Isomerization of Saturated Hydrocarbons. XIII.[1] γ-Ray Irradiation as a Means of Initiating the Isomerization of Methylcyclopentane

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It has been reported previously[3] that methylcyclopentane does not isomerize to cyclohexane when shaken in a sealed tube for 19 hours at 25° in the presence of aluminum bromide and hydrogen bromide. However, the addition of trace amounts of olefins such as cyclohexene or an alkyl halide such as *sec*-butyl bromide[1] was found to initiate the isomerization reaction. It was suggested that isomerization is a chain reaction and that the function of the olefin or alkyl halide is to form a carbonium ion which initiates the isomerization.

It was reported[4] that the isomerization of methylcyclopentane can also proceed without the addition of a chain initiator, such as olefins or alkyl halides, if the reaction is conducted in the presence of ultraviolet light. It was postulated that under these conditions hydrogen bromide was dissociated partially into hydrogen and bromine atoms, and that a bromine atom then reacted with methylcyclopentane to give bromomethylcyclopentane, which could serve as a chain initiator.

Since irradiation of such a mixture by relatively high energy γ-rays would be expected to give rise to a variety of radical and ionic entities,[5] it seemed that one should be able to initiate the isomerization of methylcyclopentane in this fashion.

Results of the irradiation experiments are summarized in Tables I and II. Experiments 1 and 2 were preliminary runs and no gas analyses were made. In all experiments, small amounts of a viscous polymeric material were formed. In the experiments where aluminum bromide was used, small amounts of a reddish solid also were formed, probably as a result of conjunct polymerization.[6] The same over-all mechanism as used for the ultraviolet irradiation[4] is applicable to the results obtained in the present study. However, the initial step is undoubtedly much more complex when γ-rays of high energy are used. That is, the methylcyclopentane as well as the hydrogen bromide may undergo dissociation to give the radicals necessary to initiate the reaction. The case is further complicated by the fact that products resulting purely from the radiation-induced decomposition of the hydrocarbon will appear. The irradiation in the absence of catalysts (expt. 3) shows that in addition to hydrogen, appreciable amounts of methane, ethane and ethylene are produced.

It is of interest to note that isomerization occurred to the extent of 11% when just methylcyclopentane and aluminum bromide were irradiated (expt. 4), since no isomerization was observed in a similar experiment when the reactants were exposed to ultraviolet light.[4] It is probable that in the γ-ray irradiation hydrogen bromide is formed in the system by the reaction of hydrogen atoms with either aluminum bromide or bromine atoms. This reaction then would account for the lower yield of H_2 as compared with experiment 3. The bromine atoms for this reaction would arise from the radiation-induced dissociation of aluminum bromide, and the bromine atoms, in addition to reacting with hydrogen atoms, probably react with methylcyclopentane or its products of decomposition, such as ethylene, to give the corresponding bromide, which could initiate the isomerization.

Table I

Summary of Irradiation Experiments

Expt.	Moles Methylcyclopentane			Isomerization, %
		$AlBr_3$	HBr	
1[a]	0.0639	0.00128	.....	0
2[a]	.0640	.00128	0.00065	2
3[bc]	.0580	.....	.....	0
4[b]	.0472	.00131	.....	11
5[bd]	.0400	.00130	.00065	54
6[b]	.0431	.....	.00065	0

[a] Received 2 hours irradiation in a Co^{60} source in a position where an aqueous solution would absorb 2.9×10^{20} ev./l./min. An estimate based on the composition and density of the hydrocarbon as compared to water indicates an energy absorption of 2.2×10^{20} ev./l./min. [b] Received 16 hours irradiation in a Co^{60} source in a position where an aqueous solution would absorb 2.6×10^{20} ev./l./min. The energy absorbed by the hydrocarbon is estimated to be 2.0×10^{20} ev./l./min. [c] The yield of total gas, based on the estimated energy absorption, is 5.1 molecules/100 ev. This is consistent with values of 4.0 for cyclohexane, and 4.5 for methylcyclohexane, given by M. Burton, *J. Phys. Colloid Chem.*, **52**, 786(1948). [d] A similar experiment made without irradiation did not cause the formation of cyclohexane.

Table II

Composition of Gaseous Products

Expt.[a]	H_2	CH_4	C_2H_4	C_2H_6
3	1670	46	108	5
4	570	21	3	18
5	1912	36	2	11
6	2305	50	3	15

[a] The results are expressed in micromoles of gases produced per mole of methylcyclopentane irradiated.

Examination of the gas yields shows a marked decrease in the amount of ethylene found in the runs where aluminum bromide, hydrogen bromide or the combination was irradiated with methylcyclopentane. In the experiments where aluminum bromide was present the ethylene probably disappeared through conjunct polymerization, which is in keeping with the reddish solid formed in these runs. A portion of the ethylene produced may have served as a chain initiator in the experiments where isomerization occurred. In the hydrogen bromide run, the ethylene formed may have reacted to give ethyl bromide. Since only trace amounts of ethylene were formed in these experiments, the accuracy of these values is not great and it is questionable whether there is any significance to the difference in the ethylene yields obtained in experiments 4, 5 and 6.

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(1) For paper XII of this series see H. Pines, E. Aristoff and V. N. Ipatieff, This Journal, **75**, 4775 (1953).

(2) Universal Oil Co. Predoctoral Fellow 1951–1954.

(3) H. Pines, B. M. Abraham and V. N. Ipatieff, This Journal, **70**, 1742 (1948).

(4) H. Pines, E. Aristoff and V. N. Ipatieff, *ibid.*, **72**, 4055 (1950).

(5) For a general discussion of this topic see R. R. Williams, Jr., "Principles of Nuclear Chemistry," D. Van Nostrand Co., Inc., New York, N. Y., 1950, pp. 233–241.

(6) L. Schmerling, *Ind. Eng. Chem.*, **45**, 1447 (1953).

Experimental

Isomerization Experiments.—All operations involving addition of reactants to the reaction tube or removal of products from the reaction tube were carried out using a high vacuum technique.[7] Particular care was taken to remove all air from the hydrocarbon by repeated fractionation before distilling it into the reaction tube.

After all reactants had been introduced, the reaction tube was sealed off from the vacuum line and stored in a Dry Ice–acetone-bath. With the exception of the actual irradiation period, all reaction tubes were kept in Dry Ice–acetone-baths until the products were removed. This precaution was taken to prevent the possibility of some reaction occurring as might be the case if the samples were allowed to stand for several days at room temperature. The irradiations were carried out in a Co^{60} source at the Argonne National Laboratories.[8]

After irradiations, the reaction tube again was attached to the vacuum line and the break-off ruptured. All gases non-condensable at −78° were then removed by means of a Toepler pump and collected over mercury in a small thimble. A bead of potassium hydroxide on a platinum wire was introduced into the sample to remove any hydrogen bromide present. The thimble then was transferred to a Blacet–Leighton apparatus where the volume of the gas was measured. An aliquot was then measured out for analysis in the mass spectrometer.[9]

The liquid contents of the reaction tube were distilled out, washed with 10% potassium carbonate, followed by water, then dried over calcium chloride. The composition of the reaction product was determined by means of infrared analysis. A Beckman IR-2T spectrophotometer was used for the preliminary runs, while a Baird model AB2 spectrophotometer was used for the rest of the analyses. Calculations were based on the data observed at 7.98, 8.82, 8.62 and 10.30 μ.

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[7] H. Pines and R. C. Wackher, THIS JOURNAL, **68**, 595 (1946).

[8] The authors are indebted to Dr. Edwin J. Hart and Miss D. P. Walsh for their coöperation in making the irradiations.

[9] The authors are indebted to Dr. D. F. Mason for performing the mass spectral analyses.

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Preparation of α-*d*- and α-*l*-4-Dimethylamino-1,2-diphenyl-3-methyl-2-propionyloxybutane

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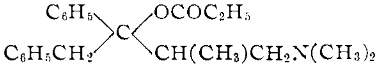
A number of esters of 4-dialkylamino-1,2-diphenyl-2-butanols have been reported to possess a high order of analgesic activity in animals.[1] One of these esters, α-4-dimethylamino-1,2-diphenyl-3-methyl-2-propionyloxybutane (I), has been found to be an effective analgesic in humans.[2]



$$(C_6H_5)(C_6H_5CH_2)C(OCOC_2H_5)CH(CH_3)CH_2N(CH_3)_2$$

I

Since β-4-dimethylamino-1,2-diphenyl-3-methyl-2-propionyloxybutane was devoid of analgesic action,[1] the optical forms of the α-diastereoisomer were prepared in order to determine which one of the four stereoisomers of I is responsible for the analgesic activity.

α-*dl*-4-Dimethylamino-1,2-diphenyl-3-methyl-2-butanol was resolved by fractional crystallization of the *d*-camphorsulfonic acid salt. The optically active carbinol hydrochlorides were prepared from the *d*-camphorsulfonic acid salts. The optically active carbinol hydrochlorides were acylated using propionic anhydride and either triethylamine or pyridine.

Preliminary pharmacological evaluation, using the rat-tail burn technique, has shown the α-*d*-isomer to give the analgesic response. Subcutaneous doses of 10 mg./kg. of the α-*d*-isomer produced an effect equal to that of 20 mg./kg. of the α-*dl*-compound. The α-*l*-isomer gave no response with subcutaneous doses from 10 to 80 mg./kg.

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Experimental[3]

Resolution of α-*dl*-4-Dimethylamino-1,2-diphenyl-3-methyl-2-butanol.—A solution of 56.7 g. (0.20 mole) of α-*dl*-4-dimethylamino-1,2-diphenyl-3-methyl-2-butanol and 46.5 g. (0.20 mole) of *d*-camphorsulfonic acid in 300 ml. of boiling absolute ethanol was prepared and allowed to stand overnight at 0°. A white crystalline solid was collected, dried *in vacuo* and melted at 171–174°, weight 55.5 g. This product after three recrystallizations from ethanol containing 30% acetone melted at 180–181°, weight 34.3 g. (66.4%), $[\alpha]^{25}_{D}$ +64.2° (*c* 0.9 in chloroform). After an additional recrystallization, the α-*d*-4-dimethylamino-1,2-diphenyl-3-methyl-2-butanol *d*-camphorsulfonate melted at 180–181°, weight 31.0 g., $[\alpha]^{25}_{D}$ +64.6° (*c* 1.0 in chloroform).

Anal. Calcd. for $C_{29}H_{41}NO_5S$: C, 67.54; H, 8.01. Found: C, 67.58; H, 7.81.

The original filtrate was concentrated to one-half its volume and diluted with 200 ml. of hot acetone. Upon cooling, a white crystalline material was obtained melting at 172–173°, weight 29.5 g. This product after three recrystallizations from acetone melted at 174–175°, weight 21.2 g. (42.0%) $[\alpha]^{25}_{D}$ −15.2° (*c* 1.0 in chloroform). After an additional recrystallization from acetone the α-*l*-4-dimethylamino-1,2-diphenyl-3-methyl-2-butanol *d*-camphorsulfonate melted at 174–175°, weight 16.0 g., $[\alpha]^{25}_{D}$ −14.3° (*c* 1.0 in chloroform).

Anal. Calcd. for $C_{29}H_{41}NO_5S$: C, 67.54; H, 8.01. Found: C, 67.79; H, 8.03.

α-*d*-4-Dimethylamino-1,2-diphenyl-3-methyl-2-butanol Hydrochloride.—A solution of 26.5 g. (0.051 mole) of α-*d*-4-dimethylamino-1,2-diphenyl-3-methyl-2-butanol *d*-camphorsulfonate in 100 ml. of water was made alkaline with concentrated ammonium hydroxide. The liberated oil was taken up in ether and dried over anhydrous magnesium sulfate. The ether solution then was saturated with anhydrous hydrogen chloride to yield the α-*d*-4-dimethylamino-1,2-diphenyl-3-methyl-2-butanol hydrochloride, m.p. 246–247°, weight 16.2 g., $[\alpha]^{25}_{D}$ +54.9° (*c* 0.7 in water).

Anal. Calcd. for $C_{19}H_{25}NO\cdot HCl$: C, 71.34; H, 8.19; N, 4.38; Cl, 11.09. Found: C, 71.07; H, 8.35; N, 4.35; Cl, 11.29.

α-l-4-Dimethylamino-1,2-diphenyl-3-methyl-2-butanol Hydrochloride.—A solution of 14.5 g. (0.028 mole) of α-*l*-4-dimethylamino-1,2-diphenyl-3-methyl-2-butanol *d*-camphorsulfonate in 50 ml. of water was made alkaline with concentrated ammonium hydroxide. The liberated oil was converted to the hydrochloride salt using the same procedure as employed with the α-*d*-isomer. The α-*l*-4-dimethylamino-1,2-diphenyl-3-methyl-2-butanol hydrochloride after three recrystallizations from methanol–ethyl acetate melted at 246–247°, weight 7.4 g., $[\alpha]^{25}_{D}$ −54.7° (*c* 0.7 in water).

Anal. Calcd. for $C_{19}H_{25}NO\cdot HCl$: C, 71.34; H, 8.19; N, 4.38, Cl, 11.09. Found: C, 71.06; H, 8.31; N, 4.16; Cl, 11.33.

α-*d*-4-Dimethylamino-1,2-diphenyl-3-methyl-2-propionoxybutane Hydrochloride.—A solution of 5.0 g. (0.017 mole) of α-*d*-4-dimethylamino-1,2-diphenyl-3-methyl-2-butanol hy-

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[1] A. Pohland and H. R. Sullivan, THIS JOURNAL, **75**, 4458 (1953).

[2] C. M. Gruber, *J. Lab. Clin. Med.*, **44**, 805 (1954).

[3] All melting points are uncorrected.