have n–π^* excited states V and VIII, respectively (note ref. 2 for "circle, dot, y" notation). V and VIII have a γ-hydrogen which may be abstracted to give species VI (or IX) in which the methylenic odd electron is conjugated with a strained, epoxide ring which should open as indicated by homolytic β-elimination, thus affording diradical VII (or X). Intramolecular disproportionation leads to the observed products II and IV, respectively. This mechanism requires proximity of benzoyl and methyl groups; and in agreement with this, cis-dypnone oxide (IIIb) (CH_3 and benzoyl groups trans) was found to be largely unreacted under the usual conditions. Finally, we emphasize that hydrogen abstraction from a saturated carbon atom is generally strongly suggestive of radical and electron-deficient oxygen rather than electron-rich oxygen.

The second reaction described[7] involves the formal migration of a methyl group to give β-diketonic product. This reaction is remarkable because the reactant (XV) differs only subtly from the cases of dimethylacrylophenone oxide (I) and dypnone oxide (IIIa) where the β-dicarbonyl product was a very minor product if formed at all. Secondly, the preferential migration of a methyl group rather than phenyl is uncommon and serves to cast mechanistic light on the reaction.

In our discussions of n–π^* excited state reactivity,[1,2] we noted that groups attached to the carbon adjacent to an excited carbonyl group might be expelled heterolytically or homolytically, i.e.
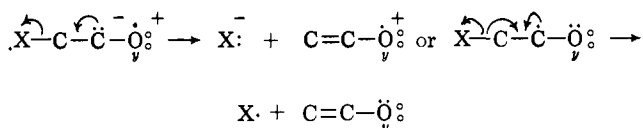
Clearly the reaction of XV begins with such a C–O fission, and the homolytic version nicely rationalizes the preferential methyl migration.[8] Whether the methyl
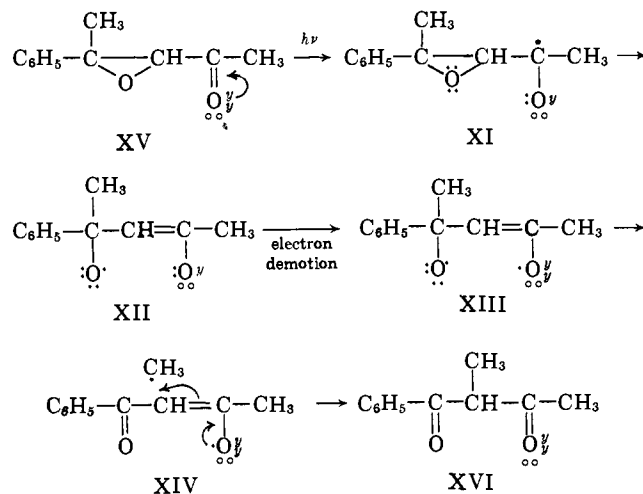
Faraday Soc., **33**, 1521 (1937)) and the Yang reaction (N. C. Yang and D. C. Yang, J. Am. Chem. Soc., **80**, 2913 (1958)).

(6) An independent conclusion regarding hydrogen abstraction by the n orbital has been noted by M. Kaska, "Comparative Effects of Radiation," M. Burton, J. Kirby-Smith, and J. Magee, Ed., John Wiley and Sons, Inc., New York, N. Y., 1960, p. 72.

(7) After our discussion of this type photochemical reaction and presentation of an example (ref. 1), W. Reusch and C. K. Johnson (Abstracts of the 142nd National Meeting of the American Chemical Society, Sept., 1962, p. 89Q) described two further cases. Some further examples have also been described by C. Lehmann, K. Schaffner, and O. Jeger, Helv. Chim. Acta, **45**, 1031 (1962). Early examples of hydrogen migration have been described by S. Bodforss, Chem. Ber., **51**, 214 (1918).

(8) (a) Preferred loss of methyl from XIII has analogy in the radical decomposition of cumene hydroperoxide (cf. M. S. Kharasch, A. Fono, and W. Nudenberg, J. Org. Chem., **16**, 113 (1951)). (b) Fission of the α,β-carbon to carbon bond appears to be a reversible epoxy ketone reaction for which evidence will be discussed elsewhere.

migration is (1) by methyl radical expulsion with intermolecular recombination, (2) expulsion and recombination within a solvent cage, or (3) direct migration of diradicaloid species XII with concomitant electron demotion is presently under study. The occurrence of C–O fission in epoxy ketone XV vs. γ-hydrogen abstraction in I and IIIa is attributed to the greater excited (π^*) electron localization in the carbonyl group of XV and hence greater probability for β-elimination. In the excited benzoyl groups of I and IIIa the excited electron is distributed throughout the phenyl group as well as the carbonyl group and is less available.

From the occurrence of C–O fission we may conclude that the carbonyl carbon of the excited state has odd electron capabilities; indeed such a fission is strongly suggestive of an electron-rich carbon rather than the reverse.

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The Biosynthesis of Cordycepin[1]

Sir:

A number of nucleoside analogs have been found in nature.[2] One of these, cordycepin (I), was isolated from culture filtrates of Cordyceps militaris and the sugar moiety reported to be a branched chain pentose.[3] More recently, Kaczka, et al.,[4] have suggested that the sugar moiety of cordycepin is 3-deoxyribose (II). Kredich and Guarino,[5] in their studies on the biosynthesis of cordycepin, reported that acetate and isovalerate were not precursors for cordycepose. Also, glucose-1-C^{14} and glucose-6-C^{14} were incorporated into cordycepose, whereas ribose-1-C^{14} was essentially not utilized. Adenine-8-C^{14} was incorporated into the purine moiety of cordycepin. Glucose was the sole carbon source.

This communication reports the results of studies on incorporation of formate-C^{14} and adenosine-U-C^{14} (III) into cordycepin and the distribution of C^{14} in the cordycepin.
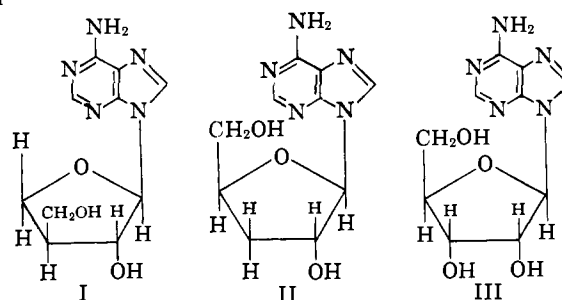
The adenosine-U-C^{14} used was obtained by hydrolysis of adenosine 5'-phosphate-U-C^{14} with snake venom and

(1) This investigation was aided by Grant G8685-03 from the National Institutes of Health, United States Public Health Service.

(2) S. S. Cohen, Science, **139**, 1017 (1963).

(3) K. G. Cunningham, S. A. Hutchinson, W. Manson, and F. S. Spring, J. Chem. Soc., 2299, 2301 (1951).

(4) E. A. Kaczka, N. R. Trenner, B. Arison, R. W. Walker, and K. Folkers, Biochem. Biophys. Res. Commun., **14**, 456 (1964).

(5) N. M. Kredich and A. J. Guarino, Biochim. Biophys. Acta, **47**, 529 (1961).

purified by paper chromatography. The adenosine-U-C[14] was eluted from the paper, sterilized, and added to cultures of *C. militaris*[6] that were rapidly synthesizing cordycepin. The formate-C[14] solution was added in a similar manner. Five to seven days after the addition of formate or adenosine, the cordycepin was isolated, purified, and crystallized to constant specific activity.[7] The radioactivity added to the flasks and the incorporation into cordycepin are shown in Table I.

TABLE I

INCORPORATION OF RADIOACTIVE COMPOUNDS INTO CORDYCEPIN[a]

Expt. no.	Compound[b]	Added mg.	μc.	μc./mmole	Cordycepin μc./mmole
1	Adenosine-U-C[14]	9.0	24	713	18.0
2	Adenosine-U-C[14]	1.5	6.0	1070	3.56
3	Adenosine-U-C[14] plus D-ribose	1.5	6.0	1070	3.58
4	Formate-C[14]	68.0	50.0	50.0	0.60

[a] Samples were counted in a Packard Tri-Carb scintillation spectrometer in dioxane–naphthalene scintillation solution. [b] Carbon source: expt. 1, 2, and 3, acetate; expt. 4, glucose.

Adenosine-U-C[14] and formate-C[14] were both incorporated into cordycepin. The similar specific activities of cordycepin in expt. 2 and 3 tend to rule out cleavage of the carbon–nitrogen glycoside bond of adenosine. Further proof of the direct conversion of adenosine to cordycepin is shown below.

To determine the distribution of radioactivity in cordycepin from the formate, adenosine-U-C[14], and adenosine-U-C[14] plus D-ribose experiments, the cordycepin and adenosine-U-C[14] were hydrolyzed, concentrated, and chromatographed on paper. The chromatograms were developed in ammonia–water (pH 10.0). One radioactive spot was observed for the adenine, ribose, or cordycepose, and these were in agreement with the R_f values of authentic adenine, ribose, and cordycepose obtained by hydrolysis of nonradioactive nucleosides. These spots were eluted and the radioactivity measured. The distribution of C[14] in cordycepin and adenosine is shown in Table II.

TABLE II

THE DISTRIBUTION OF C[14] IN ADENOSINE AND IN CORDYCEPIN FROM ADENOSINE-U-C[14] AND FORMATE-C[14]

Expt. no.	Substrate	Compound hydrolyzed	% C[14] in Adenine	Ribose	Cordy- cepose
		Adenosine	36.6	63.4	
1	Adenosine-U-C[14]	Cordycepin	40.6		59.4
2	Adenosine-U-C[14]	Cordycepin	33.5		66.5
3	Adenosine-U-C[14] plus D-ribose	Cordycepin	37.0		63.0
4	Formate-C[14]	Cordycepin	98.0		2.0

Although formate-C[14] (expt. 4) was incorporated into cordycepin, 98.0% of the radioactivity resided in the adenine. This indicates that the formate entered the C-1 pool of the fungus, but the low incorporation into cordycepose suggests that this pentose does not arise by a C-1, C-4 condensation. If cordycepin arises from the direct conversion of adenosine, then the distribution of radioactivity between adenine and the sugar should be the same for the isolated cordycepin as for the adenosine regardless of the structure of cordycepin (I or II). Hydrolysis of the added adenosine-U-C[14] resulted in 36.6% of the C[14] in adenine and 63.4% in ribose (Table II). Similarly, distribution of C[14] in cordycepin from expt. 1 and 2 compares with that

(6) Kindly supplied by Dr. A. J. Guarino, Dept. of Biochemistry, Woman's Medical College of Pennsylvania, Phila., Pa.

(7) A. J. Guarino and N. M. Kredich, *Biochim. Biophys. Acta*, **68**, 317 (1963).

of adenosine. The distribution of radioactivity in cordycepin was not affected when 10 mg. of ribose was added along with adenosine-U-C[14] (expt. 3). An average of 98.8% (expt. 1, 2, and 3) of the radioactivity of the ribose from adenosine was found in the cordycepose. The ribose moiety from the adenosine-U-C[14] was isolated, converted to the osazone,[8] and degraded[9] in order to determine the distribution of radioactivity in the sugar. The distribution of C[14] obtained from the ribose of adenosine-U-C[14] is given in Table III.

TABLE III

DISTRIBUTION OF C[14] FROM RIBOSE-U-C[14]

Derivative	Carbon atoms	C.p.m./mmole[a]	% C[14] Exptl.	Theoret- ical
Ribosazone	1,2,3,4,5	19,550	100	100
Mesoxaldehyde 1,2-bisphenylosazone	1,2,3	11,394	58.4	60
Formaldimedon	5	3,636	18.6	20
Formic acid	4	[b]		20

[a] Crystallized to constant specific activity. [b] Not analyzed.

These findings rule out the hydrolysis of adenosine prior to the formation of cordycepin and *demonstrate that none of the carbon atoms of ribose is lost.*

Studies are in progress to define the reaction sequence and to determine if the biosynthesis of this deoxynucleoside proceeds in a manner similar to that of deoxyribonucleotides.[10]

(8) W. T. Haskins, R. M. Hann, and C. S. Hudson, *J. Am. Chem. Soc.*, **68**, 1766 (1946).

(9) Y. J. Topper and A. B. Hastings, *J. Biol. Chem.*, **179**, 1255 (1949).

(10) A. Larsson, *ibid.*, **238**, 3414 (1963).

(11) Research Career Development Awardee of the United States Public Health Service (5-K3-GM-7100-03).

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On the Enantiomorphism of Organic Peroxy Compounds in the Crystalline State

Sir:

Because of the dihedral angle of the peroxy group, a molecule of an organic peroxy compound is not identical with its mirror image. In solution, the low barrier[1] to rotation about the peroxy link results in frequent interconversion between the mirror-related configurations, so that although nonzero dipole moments have been reported,[2] D,L isomerism has not. In the crystalline solid, this is not so, and we have found by X-ray structure analysis both enantiomorphic and racemate crystal structures.

In the crystal structure of dibenzoyl peroxide we find a peroxy dihedral angle of 93°. The crystals have the space group $P2_12_12_1$ and the molecules in any one crystal are all of the same sense. The same is probably true for the crystals of p-nitroperoxybenzoic acid, which also have the symmetry $P2_12_12_1$.

In the crystal structures of peroxypelargonic acid and *o*-nitroperoxybenzoic acid,[3] on the other hand, there are equal numbers of left and right handed molecules. In the fatty peroxy acid crystals, the molecules of the same sense are hydrogen bonded in spirals and there are an equal number of left and right handed spirals. In the *o*-nitroperoxybenzoic acid, alternate left and right handed molecules form a hy-

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(2) F. D. Verderame and J. G. Miller, *J. Phys. Chem.*, **66**, 2185 (1962).

(3) D. Belitskus, S. Chu, G. A. Jeffrey, and M. Sax, unpublished work.