, Inc., New York, N. Y., 1964.

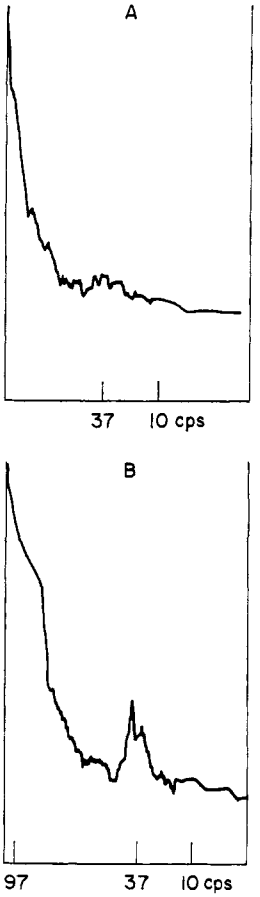
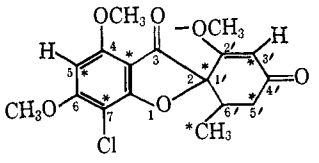


Figure 1. (A) ^{13}C-satellite pattern of unlabeled griseofulvin recorded on the HA-100 spectrometer at 80 scans. The upfield C_6'–CH_3 satellite signal appears at 37 cps. (B) ^{13}C-satellite pattern of labeled griseofulvin recorded as in (A). The integrated ratio of A:B is approximately 1:3.

were isolated as barium carbonate by nitration and subsequent oxidation with barium hypobromite.

This report describes an alternative method for studying the biosynthesis of microbial metabolites employing ^{13}C-labeled acetate. The location of the incorporated ^{13}C label in excess over that of natural abundance (1.1%) in the metabolite can be determined by proton nuclear magnetic resonance spectroscopy. The nondegradative spectroscopic method eliminates the necessity of chemical reactions to isolate specific labeled carbon atoms. The detection of the excess ^{13}C label in a metabolite is dependent upon the large range of coupling constants, 120–250 cps, associated with $J_{^{13}C-H}$. These values have a near-linear dependence on the per cent s character of the bond.[4] The increase in the coupling constant with increasing s character is of considerable value in the location of specific carbon atoms.



(I)

(4) J. N. Shoolery, *J. Chem. Phys.*, **31**, 1427 (1959); N. Muller and D. E. Pritchard, *ibid.*, **31**, 768, 1471 (1959).

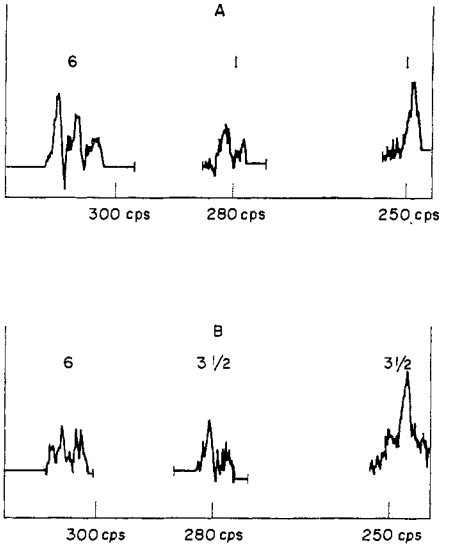


Figure 2. (A) ^{13}C-satellite pattern of unlabeled griseofulvin, recorded on the A-60 spectrometer with 800 scans. Two downfield methoxyl satellite signals, utilized as an internal standard, appear at 305 cps and the upfield C_3'–H and C_5–H satellite signals at 280 and 250 cps, respectively, with relative intensities of 6:1:1. (B) ^{13}C-satellite pattern of labeled griseofulvin recorded under the same conditions as in (A). The relative intensities are 6:3.5:3.5.

From cultures of *Penicillium urticae* (NRRL 989) with sodium acetate-2-^{13}C of 55% isotopic purity included in the medium, the antibiotic griseofulvin (I) was isolated.[5] The details of the nmr data of griseofulvin are indicated in Table I.

Table I. Nuclear Magnetic Resonance Data of Griseofulvin

	τ	$J_{^{13}C-H}$, cps[a]	Yield,[b] %
C_6'–CH_3	9.03 $J = 6$ cps	120[c]	~2.5
C_6'–H, C_5'–CH_2	6.8–7.7[d]		
C_2'–OCH_3	6.41[e]		
C_4–OCH_3	6.06	140[e]	
C_6–OCH_3	6.01	140[e]	
C_3'–H	4.49	160	~2.5
C_5–H	3.88	160	~2.5

[a] These values were determined in 5% deuteriochloroform solutions of griseofulvin on a Varian Associates HA-100 or A-60 nmr spectrometer with the aid of a time-averaging computer (Varian C-1024 CAT). Approximately 80 scans of labeled and unlabeled materials were made with the 100-Mc instrument, 800 scans with the A-60 (Figures 1 and 2). [b] The approximate incorporation yield was determined by comparison of the area of the ^{13}C-satellite bands with material of natural abundance with the labeled product. [c] Experimentally, only the upfield side of this methyl doublet could be observed. [d] The C_5'–CH_2 contains excess ^{13}C, but the complexity of the splitting pattern causes difficulty in spectral determination. [e] The chemical shift values for the three methoxyl groups were arbitrarily assigned. Incorporation yields at C_3' and C_5 were also determined with the use of the two integrated downfield methoxyl ^{13}C–H satellite signals as internal standards. This method also gave the same approximate incorporation yields. The methoxyl groups would not be expected to contain excess ^{13}C since feeding experiments with ^{14}C-labeled choline indicate that the methoxyl carbons of griseofulvin arise from the one-carbon metabolic pool: D. J. P. Hockenhall and W. F. Faulds, *Chem. Ind.* (London), 1390 (1955).

(5) We thank Dr. C. W. Hessletine of the North Regional Research Laboratories, Peoria, Ill., for samples of this culture. After an initial growth period of 14 days, griseofulvin was produced in a medium containing sodium acetate as the sole carbon source.

The nmr data clearly indicate that $C_{3'}$, C_5, and the $C_{6'}$-methyl group are derived from the methyl group of acetate. The magnitude of the observed coupling constants is in accord with the degree of s character at these respective carbon atoms. These results from the ^{13}C study are in accord with the prior biogenetic study of griseofulvin employing the conventional ^{14}C-labeling method.[6]

The application of this ^{13}C method for the study of the biosynthesis of other microbial products is now in progress in this laboratory.

(6) A. J. Birch, R. A. Massy-Westropp, R. W. Richards, and H. Smith, *J. Chem. Soc.*, 360 (1958). In this study acetic acid-1-^{14}C was employed. We have made a similar study with sodium acetate-1-^{13}C; observations of the ^{13}C satellite bands of the $C_{6'}$–H in the griseofulvin obtained in this manner was precluded by the complexity of the $C_{6'}$–H splitting pattern. The biosynthesis of griseofulvin using sodium acetate-2-^{14}C has been reported by R. W. Rickards in "The Chemistry of Natural Phenolic Products," W. D. Ollis, Ed., Pergamon Press, London, 1964, p 6. A slight redistribution of the label was reported in this case, apparently arising from participation of acetic acid in the tricarboxylic acid cycle.

Masato Tanabe, George Detre

Stanford Research Institute
Menlo Park, California

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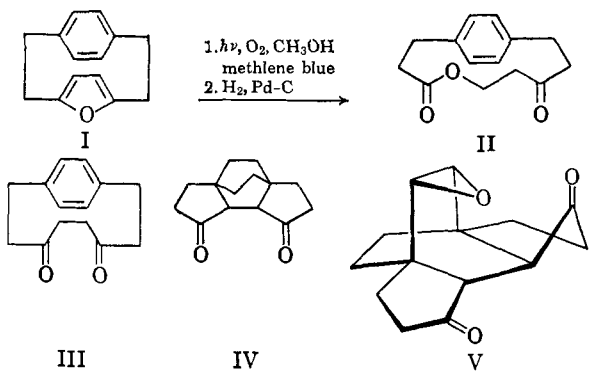
A Novel Oxygen-Transfer Reaction in a Photosensitized Autoxidation

Sir:

We wish to report a novel conversion of the furano-paracyclophane I[1] during photosensitized autoxidation leading to a benzene epoxide as a transient oxidation product.



A methanolic solution of I was irradiated in the presence of methylene blue for 18 hr at 25° with a 150-w flood lamp while air was bubbled through the reaction medium. The solution was concentrated under reduced pressure and hydrogenated over palladium on charcoal for 24 hr.[2] Chromatography of the crude hydrogenated material over silica gel gave three products, A (26%), B (11%), and C (5%).

Compound A, mp 118–120°, was shown to be the keto lactone, II. *Anal.* Calcd for $C_{14}H_{16}O_3$: C, 72.39; H, 6.94. Found: C, 72.50; H, 6.93. The infrared spectrum ($CHCl_3$) shows strong absorption at 1725 (sh), 1710, and 1134 cm^{-1}. The nmr spectrum ($CDCl_3$) shows a singlet at τ 2.90 (4 H), triplets at 6.01 (2 H), 7.47 (4 H), and 8.02 (2 H), and a complex multiplet centered at 7.02 (4 H). Reduction of II to the triol with lithium aluminum hydride followed by tosylation and then further reduction with lithium aluminum hydride led to 1-propyl-4-amylbenzene. This product is identical with the hydrocarbon prepared by the Friedel–Crafts acylation of propylbenzene followed by Wolff–Kishner reduction. *Anal.* Calcd for $C_{14}H_{22}$: C, 88.35; H, 11.85. Found: C, 88.50; H, 11.79. The mass spectrum shows a parent peak at *m/e* 190 and the expected peaks at *m/e* 133 and 161.

Compound B was shown to be identical with III (infrared, nmr, mixture melting point), a product previously prepared from I by Cram.[1]

Compound C, mp 145–147°, formed in low yield, was unstable to acid or base. *Anal.* Calcd for $C_{14}H_{16}O_3$: C, 72.39; H, 6.94; mol wt, 232. Found: C, 72.21, 72.41; H, 6.93, 6.94; mol wt (mass spectrum), 232. While transparent in the ultraviolet, compound C shows peaks in the infrared at 1730 and 1245 cm^{-1} suggesting the presence of a five-membered ring ketone and an ether linkage. A most interesting feature of its structure, shown by the nmr spectrum, is the complete absence of all aromatic protons.

While the above spectroscopic data and our earlier work on the photooxidation of a related furanoheterocyclophane system[3] led us to believe that C contains the main structural features of IV, the final location of the ether oxygen in V and the stereochemistry of the molecule rest on the results of a single-crystal X-ray structure determination.

Compound C crystallizes in the monoclinic system, with cell dimensions $a = 12.97$, $b = 11.03$, $c = 9.17$ A, $\beta = 117.98°$, and four molecules in the unit cell. The observed and calculated densities are 1.32 and 1.33 g/cm^3, respectively. The systematic absences (*hkl* for $h + k = 2n + 1$ and *h0l* for $l = 2n + 1$) are consistent with either of the space groups Cc or C2/c. Using a General Electric XRD-6 diffractometer equipped with single-crystal orienter and a balanced Ni-Co filter pair, three-dimensional intensity data were collected, by the stationary crystal–stationary counter method, to the limit $2\theta = 110°$; orienter settings were computed using λ 1.5405 A (Cu $K\alpha_1$). Due to rather poor crystal quality, only 683 of the 861 possible independent reflections were considered to have observable intensity.

The usual correction factors were applied to produce a set of structure amplitudes ($|F|$) from the intensity data. These structure amplitudes were then converted by use of a K(s) curve[4] to normalized structure amplitudes ($|E|$). The statistical averages[5] (Table I) and distributions[5] (Table II) of the normalized structure factors imply that the crystal is centrosymmetric and that the correct space group is C2/c. Since this space group has eightfold general multiplicity and the unit cell contains only four molecules, the molecule must be centered at a twofold symmetry position (*i.e.*, an inversion center or a twofold rotation axis). Each asymmetric unit of the cell, therefore, contains one-half a chemical molecule, or $^1/_2(C_{14}H_{16}O_3)$. Since the mole-

(1) D. J. Cram and G. R. Knox, *J. Am. Chem. Soc.*, **83**, 2204 (1961); D. J. Cram, C. S. Montgomery, and G. R. Knox, *ibid.*, **88**, 515 (1966).

(2) The unhydrogenated reaction mixture tended to decompose rapidly on work-up, giving polymeric material.

(3) H. H. Wasserman and A. R. Doumaux, *J. Am. Chem. Soc.*, **84**, 4611 (1962).

(4) J. Karle and H. Hauptman, *Acta Cryst.*, **6**, 473 (1953).

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