creted unaltered. Aminoacetonitrile, 2,2′-iminodiacetonitrile and γ-aminobutyronitrile failed to give rise to cyanoacetic acid. It appears that in the metabolism of BAPN and certain other aliphatic nitriles by the rat the organic cyano group is largely unaffected and that deamination and/or oxidation occur at the other end of the molecule. Results to date tend to indicate that aliphatic nitriles are metabolized in the animal body to form ω-carboxynitriles which then undergo cleavage as proposed for the fatty acids.[5] The color reaction with diazotized sulfanilic acid affords a very sensitive method for detecting cyanoacetic acid and may be useful for studying the metabolism of other organic cyano derivatives. A detoxication product of *inorganic* cyanide, 2-imino-4-thiazolidine carboxylic acid,[6] gives a somewhat similar color with this reagent but is easily distinguished from cyanoacetic acid. Neither cyanoacetic acid or cyanacetamide produced any of the symptoms of BAPN toxicity when fed to weanling rats at the rate of 2 mg. per ml. of drinking water for seven weeks.[7] Cyanoacetic acid may be a detoxication product of BAPN. Its relationship, if any, to the connective tissue degeneration characteristic of BAPN toxicity is not known.

(5) D. E. Green, *Biol. Revs.*, **29**, 330 (1954).
(6) J. L. Wood and S. L. Cooley, *J. Biol. Chem.*, **118**, 449 (1956).
(7) J. J. Lalich, unpublished experiments.

DEPARTMENTS OF BIOCHEMISTRY AND PATHOLOGY — S. H. LIPTON
UNIVERSITY OF WISCONSIN — J. J. LALICH
MADISON, WISCONSIN — F. M. STRONG

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UO_2–PuO_2 SOLID SOLUTIONS[1]

Sir:

An X-ray diffraction investigation has been made of the solid phase relationships in the UO_2–PuO_2 system. The results show that a continuous solid solution exists, and that the lattice parameter varies essentially linearly with composition. A slight negative deviation from linearity may exist.

Some trouble was experienced in preparing satisfactory samples of the mixed oxide. Plutonia is an extremely inert substance, and at 1000° the reaction rate between PuO_2 and UO_2 is very slow. Various ways of producing an intimate mixture of plutonium and uranium compounds that could be converted to oxide were tried. The method which seemed best was to co-precipitate $Pu(OH)_4$ and $(NH_4)_2U_2O_7$ by dropping a Pu(IV)–U(VI) solution (total metal concentration *ca.* 14 g./l.) into hot ammonium hydroxide, taking care to keep the *p*H always above 8. The mixed precipitate was dried in air at 70°, then fired in hydrogen by raising the temperature to 1000° over 6 or 7 hours and holding at 1000° overnight. Samples were furnace-cooled in hydrogen.

It appears to be quite important that the firing be done in such a way as to avoid the production of well crystallized PuO_2 as a separate phase. For example, a solid solution was not produced by initial firing of the hydroxide precipitate in air followed by hydrogen reduction of the U_3O_8 to UO_2, nor by hydrogen firing of mixtures produced by evaporation of various solutions containing U and Pu. Coprecipitation of the U and Pu as peroxide was also tried and was not successful.

After the samples were examined by X-ray diffraction, a radiochemical Pu assay was done to check the composition. The Pu assay agreed with the compositions as made in each case.

X-Ray powder patterns were taken in a 114.6 mm. diameter powder camera using filtered copper K-radiation. (Wave lengths, $\alpha_1 = 1.54051$, $\alpha_2 = 1.54433$, mean $\alpha = 1.5418$ Å.) The lattice parameter was determined in most cases by graphical extrapolation of the values found for the high-angle lines on each pattern. Results are presented in Table I. The error limits on the compositions are estimated, those on the lattice parameters are estimated uncertainties in the graphical extrapolation. The solid solution has the fluorite structure, the same as PuO_2 and UO_2.

TABLE I

UO_2–PuO_2 SOLID SOLUTION FLUORITE STRUCTURE

Compn. (mole % PuO_2)	Lattice parameter (Å., 25°)
0	5.4700 ± 0.0001
12.6 ± 0.3	5.449 ± .003
20.0 ± .3	5.4544 ± .0006
35.9 ± .3	5.441 ± .003
48.1 ± .3	5.4345 ± .0005
63.1 ± .3	5.420 ± .003
73.8 ± .3	5.414 ± .002
79.4 ± .3	5.407 ± .003
100.0	5.3960 ± .0003

Thanks are due the Misses Marian Gibbs and Gladys Sturdy for measuring the films and preparing the samples, respectively; and Mr. A. Zerwekh for the Plutonium assays.

UNIVERSITY OF CALIFORNIA — ROBERT N. R. MULFORD
LOS ALAMOS SCIENTIFIC LABORATORY
LOS ALAMOS, NEW MEXICO — F. H. ELLINGER

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S-ADENOSYLMETHIONINE AND ERGOSTEROL SYNTHESIS[1]

Sir:

The side-chain C-28 methyl group of ergosterol have been shown to arise intact from methionine.[2,3] This transfer of a methyl group was of interest since this was the first demonstration that a carbon atom may act as the acceptor of a methyl group. In order to participate in certain methyl additions, methionine must first react with ATP[4] to form an adenosylsulfonium compound, S-adenosylmethionine,[5] which may then act as the methyl donor to the appropriate acceptor. Involvement of S-adenosylmethionine as the actual donor in the transfer of methyl groups to sulfur[6] and nitrogen[7] has been de-

(1) Work done under the auspices of the Atomic Energy Commission.

(1) This work was performed under the auspices of the U. S. Atomic Energy Commission.

(2) G. J. Alexander, A. M. Gold and E. Schwenk, THIS JOURNAL, **79**, 2967 (1957).
(3) G. J. Alexander and E. Schwenk, *ibid.*, **79**, 4554 (1957).
(4) H. Borsook and J. W. Dubnoff, *J. Biol. Chem.*, **171**, 363 (1947).
(5) G. L. Cantoni, THIS JOURNAL, **74**, 2942 (1952).
(6) S. K. Shapiro, *Bacteriol. Proc. Am. Bacteriologists*, 116 (1957).
(7) G. L. Cantoni, *Phosphorus Metabolism*, **2**, 129 (1952).

scribed. A further study of transmethylation in the ergosterol-synthesizing system was desirable to determine whether the sulfonium derivative is of importance there also.

Methods developed in this Laboratory were used for the preparation of S-adenosylmethionine in high purity.[8] S-Methylmethionine was prepared according to the procedure of Toennies and Kolb.[9] Methionine and $C^{14}H_3$-methionine were obtained from commercial sources. A cell-free ergosterol-synthesizing system was prepared from bakers yeast.[10] Cells were disrupted by sonic treatment. Methyl donors were allowed to react in the enzyme system for 5 hours at 30°. Reaction vessel contents were then saponified with KOH and the non-saponifiable fraction extracted with petroleum ether. A Packard Tri-Carb liquid scintillation counter was used for radioactivity measurements. The results are shown in the Table I.

TABLE I

C-14 INCORPORATED INTO ERGOSTEROL FROM VARIOUS METHYL DONORS

C-14 methyl donor[a]	Non-radioactive substrate[b]	C-14 in ergosterol, c.p.m.
S-Adenosylmethionine	None	3795
	Methionine	3400
	Serine	3345
Control[c]	None	15
Methionine	None	1670
	S-Adenosylmethionine	90
	Serine	1235
Control	None	50
S-Methylmethionine	None	60
	S-Adenosylmethionine	25
	Methionine	10
	Serine	30
Control	None	40

[a] Each complete reaction mixture in a total volume of 4.5 ml. contained 3 ml. of enzyme representing 37.5 mg. of protein; 100 μmoles of potassium acetate; 20 μmoles of ATP; and 0.2 μc. C-14 representing 7.5 μmoles of the substrate. [b] 7.5μ moles of the non-radioactive substrate was added. [c] Control flasks were stopped at 0 time with KOH.

In these experiments S-adenosylmethionine is more efficient as a methyl group donor than is methionine. Incorporation of the labeled methionine does occur however, probably because of adenosylmethionine synthesis in the extracts since *Saccharomyces* extracts possess a methionine-activating system operable under the conditions of these experiments. Added non-radioactive adenosylmethionine greatly suppresses the methyl incorporation from free methionine, demonstrating preferential incorporation from the adenosyl sulfonium derivative. While methylmethionine has been found under certain conditions to be an excellent methyl source in the synthesis of methionine[11] it is virtually inactive in ergosterol synthesis.

(8) F. Schlenk and R. DePalma, *J. Biol. Chem.*, **229**, 1037 (1957).

(9) G. Toennies and J. J. Kolb, THIS JOURNAL, **67**, 849 (1945).

(10) H. P. Klein and Z. K. Booher, *Proc. Soc. Exptl. Biol. Med.*, **89**, 43 (1955).

(11) S. K. Shapiro, *J. Bacteriol.*, **72**, 730 (1956).

DIVISION OF BIOLOGICAL AND MEDICAL RESEARCH
ARGONNE NATIONAL LABORATORY L. W. PARKS
LEMONT, ILLINOIS

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REACTIONS OF 1,1-DIHALOCYCLOPROPANES WITH ELECTROPHILIC REAGENTS. SYNTHETIC ROUTE FOR INSERTING A CARBON ATOM BETWEEN THE ATOMS OF A DOUBLE BOND

Sir:

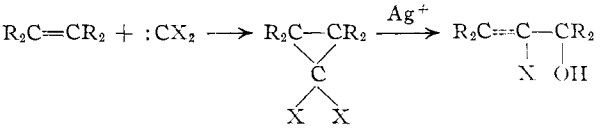
The chance observation that 2,2-dibromobicyclo-[3,1,0]hexane (I) reacted rapidly with alcoholic silver nitrate[1] indicated the desirability of further examination of this reaction.

Shaking I with aqueous or alcoholic silver nitrate results in the rapid precipitation of 1 mole of silver bromide per mole of I, the second bromine being unreactive. In aqueous alcoholic media a mixture of a bromoalcohol and a bromoether is obtained. In the aqueous media I is cleanly converted to the bromoalcohol, to which the structure 2-bromo-2-cyclohexen-1-ol (II) is assigned. Infrared (3.05, 6.12 μ) and proton magnetic resonance spectra are

I II

consistent with this assignment. The analogous 1,1-dichlorobicyclo[3,1,0]hexane (III) reacts similarly to produce the known 2-chloro-2-cyclohexen-1-ol (IV),[2] compared as the alcohol and the acetate.

This reaction has been extended to other systems and appears to be general for electrophilic attack on 1,1-dihalocyclopropanes. Thus a sequence of reactions of general character is available for extending a carbon chain[3] through insertion of a carbon atom *between* the double-bonded atoms. Isobutylene, styrene, *cis*- and *trans*-2-butene have been studied and the reaction is being extended to other olefins.



The strain in the 5–3 ring system of I results in greatly enhanced reactivity, I being 200 times as reactive as the analogous 2,2-dihalobicyclo[4,1,0]-heptane (V) which has a 6–3 ring system. Monocyclic dihalocyclopropanes have reactivities similar to V. The driving force for this reaction, in addition to the formation of an allylic cation, is derived

(1) A. Y. Garner, Pennsylvania State University Thesis, 1956. This compound is not dehydrohalogenated by alcoholic alkoxides at room temperature.

(2) M. Mousseron and R. Jacquier, *Bull. soc. chim. France*, 648 (1950).

(3) Specific applications of this reaction are known. (a) Indenes to β-halonaphthalenes: W. E. Parham and H. E. Reiff, THIS JOURNAL, **77**, 1177 (1955); W. E. Parham, H. E. Reiff and P. Swartzentruber, *ibid.*, **78**, 1437 (1956); W. E. Parham and R. R. Twelves, *J. Org. Chem.*, **22**, 730 (1957); W. E. Parham and C. D. Wright, *ibid.*, **22**, 1473 (1957). (b) Pyrroles to β-substituted pyridines: J. Hine, THIS JOURNAL, **72**, 2444 (1950); E. R. Alexander, A. B. Herrick and T. M. Roder, *ibid.*, **72**, 2760 (1950); G. L. Ciamician, *Ber.*, **37**, 4234 (1904); G. L. Ciamician and M. Dennstedt, *ibid.*, **14**, 1153 (1881); **15**, 1172 (1882); G. L. Ciamician and P. Silber, *ibid.*, **20**, 191 (1887); M. Dennstedt and J. Zimmermann, *ibid.*, **18**, 3316 (1885); G. Plancher and U. Ponti, *Atti. accad. naz. Lincei*, [5] **18**, II, 469 (1909); O. Bocchi, *Gazz. chim. ital.*, **30**, [1] 89 (1900). (c) Indoles to β-haloquinolines: G. Magnanini, *Ber.*, **20**, 2608 (1887); A. Ellinger, *ibid.*, **39**, 2517 (1906); G. Plancher and O. Carrasco, *Atti. accad. naz. Lincei*. [5] **13**, I, 573, 632 (1904).