biological studies, as well as *in vivo* metabolism experiments. It would appear that the reproducibility and uniformity of the plates obtained depend upon the organic component of the biological fluids as curves with saline alone are not reproducible to better than 10%.

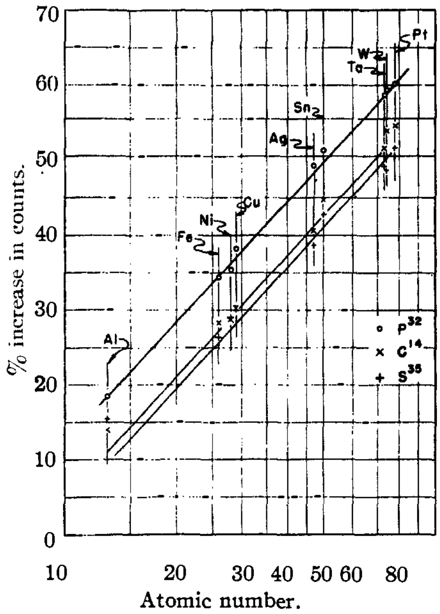

Fig. 3.

Figure 3 shows the relation of composition of the background plate to the total count of a standard sample containing C^{14}, S^{35} or P^{32}. The per cent. increase in count is plotted against the logarithm of the atomic number of the background plate. It can be seen that the amount of back-scattering and, therefore, the total recorded count is a function of the atomic number of the background material. This, too, is of great importance in obtaining reliable determinations of radioactivity. Standard plates and all subsequent plates for analysis should be made on the same background material. If this is not done, the difference in back-scattering should be appreciated and appropriate corrections made, as errors of as much as 50% may be introduced. The sensitivity of the counting system may be increased by using background discs of a higher atomic number.

As plating in this Laboratory was done on copper discs with an oxidized surface, it was felt that the effect of copper oxide on back-scattering should be evaluated. No difference between the polished copper and oxide surfaces could be detected.

The authors wish to express their appreciation to Dr. Frederick Reines for his suggestions in the course of this work.

Summary

1. An evaluation of a method for direct plating and analysis of biological fluids containing radioactive isotopes is presented.

2. Calibration curves for such analysis are discussed. It is essential that in all work of this type calibration curves be made for the fluids to be analyzed and for all different isotopes used.

3. The amount of back-scattering and hence the total count recorded is a function of the atomic number of the background plate, the amount of back-scattering increasing with the atomic number.

P. O. Box 1663, Los Alamos, N. M.

Received July 12, 1948

[Contribution from the Noyes Chemical Laboratory, University of Illinois]

2-Alkyl-1,3-butadienes[1]

By C. S. Marvel and Jack L. R. Williams

In a recent communication[2] from this Laboratory the preparation of three members of the 2-alkyl-1,3-butadiene series was described. Two reactions were used in their preparation. One involved the thermal cracking of the 2-alkyl-3-acetoxy-1-butene and the other, the catalytic dehydration of the 2-alkyl-1-hydroxy-3-butene over alumina or potassium acid sulfate. Further work on these reactions has shown that pure 2-alkyl-1,3-butadienes are obtained by thermal cracking of the acetates. Dehydration of the alcohols gives dienes of doubtful purity due to rearrangement of the double bonds. The extent of this rearrangement appears to vary in different experiments depending on the individual member of the series used in dehydration, the temperature of the reaction, and on other factors of uncertain nature.

It has now been found that dehydration of 2-ethyl-3-hydroxy-1-butene (I) over potassium acid sulfate at 175–200° gives almost entirely 3-methyl-1,3-pentadiene (II) and little, if any, 2-ethyl-1,3-butadiene (III). Merling[3] and Dumoulin[4] have observed similar rearrangements in related compounds. The 3-methyl-1,3-pentadiene obtained by the dehydration reaction has been compared with a sample prepared by the process of Nichol and Sandin.[5] The two samples give the same mal-

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(1) This investigation was carried out under the sponsorship of the Office of Rubber Reserve, Reconstruction Finance Corporation, in connection with the Government Synthetic Rubber Program.

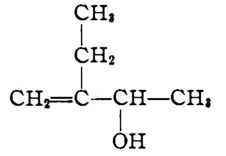
(2) Marvel, Myers and Saunders, This Journal, **70**, 1694 (1948).

(3) Merling, *Ann.*, **264**, 310 (1891).

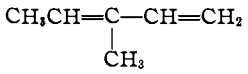
(4) Dumoulin, *Compt. rend.*, **182**, 974 (1926).

(5) Nichol and Sandin, This Journal, **69**, 2256 (1947).

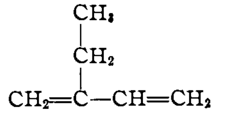
eic anhydride adduct (V) melting at 67–68° which has been reported by Brunner, Hofer and Stein.[6] The diene obtained by catalytic dehydration of 2-ethyl-3-hydroxy-1-butene did not polymerize in the GR-S system.[7]


$CH_2{=}C(CH_2CH_3){-}CH(OH){-}CH_3$

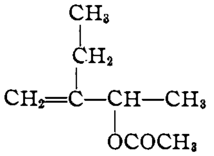
I


$CH_3CH{=}C(CH_3){-}CH{=}CH_2$

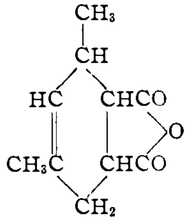
II

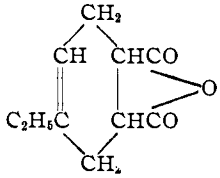

$CH_2{=}C(CH_2CH_3){-}CH{=}CH_2$

III


$CH_2{=}C(CH_2CH_3){-}CH(OCOCH_3){-}CH_3$

IV


V


VI

The diene prepared by pyrolysis of 2-ethyl-3-acetoxy-1-butene (IV) over glass beads at 400–420° also gave a maleic anhydride addition product (VI) which melted at 67–69°. However, this diene had a lower boiling point and a lower refractive index than 3-methyl-1,3-pentadiene and, moreover, it did polymerize readily in the GR-S system. Mixed melting point of this maleic anhydride adduct with that of 3-methyl-1,3-pentadiene showed they were not identical. There are several cases reported in the literature[8,9,10] in which acetate pyrolysis has been shown to give olefins which have the double bonds in the expected positions.

The diene[2] prepared by the dehydration of 2-*n*-amyl-3-hydroxy-1-butene did not polymerize in the GR-S system nor give a crystalline maleic anhydride adduct. Presumably it is not the desired 2-*n*-amyl-1,3-butadiene. Cracking the corresponding acetate has yielded a diene which polymerizes smoothly, gives a crystalline maleic anhydride adduct, and has a different refractive index from that of the diene prepared from the alcohol. The boiling point of this new diene is also lower than that of the earlier sample.

In the earlier work 2-isopropyl-1,3-butadiene was prepared both from the acetoxy and the hydroxy derivatives. The physical properties of these samples were quite similar, but we have now found that only the material prepared from the acetoxy derivative will polymerize smoothly, and hence it is presumably the desired pure butadiene derivative.

In Table I are collected the properties of the dienes prepared from the alcohols and those of the dienes prepared from the acetates.

TABLE I

PROPERTIES OF DIENES FROM ALCOHOLS AND ACETATES

	B. p., °C.	$n^{20}D$	Polymerization in twenty-four hours in GR-S system, %
Diene from dehydration of			
2-Ethyl-3-hydroxy-1-butene	76–78	1.4490	0
2-*n*-Amyl-3-hydroxy-1-butene	146–149	1.4380–1.4412	0
2-Isopropyl-3-hydroxy-1-butene	83–89.5	1.4225–1.4290	0
Diene from pyrolysis of			
2-Ethyl-3-acetoxy-1-butene	66	1.4325	82
2-*n*-Amyl-3-acetoxy-1-butene	140–142	1.4450	67
2-Isopropyl-3-acetoxy-1-butene	85–87	1.4337	66

Confirmatory evidence that those dienes prepared by cracking the acetate are really the desired 2-alkyl-1,3-butadienes has been obtained by comparing the infrared absorption spectra of the three new dienes with those of isoprene[11] and of 3-methyl-1,3-pentadiene (curves I–IV).[12] Details of the polymerization and copolymerization of these new butadiene derivatives will be reported later.

Experimental

Dehydration of 2-Ethyl-3-hydroxybutene-1.—Dehydration of 2-ethyl-3-hydroxybutene-1[2] was accomplished by dropping it through a 20-mm. outside diameter Pyrex tube packed for a distance of 46 cm. with crystalline potassium acid sulfate and heated to the desired temperature by means of an electrically heated jacket. The crude product was collected in a Dry Ice–methanol trap. The organic material was then separated, dried over anhydrous magnesium sulfate, and distilled through a 46-cm. helices-packed column. All temperatures were recorded with the thermometer built in the jacket 1 cm. from the dehydration tube.

Run 1 of 57 g. of 2-ethyl-3-hydroxy-1-butene over the catalyst at 205–215° gave the following on fractional distillation: 1, b. p. 55–70°, 1.0 g.; 2, b. p. 70–74°, $n^{20}D$ 1.4395, 2.0 g.; 3, b. p. 74–77°, $n^{20}D$ 1.4478, 3.5 g.; 4, b. p. 77–79°, $n^{20}D$ 1.4503, 1.5 g.; 5, b. p. 113–114°, $n^{20}D$ 1.4005, 10 g. The last fraction is undoubtedly methyl *s*-butyl ketone.[2]

Run 2 at 190–200°, 167 g. of the same alcohol gave the following on fractional distillation: 1, b. p. 69–71°, $n^{20}D$ 1.4352, 3 g.; 2, b. p. 71–74°, $n^{20}D$ 1.4422, 10 g.; 3, b. p. 74–76°, $n^{20}D$ 1.4475; 4, b. p. 76–77°, $n^{20}D$ 1.4500; 5, b. p. 77–78°, $n^{20}D$ 1.4508; 3, 4, and 5 combined 15 g.; 6, b. p. 78–90°°, $n^{20}D$ 1.4100, 2 g.; 7, b. p. 113°, $n^{20}D$ 1.4006, 20 g.

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[6] Brunner, Hofer and Stein, *Monatsh.*, **63**, 79 (1933).

[7] Marvel, Inskeep, Deanin, Juve, Schroeder and Goff, *Ind. Eng. Chem.*, **39**, 1486 (1947).

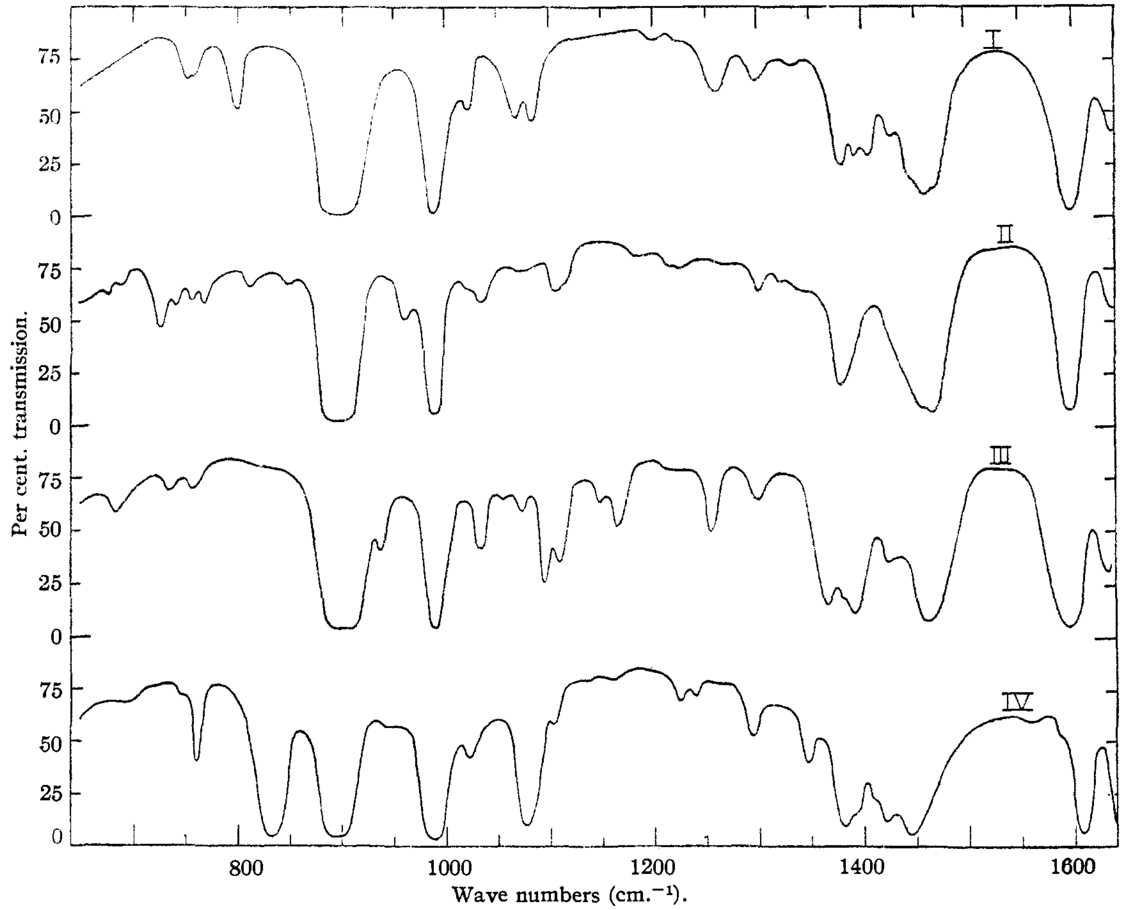
[8] Hurd and Blunck, THIS JOURNAL, **60**, 2419 (1938).

[9] Houtman, Van Steenis and Heertjes, *Rec. trav. chim.*, **65**, 781 (1946).

[10] Frank, Adams, Blegen, Deanin and Smith, *Ind. Eng. Chem.*, **39**, 887 (1947).

[11] Infrared Absorption Spectrograms issued by the American Petroleum Institute, National Bureau of Standards, March 31, 1946.

[12] We are indebted to Mrs. J. L. Johnson for these infrared absorption spectra curves and their interpretation.



Figs. 1 and 1a.

Curve no.	Diene	Curve no.	Diene
I	2-Ethyl-1,3-butadiene	III	2-Isopropyl-1,3-butadiene
II	2-*n*-Amyl-1,3-butadiene	IV	3-Methyl-1,3-pentadiene

Run 3 of 36 g. of alcohol at 170–173° on fractional distillation gave: 1, b. p. 68–74°, n^{20}D 1.4382, 3 g.; 2, b. p. 74–76°, n^{20}D 1.4483, 3 g.; 3, b. p. 76°, n^{20}D 1.4462, 2 g.; 4, b. p. 110–120°, n^{20}D 1.4005, 9 g.; 5, residue 4 g.

Redistillation of combined fractions 2 and 3 from run 3 gave material boiling from 67° to 77° with a refractive index varying from 1.4375 for the lowest boiling fraction to 1.4104 for the highest boiling fraction.

Fractions 1 and 2 and 3, 4, and 5 of run 2 were combined and portions were treated with maleic anhydride. Both products gave maleic anhydride adducts in about 60% yield, melting at 67–68° and mixed melting points showed they were identical with each other and with the adduct of 3-methyl-1,3-pentadiene.[6] Likewise, fractions 1–7 from run 3 were combined and treated with maleic anhydride to give a 60% yield of the 3-methyl-1,3-pentadiene adduct. Fractions 3–5 from run 1 and 3–5 of run 2 were combined and redistilled to give a product b. p. 76–78°, n^{20}D 1.4490. This sample did not produce an appreciable amount of polymer in ninety-six hours in a standard 50° GR-S polymerization.[7]

Attempted Rearrangement of 2-Ethyl-1,3-butadiene over Hot Potassium Acid Sulfate.—Twenty-eight grams of 2-ethylbutadiene (obtained from Carbide and Carbon Chemicals Corporation[13]), n^{20}D 1.4253, was passed dropwise through a 20-mm. Pyrex tube packed for a distance of 46 cm. with potassium acid sulfate and heated to a temperature of 190–200° by means of an electrically heated jacket. The crude product was trapped in a flask cooled by means of a Dry Ice–methanol mixture. It was then dried over anhydrous magnesium sulfate and distilled through a 25-cm., helices-packed column. The following fractions were collected: 1, b. p. 66–68°, n^{20}D 1.4254, 5 g.; 2, b. p. 68–72°, n^{20}D 1.4280, 15 g.; 3, b. p. 72–74°, n^{20}D 1.4320, 1 g.; 4, b. p. 74–75°, n^{20}D 1.4419, 0.5 g.; 5, b. p. 75–77°, n^{20}D 1.4450, 0.5 g.

The original 2-ethylbutadiene all boiled between 65 and 66.6°, n^{20}D 1.4253. The higher boiling material obtained by the action of hot potassium acid sulfate approaches the boiling point and refractive index (1.4515) of 3-methyl-1,3-pentadiene.

2-Ethyl-3-acetoxy-1-butene.—In a round-bottomed flask, equipped with reflux condenser and calcium chloride tube, were placed 84 g. (0.84 mole) of 2-ethyl-3-hydroxy-1-butene, 250 g. (2.42 moles) of acetic anhydride, and 1 cc. of pyridine. The reaction mixture was heated on the steam cone for twelve hours, poured into water, separated, and washed with saturated sodium carbonate solution. The separated organic material was dried over anhydrous sodium sulfate and distilled through a 46-cm., helices-packed column at reduced pressure. The fraction boiling at 74° (50 mm.), n^{20}D 1.4209, was collected and amounted to 113 g. (88%).

Anal.[14] Calcd. for $C_8H_{14}O_2$: C, 67.57; H, 10.02. Found: C, 67.49; H, 10.01.

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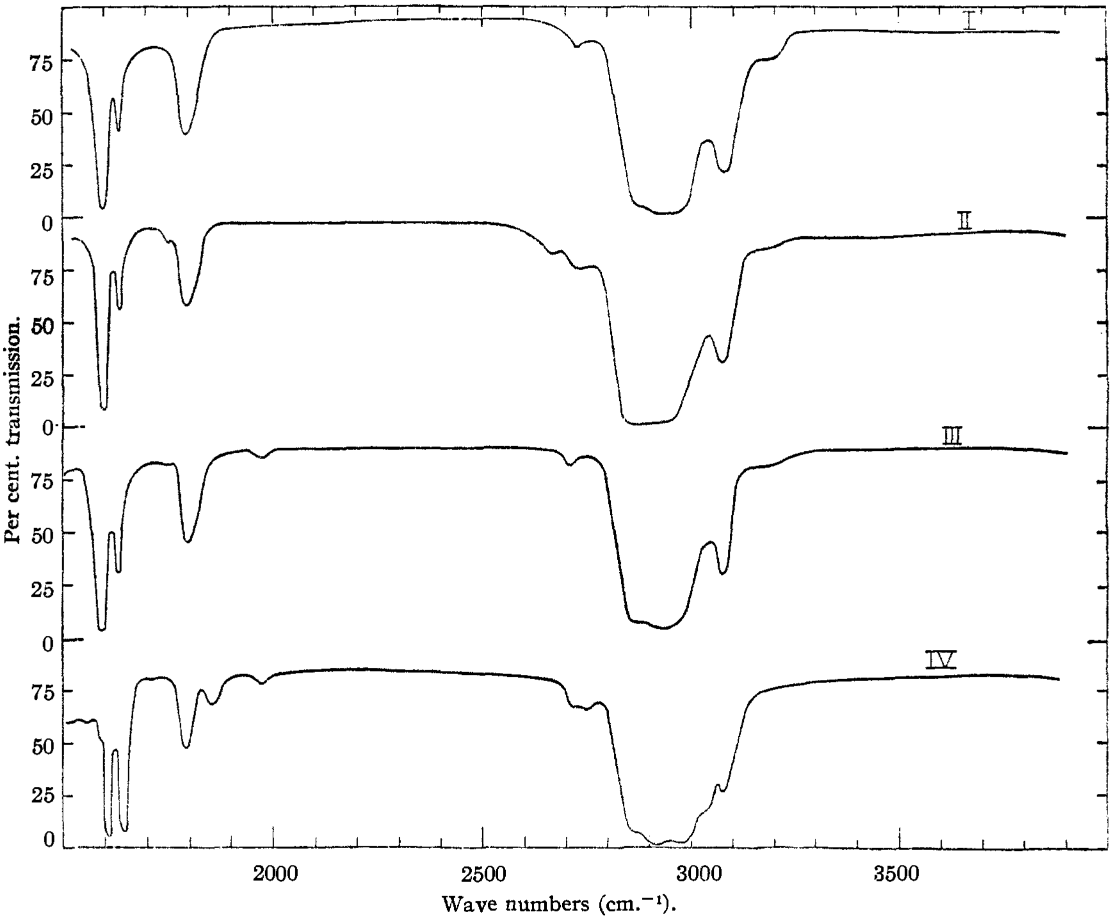
[13] We are indebted to Mr. L. C. Shriver for a generous sample of 2-ethyl-1,3 butadiene.

[14] Analyses by Clark Microanalytical Laboratory, Urbana, Illinois.



2-Ethylbutadiene.—Eighty-four grams (0.59 mole) of 2-ethyl-3-acetoxy-1-butene was passed dropwise through a 20-mm. Pyrex tube packed for a distance of 46 cm. with glass beads and heated to a temperature of 400–420° by means of an electrically heated jacket. The pyrolysate was collected in a Dry Ice–methanol trap and was washed with three 150-cc. portions of water and twice with 150-cc. portions of 15 per cent sodium hydroxide. After the crude product had been dried over anhydrous magnesium sulfate, the material boiling below 67° was distilled through a 25-cm., helices-packed column. The higher boiling material was recycled through the pyrolysis step and in this way additional material boiling below 67° was obtained. The combined low-boiling fractions were distilled through a 46-cm., helices-packed column and the fraction boiling at 65–66° collected. Very little material boiling lower than 65° was present. The yield of 2-ethyl-1,3-butadiene (n^{20}D 1.4325) was 16 g. (23.2%).

Anal. Calcd. for C_6H_{10}: C, 87.73; H, 12.27. Found: C, 87.53; H, 12.34.

A sample of 4.9 g. of this diene was treated with 5.8 g. of maleic anhydride in 25 cc. of dry ether containing a trace of picric acid in a 2-oz., screw-capped polymerization bottle sealed with a rubber gasket protected with tin foil for forty-eight hours at 50°. The bottle was cooled, opened, and the ether evaporated. The crystalline residue was recrystallized from petroleum ether until further crystallization did not change the melting point, 67–69°. The yield was 8.7 g. (81%).

Anal. Calcd. for $C_{10}H_{12}O_3$: C, 66.65; H, 6.72. Found: C, 66.86; H, 6.81.

A mixture of equal parts of this maleic anhydride adduct and that from 3-methyl-1,3-pentadiene[6] melted at 49°.

2-*n*-Amyl-3-acetoxy-1-butene.—The acetylation of 142 g. (1.0 mole) of 2-*n*-amyl-3-hydroxy-1-butene with 300 g. (2.73 moles) of acetic anhydride and 1 cc. of pyridine was carried out according to the procedure described above for 2-ethyl-3-acetoxy-1-butene. Distillation of the crude product yielded 131.5 g. (71%) of 2-*n*-amyl-3-acetoxy-1-butene boiling at 104° (28 mm.), n^{20}D 1.4313. A quantity of this material was redistilled for analysis, b. p. 78° (4 mm.), n^{20}D 1.4330.

Anal. Calcd. for $C_{11}H_{20}O_2$: C, 71.69; H, 10.94. Found: C, 71.74; H, 11.17.

2-*n*-Amyl-1,3-butadiene.—The pyrolysis of 124 g. (0.68 mole) of 2-*n*-amyl-3-acetoxy-1-butene at 400–420° was carried out according to the procedure described above for 2-ethyl-1,3-butadiene and yielded 29 g. of material boiling between 135° and 143°, n^{20}D 1.4448. The high boiling material was recycled through the pyrolysis step and yielded another 16 g. of material, b. p. 135–143°, n^{20}D 1.4445. The two diene fractions were combined and shaken with 15% sodium hydroxide, dried over anhydrous magnesium sulfate, and distilled at reduced pressure. The fraction boiling at 68–69.5° (65 mm.), n^{20}D 1.4450, was collected. The yield was 29 g. (42.5%).

Anal. Calcd. for C_9H_{16}: C, 87.01; H, 12.99. Found: C, 86.55; H, 13.20.

Treatment of 5.0 g. of this diene with 6.0 g. of maleic anhydride as described above gave 10 g. of adduct, m. p. 49–50°.

Anal. Calcd. for $C_{13}H_{18}O_3$: C, 70.25; H, 8.15. Found: C, 69.96; H, 8.10.

No crystalline maleic anhydride adduct could be obtained from diene prepared from 2-*n*-amyl-3-hydroxy-1-butene.[3]

2-Isopropyl-1,3-butadiene.—Pyrolysis of 87 g. of 2-isopropyl-3-acetoxy-1-butene as previously described[2] gave 29 g. (54%) of 2-isopropyl-1,3-butadiene, b. p. 85–87°, $n^{20}D$ 1.4337. This material polymerized readily and gave an infrared spectrum related to that of isoprene. This sample of 2-isopropyl-1,3-butadiene gave the same crystalline maleic anhydride adduct, m. p. 86–86.5°, which was reported earlier.[2]

Diene prepared by dehydration of 2-isopropyl-3-hydroxy-1-butene over either potassium acid sulfate or alumina boiled over a wide range, had a variable index of refraction depending on the fraction examined, and did not polymerize in the GR-S system. A considerable fraction of ketone was always obtained in the attempted dehydration.

3-Methyl-1,3-pentadiene.—This diene was prepared by the method of Nichol and Sandin.[5] Its maleic anhydride adduct was prepared in 61% yield by the procedure used for the adduct of 2-ethyl-1,3-butadiene instead of by the sealed tube method previously described.[6] The product melted at 67–68° as reported.[6]

Summary

Dehydration of 2-alkyl-3-hydroxy-1-butenes produced dienes of uncertain purity. Thermal cracking of the corresponding acetates gave pure 2-alkyl-1,3-butadienes in case of the ethyl, isopropyl and 2-*n*-amyl derivatives.

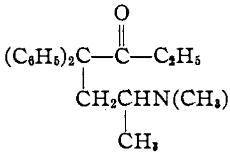
URBANA, ILLINOIS RECEIVED AUGUST 19, 1948

[CONTRIBUTION FROM THE LABORATORIES OF THE STERLING-WINTHROP RESEARCH INSTITUTE]

The Preparation and Properties of Some Benzohydryl Sulfones

BY MABEL M. KLENK, C. M. SUTER AND S. ARCHER

Reports which emanated from Germany at the end of the war[1] and later confirmed in this country[2] revealed that the ketone, I, known as methadone or 10,820 was an analgesic more potent than morphine. As part of an analgesic program under way

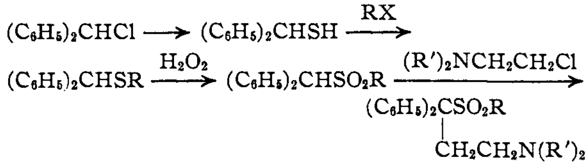


$$\begin{array}{l} \qquad\qquad\quad O \\ \qquad\qquad\quad \| \\ (C_6H_5)_2C—C—C_2H_5 \\ \qquad\quad\ | \\ \qquad\quad CH_2CHN(CH_3)_2 \\ \qquad\qquad\quad | \\ \qquad\qquad\quad CH_3 \end{array}$$

I

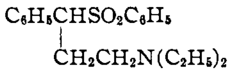
in these laboratories it was decided to prepare a series of aminoalkyl benzohydryl sulfones.

The compounds were prepared according to the equations



$$(C_6H_5)_2CHCl \longrightarrow (C_6H_5)_2CHSH \xrightarrow{RX}$$
$$(C_6H_5)_2CHSR \xrightarrow{H_2O_2} (C_6H_5)_2CHSO_2R \xrightarrow{(R')_2NCH_2CH_2Cl} \begin{array}{l} (C_6H_5)_2CSO_2R \\ \quad\ | \\ \quad CH_2CH_2N(R')_2 \end{array}$$

Eisleb[3] alkylated benzyl phenyl sulfone with diethylaminoethyl chloride with the aid of sodium amide and obtained the sulfone, II. Later,[4]



$$\begin{array}{l} C_6H_5CHSO_2C_6H_5 \\ \quad\ | \\ \quad CH_2CH_2N(C_2H_5)_2 \end{array}$$

II

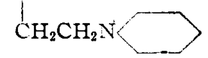
it was shown that sulfones such as methyl phenyl sulfone could also be alkylated with sodium amide as the condensing agent.

Benzohydryl mercaptan was previously prepared by Staudinger from diphenyldiazomethane and hydrogen sulfide.[5] We obtained this thiol in quantity by employing the thiourea synthesis.[6] Iodometric titration after distillation indicated that the thiol was about 85% pure. This material was satisfactory for the next step. It was smoothly alkylated in sodium ethylate solution with alkyl halides to yield the corresponding sulfides of approximately the same purity as the starting thiol. When the sulfides were oxidized with hydrogen peroxide in acetic acid solution, the resulting alkyl benzohydryl sulfones were readily isolated in crystalline form and could be purified easily. It was subsequently found that best results were realized when the distillations of the intermediate thiol and sulfides were avoided. When undistilled mercaptan and sulfide were employed in the preparation of ethyl benzohydryl sulfone the over-all yield based on benzohydryl chloride was 81%.

9-Fluorenyl mercaptan, a nicely crystalline solid, was converted to ethyl 9-fluorenyl sulfone by the procedures used in the benzohydryl series. Benzohydryl *p*-tolyl sulfone was prepared from sodium *p*-toluenesulfinate and benzohydryl chloride.[7]

Alkylation of the sulfones was effected in toluene solution in the presence of sodium amide. Details of the procedure are given in the Experimental Part.

Since the methyl group in methyl phenyl sulfone underwent alkylation under conditions similar to ours,[4] it was necessary to prove that the entering aminoalkyl group replaced the benzohydryl hydrogen rather than the hydrogen of the alkyl group in the alkyl benzohydryl sulfones. The product obtained from the reaction between pi-



III

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(1) Report No. PB-981, Office of the Publication Board, Dept. of Commerce, Washington, D. C., p. 91.

(2) Scott and Chen, *J. Pharmacol. Exptl. Therap.*, **87**, 63 (1946).

(3) Eisleb, *Ber.*, **74B**, 1433 (1941).

(4) German patent 735,866; *C. A.*, **38**, 4101 (1944).

(5) Staudinger and Stewart, *Ber.*, **49**, 1918 (1916).

(6) "Organic Syntheses," **21**, 36 (1941).

(7) Balfe, Doughty, Kenyon and Poplett, *J. Chem. Soc.*, 605 (1942).