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MECHANISM OF REACTION OF METHYLENE WITH THE CARBON-HYDROGEN BOND

EVIDENCE FOR DIRECT INSERTION

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Abstract—The photolysis of diazomethane in 2-methylpropene-1-^{14}C leads predominantly to 2-methylbut-1-ene-1-^{14}C whether the reaction be run in the liquid or gas-phase. This result is the first unequivocal evidence in support of mechanisms involving direct insertion of methylene into the carbon–hydrogen bond.

In the gas-phase, recovered 2-methylpropene shows a small amount of mixing of radioactivity while the 2-methylbutene-1 shows as much as 8 per cent. The intervention of free radicals as a side-reaction is indicated.

MEERWEIN and his coworkers[1,2] discovered that the photochemical decomposition of diazomethane in organic solvents can lead to the formation of methyl groups. Superficially the reaction involves the insertion of methylene into the carbon–hydrogen bond. However, the presence of oxygen in their examples makes it conceivable[3] that an intermediate "ylid" may have been involved.[†] Examples of the reaction of the saturated carbon–hydrogen bond of aliphatic hydrocarbons with diazomethane[4] and methyl diazoacetate,[5] brought to light later, brook no question of the formation of "ylids" or other prior complexes.[‡]

The mechanism of the reaction is most simply conceived as a direct insertion and has been represented accordingly (Chart 1, A).[5,8,9] The possibility of free radical mechanisms is also reasonable. A chain mechanism (Chart 1, B–B″) receives its clearest support in the fine work of Urry and Eiszner[10] and is given general formulation in Chart 1. A non-chain scheme (Chart 1, B–B′) has been constructed by Frey and

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[†] In the reaction of tetrahydrofuran with diazomethane, the absence of tetrahydropyran (more than 0·05% could have been detected) leaves one with no compelling reason to invoke an "ylid" (W. von E. Doering, L. H. Knox and M. Jones, *J. Org. Chem.* In press).

[‡] The question of whether methylene reacts directly with methane to give ethane is still unresolved.[6,7,8]

[1] H. Meerwein, H. Rathjen and H. Werner, *Ber.* **75**, 1610 (1942).

[2] H. Meerwein, H. Disselnkoetter, F. Rappen, H. v. Rintelen and H. van de Vloed, *Liebigs Ann.* **604**, 151 (1957).

[3] R. Huisgen, *Angew. Chem.* **67**, 439 (1955).

[4] W. von E. Doering, R. G. Buttery, R. G. Laughlin and N. Chaudhuri, *J. Amer. Chem. Soc.* **78**, 3224 (1956).

[5] W. von E. Doering and L. H. Knox, *J. Amer. Chem. Soc.* **78**, 4947 (1956).

[6] F. Grard and M. Vanpee, *Bull. Soc. Chim. Belg.* **60**, 208 (1951).

[7] C. Rosenblum, *J. Amer. Chem. Soc.* **63**, 3322 (1941).

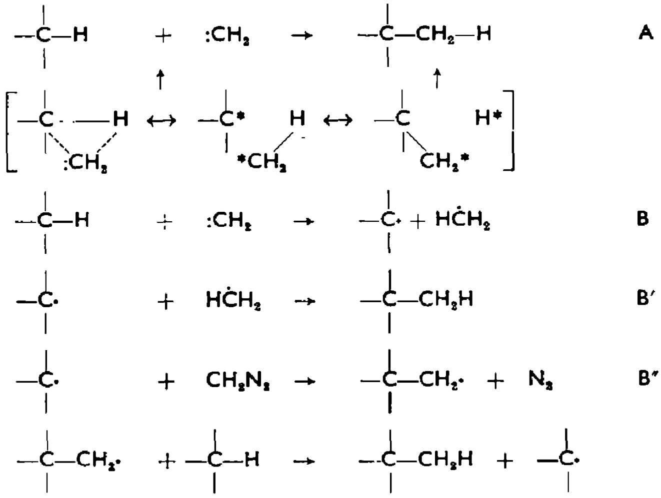
[8] J. Chanmugam and M. Burton, *J. Amer. Chem. Soc.* **78**, 509 (1956).

[9] J. H. Knox and A. F. Trotman-Dickenson, *Chem. & Ind.* 268 (1957). These workers invoke a similar mechanism for the reaction of CH_2 with H_2.

[10] W. H. Urry and J. R. Eiszner, *J. Amer. Chem. Soc.* **73**, 2977 (1951); **74**, 5822 (1952).

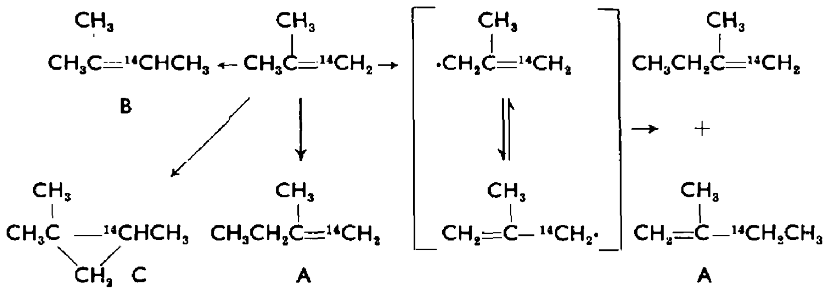
Kistiakowsky[11] as an explanation for the production of ethane in the reaction of methylene with propane and butane.

CHART 1



Distinction between the radical mechanisms and direct insertion—the first involving intermediate fragmentation; the other not—is a step in understanding the mechanism of the reactions of methylene. The distinction can be made with a molecule capable of giving a radical, which, if free, could then react further at a site other than the one involved in its initial formation. Such a molecule cannot consist only of saturated, alkyl carbon–hydrogen bonds and, most simply, is an olefin, whereupon, to be precise, the investigation becomes a study of the allyl carbon–hydrogen bond. 2-Methylpropene-1-^{14}C was the specific molecule chosen. Here, the product of interest, 2-methylbutene-1 (Chart 2, A), is expected to show radioactivity in the 1-position alone, if the mechanism be concerted, and activity in the 3-position as well, if a step-wise process with free intermediates or their equivalent be involved.

CHART 2



2-Methylpropene-1-^{14}C seemed advantageous from several points of view. Its vapor-pressure makes it suitable for study in both the liquid and gas-phase, a consideration of importance in view of the significant differences uncovered by Frey and Kistiakowsky[11] and by Knox and Trotman-Dickenson.[9] The products—2-methylbutene-1 (A), 2-methylbutene-2 (B) and 1:1-dimethyl*cyclo*propane (C)—are

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[11] H. M. Frey and G. B. Kistiakowsky, *J. Amer. Chem. Soc.* **79**, 6373 (1957).

of sufficiently high volatility to be separable by gas–liquid-partition-chromatography (g.l.p.c.). The three main reaction products can be separated on a 4 meter column of dioctyl phthalate from each other and from the remaining starting material, from all the decomposition products of diazomethane and from small amounts of C_6-compounds formed as by-products. The products are identified by comparing their infrared spectra with those of authentic samples. Further purification of the 2-methylbutene-1 is effected on a silicone column and affords material having an infrared spectrum completely indistinguishable from that of the authentic material. The ratio of 2-methylbutene-2 to 2-methylbutene-1 to 1:1-dimethyl*cyclo*propane in the liquid phase reaction was roughly 1 : 2·5 : 8 whereas in the gas-phase the ratio of the latter two products was 1 : 3·5.

Labeled 2-methylpropene-1-^{14}C has been synthesized by Reeve and Chambers[12] from 2-methylpropan-1-ol-1-^{14}C by treatment with phosphorus and iodine followed by elimination with potassium hydroxide. Since there was no indication of the accuracy of their analyses and some reason to expect the formation of *t*-butyl iodide in the transformation of the carbinol, we did not rely on this method. Labeled 2-methylpropene has also been reported by Andrianova and Andreev[13] as the product of dehydrating 2-methylpropan-1-ol-1-^{14}C over alumina at 415°. In view of the experiences of Fries and Calvin[14] in dehydrating propan-1-ol-1-^{14}C under similar conditions and the lack of explicit indication of the distribution of radioactivity in the resulting 2-methylpropene, this method was also rejected.

In this work the general olefin synthesis of Wittig[15] was applied to acetone. Labeled triphenylphosphinemethylene was prepared from radioactive methyl iodide and triphenylphosphine followed by treatment of the phosphonium iodide with phenyl lithium. (The use of butyl lithium led to difficultly separable butane as a by-product.) The reaction of acetone and the "ylid" proceeded smoothly and led to 2-methylpropene-1-^{14}C which could be isolated in a pure state by g.l.p.c. By a method to be described in detail below, it was found to have all radioactivity at C_1 and no significant activity in the remainder (Table 1). This method is quite convenient for the preparation of small quantities of material, makes efficient use of radioactive methyl iodide (60–70 per cent of theory) and is therefore suitable for the preparation of material of high specific activity.

In this synthesis one has incontrovertible support for the hypothesis that the elimination in the final stage of the Wittig reaction proceeds without rearrangement. Although the gross structural outcome of the Wittig reaction has been abundantly clear in the numerous examples in the literature, it seems helpful to have rearrangement eliminated even as a minor side-reaction.

Radioactivity was determined by the new procedure of Wolfgang and Rowland.[16] The elegance, convenience and reliability of this method for organic chemical problems involving volatile materials cannot be overemphasized. By coupling a g.l.p.c. system in series with an integrating proportional flow counter Wolfgang and Rowland combined the powerful separating qualities of gas–liquid partition–chromatography

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[12] W. Reeve and D. H. Chambers, *J. Amer. Chem. Soc.* **73**, 4499 (1951).

[13] T. I. Andrianova and E. A. Andreev, *Dokl. Akad. Nauk SSSR* **87**, 45 (1952); *Chem. Abstr.* **48**, 106c (1954); *Chem. Zentr.* 7515 (1953).

[14] B. A. Fries and M. Calvin, *J. Amer. Chem. Soc.* **70**, 2235 (1948).

[15] G. Wittig and U. Schoellkopf, *Ber.* **87**, 1318 (1954).

[16] R. Wolfgang and F. S. Rowland, *Analyt. Chem.* **30**, 903 (1958).

TABLE 1. DISTRIBUTION OF RADIOACTIVITY IN 2-METHYLPROPENE (C_4) AND 2-METHYLBUTENE-1 (C_5)

	αC_1OH[a,b]	αC_3OH	αC_4OH
Starting C_4	40,050	0[c]	
Rec. C_4 liquid dil	5,280	37	
Rec. C_4 liquid conc	45,530	906	
C_5 liquid conc	20,060		170
Rec. C_4 gas (400 mm)	13,525	420	
C_5 gas (400 mm)	10,435		892

[a] Activities, α, are in disintegrations per second per millimole calculated from the formula: $\alpha = N(F_{He} + F_{Me})/60\, V_m$. N is the total number of counts recorded from a given sample peak flowing through the counter; F_{He} and F_{Me} are flow rates in ml per minute of helium and methane, V is the volume of the counter and m is the quantity of substance in millimoles.

[b] Subscripts C_1OH, C_3OH and C_4OH denote methanol, propanol-2 and butanol-2 obtained by the ozonolysis-reduction of the olefin.

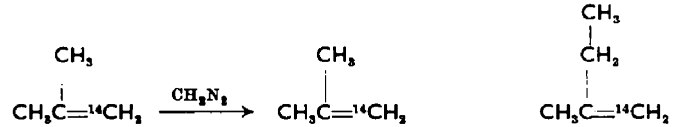
[c] The background is in the order of magnitude of 40 to 60 counts per minute. A minimum of 20 cpm can be observed with assurance (corresponding to 1·4 dps for a flow rate of 27 ml/min of helium and methane respectively).

with rapid, reliable counting. The method avoids tedious preliminary separation and the preparation of solid derivatives and is thus extraordinarily well suited to work with small quantities of material. The method has permitted all phases of this problem to be carried out on the small scale necessary to profit conveniently from the advantage of the powerful g.l.p.c. method.

Distribution of radioactivity in starting material and product was determined by ozonizing the olefin in pentane, reducing the ozonide with lithium aluminum hydride and passing the resulting solution of alcohols into the Wolfgang train without any prior separation.

The irradiation in the liquid phase was carried out in the usual way with sunlamps as the source of ultraviolet light but at considerably higher concentrations than those required for optimum yield of products. The gas-phase irradiations were carried out at a total pressure of 400 mm. The results of irradiation in the liquid phase and in the gas phase are shown in Chart 3 and in somewhat greater detail in Table 1. In both cases it is clear that the distribution of radioactivity in the 2-methylbutene-1 is far from the 0·50–0·50 values predicted on the basis of a free radical intermediate. These results constitute the first demonstration that methylene can react with a carbon–hydrogen bond by direct insertion (Chart 2, A). The results in the gas-phase are the more striking because in that phase there is no solvent cage to force the return of incipient free radicals (Chart 2, B-B′).

CHART 3



$$CH_3\overset{CH_3}{\overset{|}{C}}{=}{}^{14}CH_2 \xrightarrow{CH_2N_2} CH_3\overset{CH_3}{\overset{|}{C}}{=}{}^{14}CH_2 \qquad CH_3\overset{CH_3}{\overset{|}{\overset{CH_2}{\overset{|}{C}}}}{=}{}^{14}CH_2$$

Liquid phase	0·00	1·00	0·02	0·98	0·01	0·99
Gas phase	0·00	1·00	0·03	0·97	0·08	0·92

The gas-phase reaction is, however, not clean cut. Redistribution in the 2-methylbutene-1 occurs to the extent of 8 per cent. Its seems unlikely for a number of reasons that this mixing occurs by the decomposition of initially formed "hot" 1:1-dimethyl*cyclo*propane. 3-Methyl-butene-1 would be expected among the products of this decomposition, but, in fact, cannot be detected (less than 0·05 per cent). The total pressure (400 mm) of the reactions is considerably higher than the range in which decomposition of "hot" 1:2-dimethyl*cyclo*propanes occurs to an appreciable extent.* It is much more reasonable to ascribe the mixing to the intervention of free radicals. It is significant that mixing occurs to an appreciable extent in the 2-methylpropene-1 recovered from the gas-phase reaction. A similar rearrangement is to be seen in the observation that one of the minor products of the reaction of *cis*-butene with diazomethane is butene-1.[17] These reactions are almost certainly brought about by free radicals. A chain process (Chart 2, B-B″) is a simple way of accommodating the observations.

EXPERIMENTAL

Photochemical decomposition of diazomethane and 2-methylpropene

In all experiments diazomethane is prepared in the following way: 10 g of nitrosomethylurea[18] is added in small amounts with vigorous stirring during 15 min to 30 ml of 50% potassium hydroxide and 75 ml of distilled decalin at 0°. The decalin-diazomethane layer is decanted and dried over potassium hydroxide. Such a solution can be kept at −70° without decomposition. Out of such a solution the diazomethane is transferred into the reaction vessels either by means of a stream of nitrogen or a vacuum system. In order to obtain products of sufficiently high specific activity the standard conditions for the reaction between diazomethane and hydrocarbons involving very dilute solutions had to be replaced by much higher concentrations of diazomethane. An illustrative procedure is given below.

Diazomethane from 10 g of nitrosomethylurea is blown by a slow stream of nitrogen into 500 mg of condensed 2-methylpropene. The reaction vessel is designed so that the Dry Ice condenser extends just to the surface of the liquid in order to minimize reaction in the gas-phase. The reaction vessel is cooled by flowing water and irradiated with 2 Westinghouse sunlamps (Type R S). After 6 hr all the diazomethane from the decalin solution has been transferred and irradiation is continued for one additional hour. The slightly yellow reaction products are separated on a 4 m column of dioctylphthalate on firebrick at 20° ("A"-column). Besides ca. 85% of recovered 2-methylpropene, decomposition products of diazomethane and small amounts of higher boiling C_6-products, three main reaction products are isolated: 1:1-dimethyl*cyclo*propane, 2-methylbutene-1 and 2-methylbutene-2. The ratio of the yields of these products roughly estimated from their peak heights is 8 : 2·5 : 1. They are finally purified on a 10 ft silicone column ("C"-column at 20° and identified by comparison of their g.l.p.c. retention times and of their infrared spectra with those of authentic samples (1:1-dimethyl*cyclo*propane was synthesized by the procedure given by Shortridge *et al.*[19]).

2-*Methylpropene*-1-^{14}C. Methyliodide-^{14}C (180 mg of methyliodide-^{14}C of 50 microcuries activity, obtained from New England Nuclear Corp., Boston, Mass., and 2·16 g of inactive methyliodide, a total of 16·5 mmole) and triphenylphosphine, (4·74 g, 18·1 mmoles) are mixed in 25 ml of anhydrous benzene at 0° in a 100 ml pressure-flask. After 2 days' standing at room temp., the salt is washed several times with anhydrous benzene: 6·55 g (theoret. yield); m.p. 189–191°.[20]

Triphenylmethyl-^{14}C-phosphonium iodide (6·55 g, 16·5 mmoles) is dissolved in 25 ml of anhydrous ether (freshly distilled from phenylmagnesium bromide) in a 150 ml Schlenk-tube. Under a nitrogen atmosphere 15 mmole of phenyllithium—made from diphenylmercury[21] in 40 ml of anhydrous ether—is added. Stirring the mixture magnetically dissolves the salt within a few minutes. To this orange solution 1·04 g (18·0 mmoles) of anhydrous acetone in 10 ml of ether is added at −30°. The

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* Very little change in product composition with pressure is observed in the reaction of *cis*- and *trans*-butene with diazomethane above a total pressure of 60 mm.[17]

[17] W. von E. Doering and D. MacDuffie, unpublished results.

[18] *Organic Syntheses* Coll. Vol. II, p. 165. Wiley, New York.

[19] R. W. Shortridge, R. A. Craig, K. W. Greenlee, J. M. Derfer and C. E. Boord, *J. Amer. Chem. Soc.* **70**, 946 (1948).

[20] A. Michaelis and L. Gleichmann, *Ber.* 15, 810, (1882).

[21] W. Schlenk and J. Holtz, *Ber.* **50**, 262 (1917).

tube is sealed and the reaction mixture is homogenized by intensive shaking for 1 hr at room temp. A white product precipitates. The mixture is then heated for 20 hr at 70°; the tube is cooled in liquid nitrogen for 2 hr, opened and the 2-methylpropene—together with ca. 30% of ether and small amounts of acetone and benzene—is distilled with the use of a 20 cm "Podbielniak"-column. 2-Methylpropene is separated and purified by g.l.p.c. using a 10 ft "C"-column at 20°. The yield of 2-methylpropene varies between 60 and 70% on the basis of phenyllithium.

Ozonization of 2-methylpropene-1-^{14}C

2-Methylpropene-1-^{14}C (13·7 mg) is dissolved in 0·25 ml of purified pentane (shaken with sulfuric acid for several days), and cooled to −70°. A very small part of an ozone/oxygen stream, containing ca. 2·2 g of ozone per hr, is diverted through the methylpropene–pentane solution at −70° at a rate of ca. 1 bubble per second. As soon as the potassium iodide solution at the exit turns yellow, the oxidation is stopped, and the excess of ozone is expelled with a stream of dry nitrogen. Lithium aluminum hydride (20 mg) is added and the mixture is slowly warmed to 0°, 0·25 ml of anhydrous ether having been added in order to increase the solubility of the lithium aluminum hydride. The reaction starts vigorously and has to be cooled from time to time. It is finally kept at 0° for several hours. The mixture then is again cooled to −70° and decomposed by adding 20 mg of water. The decomposition is completed by warming up very slowly and shaking at 0° for 1 hr. The reaction vessel is attached directly to the g.l.p.c.-column and the crude mixture of ether, pentane, methanol, propanol-2 and water is introduced into the 5 ft "F"-column (tetraethyleneglycol–dimethylether on firebrick; at 50°) as quickly as possible by surrounding the flask by a bath at 220°. By fractionating two or three times the alcohols are obtained quite pure and give symmetrically shaped peaks. Radioactivity and mass are then assayed simultaneously. If the mixture is introduced into the column too slowly the peaks are very broad and prevent the radioactivity peaks from being cleanly separated and returning to the background level between peaks. The number of disintegrations N is integrated automatically and recorded on the activity chart. N is then related to the total absolute activity A by the equation $N = A(V/F_{\mathrm{He}} + F_{\mathrm{Me}})$ where V is the volume of the counter and F_{He} and F_{Me} are the flow rates (ml/min) of the carrier gases helium and methane, respectively. A counter of 12·87 ml volume was used in all our experiments. Since the precision of these determinations increases the larger N is and the larger R becomes relative to R_B (R being the average counting rate in counts/min and R_B being the background counting rate), low flow rates varying from 20–35 cc/min for the different runs were employed and the column was operated at the highest temp. consistent with satisfactory separation. It is evident that the precision of the determination of specific activities of the same material in different runs depends almost completely on the precision in achieving the same flow rates and the same operating temp. Since we have not been interested in absolute activity, we did not take special care to keep these variables constant in all experiments. As long, however, as the temp. and flow rates are kept constant within each single run, the ratio of the specific activities of the components will be constant for identical runs. In order to determine the specific activities, the corresponding peak areas on the mass chart are measured and translated into milligrams of substance on the basis of previous calibration experiments.

The sample of 2-methylpropene-1-^{14}C afforded: methanol, 5·8 mg, 435, 600 dpm: α: 40,050 dps/mmole. The activity of the propanol-2 was within the background.

Reaction between diazomethane and 2-methylpropene-1-^{14}C in the liquid phase

(a) *In dilute solution.* 2-Methylpropene-1-^{14}C (50 mg) is diluted with 450 mg of inactive material (Phillips, pure grade, 99%) and allowed to react in the described way with diazomethane from 10 g of nitrosomethylurea. 2-Methylpropene-1 (29·6 mg) recovered from this reaction, is purified on a 4 m "A"-column at 20° and a 10 ft "E"-column (dimethylformamide on firebrick) at 0° and degraded. Methanol and propanol-2 are fractionated three times on the 5 ft "F"-column at 50° and analyzed as described above. Methanol, 8·1 mg, 78, 120 dpm: α: 5280 dps/mmole; propanol-2, 50 mg (from two identical runs), 1846 dpm: α: 37 dps/mmole. (With this highly diluted starting material, any activity distribution in the 2-methylbutene-1 could not be detected. Therefore, additional experiments in concentrated solution were carried out).

(b) *Concentrated solution.* 2-Methylpropene-1-^{14}C (42·3 mg) is condensed with 10 mg of diazomethane and irradiated for 2 hr in a closed system. Diazomethane, 20 mg, is added in 2 portions and the irradiation continued for 2 hr in each case. Recovered 2-methylpropene (4·7 mg), purified on the 10 ft "E"-column at 0° is ozonized and analyzed in the usual way: methanol, 0·4 mg, 34,160 dpm: α: 45,530 dps/mmole; propanol-2, 0·6 mg, 776 dpm: α: 906 dps/mmole.

2-Methylbutene-1, 2·7 mg, isolated from this run and purified on the 10 ft "E"-column at 0° is diluted with 2·2 mg of inactive material (Mathieson, 99% pure), ozonized and worked in the described manner: methanol and butanol-2, fractionated twice on the 5 ft "F"-column at 80° show the following activity: methanol, 1·6 mg, 64,180 dpm: α: 20,060 dps/mmole; butanol-2, 3·7 mg, 810 dpm: α: 170 dps/mmole.

Reaction between diazomethane and 2-methylpropene-1-^{14}C in the gas-phase

2-Methylpropene-1-^{14}C, 20·2 mg and 47·0 mg of inactive material is condensed with 50 mg of diazomethane in a 450 ml flask and irradiated for 2 hr under a partial pressure of purified nitrogen of 350 mm, the reaction flask being cooled with running water. Diazomethane, 50 mg, is added again and the irradiation continued for 2 hr more. The reaction products are separated and purified on the 10 ft "C"-column at 20° and the 10 ft "E"-column at 0°. (Besides the earlier described reaction products of the liquid-phase reaction, in this case, a small amount of radioactive 2-methylpropane was isolated and identified). 2-Methylpropene (20 mg) recovered and purified is degraded. The alcohols are fractionated three times on the 5 ft "F"-column at 50°: methanol, 3·9 mg, 99,930 *dpm*: α: 13,525 *dps*/mmole; propanol-2, 11 mg, 4627 dpm: α: 420 *dps*/mmole.

2-Methylbutene-1 (10·29 mg), isolated from two such runs, and purified on the 10 ft "E"-column at 0° is degraded and the alcohols fractionated at the 5 ft "F"-column at 80°: methanol, 3·2 mg, 62,610 *dpm*: α: 10,435 *dps*/mmole; butanol-2, 7·3 mg, 5320 *dpm*: α: 893 *dps*/mmole.