Identification and quantitative estimation is achieved by gas–liquid chromatography using a Trend[4] (a commerical detergent) column and three different silicone oil-on-firebrick columns, infrared examination of fractions from preparative gas-liquid chromatography, and separation of olefinic materials by solution chromatography on silica gel.

Different ratios of products are obtained from VI and XII, large quantities of hydrocarbon with unaltered carbon skeleton resulting from each starting material. In *n*-hexadecane at 287°, for example, the relative product distribution (on a weight basis) from XII at 0.172 *M* initial concentration is II, 1.0: X, 2.1: VII, 0.50: VIII, 0.34: IV, 0.29: III, trace. Under the same conditions, the distribution from VI is II, 1.0: X, present (>0.01)[5]: VII, 0.035: VIII, 0.17: IV, $\sim$ 0.01: III, 0.02. Further, isocamphane (VII) is formed from either VI or XII as a mixture of both stereoisomers in a ratio that is essentially the same as that produced by the catalytic hydrogenation of camphene. The dependence of the product distribution on the starting material and the non-stereospecificity of hydrogen abstraction by the radical precursor of VII are evidence against a mesomeric bridged radical (XIII) as the sole intermediate and in favor of a cleavage–re-cyclization mechanism for the rearrangement. From what is known of the behavior of simple alkyl radicals,[6] it is reasonable to assume that the activation energy for β-elimination in the radical V should be substantially higher than those for disproportionation or hydrogen abstraction. The observation that products of β-elimination (VIII and the rearrangement product VII) occur only at high temperatures is thus also consistent with the cleavage–re-cyclization mechanism.

The formation of VII from VI is the first clearly intramolecular example of a free radical alkyl group rearrangement.[7]

[4] We are indebted to Dr. Robert Petterson of Purex Corporation for a sample of this material and to Dr. A. Hussey of Northwestern University for an authentic sample of *p*-menthene.

[5] Olefin X is not well resolved from IV and II on our columns and can therefore be determined readily only when present in substantial quantity, as in the mixture of products from XII.

[6] (a) E. W. R. Steacie, "Atomic and Free Radical Reactions," Reinhold Publishing Corporation, New York, N. Y., 1954, 2nd Edition, Volume 2, Chapter VI; (b) J. G. Calvert and W. C. Sleppy, THIS JOURNAL, **81**, 1544 (1959); (c) J. A. Kerr and A. F. Trotman-Dickenson, *J. Chem. Soc.*, 1602 (1960).

[7] For other alkyl group rearrangements (in acyclic systems) in which an intermolecular path is postulated or at least not excluded, see F. F. Rust and D. O. Collamer, THIS JOURNAL, **76**, 1055 (1954); S. Sato and R. J. Cvetanović, *Can. J. Chem.*, **37**, 953 (1959), and papers by R. J. Cvetanović therein cited. We are indebted to Dr. James Pitts for calling the latter work to our attention and to Dr. C. G. Overberger for several helpful suggestions on the chemistry of azo compounds.

[8] Richfield Oil Fellow, 1956–1957.

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THE REACTIVITY OF METHYLENE FROM PHOTOLYSIS OF DIAZOMETHANE

Sir:

Differences have been reported in the recent literature concerning the reactivity of methylene generated by photolysis of diazomethane. Doering, Buttery, Laughlin and Chaudhuri[1] found that the methylene produced by solution photolysis in alkanes reacted randomly with primary, secondary and tertiary carbon–hydrogen bonds. Frey,[2] on the other hand, reported that gas-phase photolysis gave a methylene which reacted selectively with carbon–hydrogen bonds in the approximate reactivity ratio $k_{\text{tert}}/k_{\text{sec}}/k_{\text{prim}}$ of 1.5/1.2/1.0. We wish to report results confirming and extending the evidence for random reactivity of methylene in alkane solution and to rationalize the difference noted above.

We have carried out the solution photolysis of diazomethane in fourteen C_7, C_8, and C_9 alkanes in the usual manner.[1] The reaction mixtures were analyzed directly by capillary gas chromatography with a squalane-coated column coupled to an argon ionization detector.[3,4] The results obtained with the four trimethylpentanes are given in Table I.

TABLE I

METHYLENE INSERTION PRODUCTS FROM THE TRIMETHYLPENTANES

Parent	Product	Precursor bond Type	Precursor bond Number	Calcd. Dist., %	Obs. Dist., %[a]
2,2,4-Trimethylpentane	2,4,4-Me$_3$C$_6$	1	9	50.0	51
	2,2,3,4-Me$_4$C$_5$	2	2	11.1	10
	2,2,4,4-Me$_4$C$_5$	3	1	5.6	4
	2,2,4-Me$_3$C$_6$	1	6	33.3	35
2,2,3-Trimethylpentane	2,2,3,4-Me$_4$C$_5$	2	2	11.1	9
	2,2,3-Me$_3$C$_6$	1	3[b]	33.3	35
	2,2-Me$_2$-3-EtC$_5$	1	3[b]		
	2,2,3,3-Me$_4$C$_5$	3	1	5.6	4
	3,3,4-Me$_3$C$_6$	1	9	50.0	52
2,3,3-Trimethylpentane	2,3,3-Me$_3$C$_6$	1	3	16.7	18
	2,2,3,3-Me$_4$C$_5$	3	1	5.6	5
	3,3,4-Me$_3$C$_6$	1	6	33.3	34
	2,3,3,4-Me$_4$C$_5$	2	2	11.1	11
	2,3-Me$_2$-3-EtC$_5$[c]	1	6	33.3	32
2,3,4-Trimethylpentane	2,2,3,4-Me$_4$C$_5$	3	2	11.1	10
	2,4-Me$_2$-3-EtC$_5$	1	3	16.7	16
	2,3,4-Me$_3$C$_6$[d]	1	12	66.7	69
	2,3,3,4-Me$_4$C$_5$	3	1	5.6	5

[a] Each product, with two noted exceptions,[c,d] was identified by comparison of its column retention time with that of an authentic sample (American Petroleum Institute Research Project 6B). The variation in isomer detector sensitivity in this molecular weight range is of the order of errors in peak area measurements; sensitivity corrections were not applied. [b] Incomplete resolution. [c] The identity of this compound was assumed. [d] The identity of this product was confirmed through alternate synthesis from 2,4-dimethylhexane by methylene insertion.

The observed product compositions are in good agreement with those expected from random insertion of methylene into carbon–hydrogen bonds. Equally good agreement between observed and calculated product distribution was obtained with ten other C_7-C_9 alkanes as solvents for the diazomethane

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[1] W. von E. Doering, R. G. Buttery, R. G. Laughlin and N. Chaudhuri, THIS JOURNAL, **78**, 3224 (1956).

[2] H. M. Frey, *ibid.*, **80**, 5005 (1958).

[3] S. R. Lipsky, R. A. Landowne and J. E. Lovelock, *Anal. Chem.*, **31**, 852 (1959).

[4] M. C. Simmons, D. B. Richardson, and I. Dvoretzky, paper presented at Third Symposium on Gas Chromatography, Edinburgh, June 8–10, 1960.

photolysis.[5] In addition to extending the number and molecular weight range of the compounds originally reported,[1] these examples include a number of alkanes which contain primary, secondary and tertiary carbon–hydrogen bonds in the same molecule. In summary, the data obtained in the present study provide excellent support for the description of this methylene by Doering *et al.*,[1] as the most indiscriminate reagent yet encountered in organic chemistry.

The difference between methylene reactivity in the gas phase and in solution can be rationalized by consideration of recent spectroscopic evidence. Herzberg[6,7] has obtained spectra of methylene from gas-phase photolysis showing both singlet and triplet states, and demonstrating the singlet state is the shorter lived. Theoretical considerations[7] indicate the excited singlet state is the first formed, the triplet state arising from a later transition.

We suggest that the random reaction of methylene with alkane carbon-hydrogen bonds[8] observed in solution arises from the excited singlet state[9] (paired non-bonding electrons) and, further, that this reaction occurs at a much higher rate than the transition of the singlet to the triplet state (unpaired non-bonding electrons). Thus, there is little or no radical component to the reaction in solution. In the gas phase, we suggest the frequency of collision is sufficiently less that the singlet–triplet transition occurs at a rate of the same order of magnitude as the random singlet insertion. Methylene in the triplet state would be expected to react selectively with carbon–hydrogen bonds as do other radicals. Therefore, methylene reacts with carbon–hydrogen bonds by two paths: a random singlet insertion and a selective triplet abstraction. The abstraction leads to methyl and alkyl radicals which can combine to give apparently selective insertion, attack diazomethane, or react in other ways typical of free radicals. The extent of insertion selectivity and of secondary product formation observed in a particular reaction will thus depend on the ratio of singlet–triplet transition to singlet carbon–hydrogen insertion.

Support for this interpretation is provided by experimental observations. (1) EFFECT OF OXYGEN.—In the photolysis of gaseous diazomethane-alkane mixtures, Frey[10] found secondary products indicating a radical component of the reaction. The presence of oxygen during photolysis prevented formation of the secondary products and altered the ratio of primary products toward that expected for random reaction. Oxygen would be expected to react selectively with methylene in the triplet state and with radicals arising from the reaction of triplet methylene with the alkane. Secondary products, therefore, should be eliminated, and the over-all reaction should exhibit more singlet or random character.

(2) EFFECT OF PRESSURE.—The above rationalization indicates that the gas-phase reaction should be pressure dependent, the triplet character of the reaction increasing as the pressure is lowered. This conclusion is in accord with results from photolysis of diazomethane—*trans*-butene-2-mixtures.[2,11] "Very similar" product compositions were reported for the liquid phase (−70°) and the gas phase (25°) at pressures greater than 1200 mm. As the pressure was lowered the yield of *trans*-1,2-dimethylcyclopropane decreased and the formation of *cis*-pentene-2, 2-methylbutene-1 and *cis*-1,2-dimethylcyclopropane was observed. These C_5 products formed at lower pressure are those expected from the reaction of methylene in the triplet state with the olefin.[12] The observed formation of ethane and other secondary products with decreasing pressure also points to the growing importance of the triplet reaction as the pressure is lowered.

(3) EFFECT OF INERT GAS.—The addition of inert gas should, according to the above interpretation, emphasize the triplet character of the reaction by increasing the ratio of singlet–triplet transition to singlet–hydrocarbon reaction. This requirement is substantiated by the formation of *cis*-1,2-dimethylcyclopropane in the photolysis of diazomethane-*trans*-butene-2 mixtures with argon or nitrogen.[11]

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(5) These data will appear in a forthcoming publication.

(6) G. Herzberg and J. Shoosmith, *Nature*, **183**, 1801 (1959).

(7) G. Herzberg, paper presented at Welch Foundation Conference on Molecular Structure, Houston, Texas, November 16–18, 1959.

(8) Doering and Prinzbach [W. von E. Doering and H. Prinzbach, *Tetrahedron*, **6**, 24 (1959)] have shown this reaction occurs by direct insertion.

(9) Skell and Woodworth [P. S. Skell and R. C. Woodworth, THIS JOURNAL, **78**, 4496, 6247 (1956)] have assigned methylene a singlet structure because of its stereospecific reaction with olefins.

(10) H. M. Frey, *Proc. Chem. Soc.*, 318 (1959).

(11) H. M. Frey, *Proc. Roy. Soc.* (*London*), **A251**, 575 (1959).

(12) R. M. Etter, H. S. Skovronek and P. S. Skell. THIS JOURNAL **81**, 1008 (1959).

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COSYNTHETIC FACTOR I, A FACTOR INVOLVED IN HYDROGEN-TRANSFER IN *STREPTOMYCES AUREOFACIENS*

Sir:

In two previous communications the accumulation of 7-chloro-5a(11a)-dehydrotetracycline[1] by *Streptomyces aureofaciens* mutant S-1308 and the biological reduction[2] of this compound to 7-chlorotetracycline were described. More recently[3] Cosynthetic Factor I, a stable, water-soluble substance elaborated by many strains of *S. aureofaciens*, was shown to be effective in enabling S-1308 to produce 7-chlorotetracycline instead of the 5a(11a)-dehydro analog. Utilizing this response (Fig. 1) as an analytical method, we have now been able to isolate Cosynthetic Factor I. The isolation and preliminary characterization of this substance are given.

Fermented mash of *S. aureofaciens* mutant W-5 was selected as the source for Cosynthetic Factor I by reason of its relatively high content of the desired product and the fact that it contained no interfering pigments. W-5 was cultivated in the

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(1) J. R. D. McCORMICK, P. A. Miller, J. A. Growich, N. O. Sjolander and A. P. Doerschuk, THIS JOURNAL, **80**, 5572 (1958).

(2) J. R. D. McCormick, N. O. Sjolander, P. A. Miller, U. Hirsch, N. H. Arnold and A. P. Doerschuk, *ibid.*, **80**, 6460 (1958).

(3) J. R. D. McCormick, U. Hirsch, N. O. Sjolander and A. P. Doerschuk, *ibid.*, **82**, 5006 (1960).