where $a = [CHX_3]_0$, $b = [OH^-]_0$, $x = \Delta[CHX_3]_t$, t = time (in seconds), and f = fraction of haloform that gives formate, shows that we need not know f nor a provided that we know the normality of haloform, $(3 + f)a$, and the change in hydroxide ion concentration, $(3 + f)x$. Each of the other nine 40-ml. samples of aqueous haloform solution was put in a 50-ml. volumetric flask at 0°. The haloform normalities of these solutions were calculated from the values found for the third and ninth samples with the assumption of a constant change in concentration between each two consecutive samples. The alternate assumption that the change is proportional to the concentration gives calculated normalities that never differ from those used by more than 0.8%. At recorded times, 10 ml. of 0.1470 *N* sodium hydroxide solution at 0° was pipetted by a cold pipet into each of the nine 50-ml. volumetric flasks. The reactions were stopped at recorded times by pouring the contents of the volumetric flasks into 25 ml. of cold 0.06200 *N* perchloric acid. Samples 1 and 2 were stopped within 30 seconds to serve as "zero points." The excess acid was titrated to the brom cresol purple end-point with 0.04877 *N* carbonate-free sodium hydroxide solution. The data obtained are given in Table *II*.

Table II

Hydrolysis of $CHBrF_2$ in Aqueous Solution at 0°[a]

Sample no.	Time[b] (sec.)	Δ Titer, ml. 0.04877 *N* NaOH	10^3k (l./mole sec.)
4	690	0.69	1.924
5	1,235	1.21	2.005
6	2,125	1.88	1.918
7	3,060	2.48	1.885
8	6,110	4.50	1.985
10	8,080	5.58	2.167
11	11,035	6.55	2.095
		Av.	1.997 ± 0.079

[a] $[NaOH]_0 = 0.02930$. [b] From the time the zero points (1 and 2) were taken.

Heats and entropies of activation were calculated from the absolute rate equation[22]

$$k = \frac{\mathbf{k}T}{h} e^{-\Delta H^{\ddagger}/RT} e^{\Delta S^{\ddagger}/R}$$

Hydrolysis of Deuterobromodifluoromethane.—The kinetics of the hydrolysis of deuterobromodifluoromethane were studied by techniques like those described for the protium compound in the previous section. The "uncorrected" rate constant of $(1.09 \pm 0.03) \times 10^{-3}$ l./mole. sec. obtained was corrected to $(1.03 \pm 0.05) \times 10^{-3}$ by allowing for the presence of the more reactive protium compound and deuterodibromofluoromethane. The isotopic analyses were carried out by extracting the aqueous reaction solution with carbon disulfide and running the infrared spectrum of the extract. The per cent. protium compound present was calculated by comparison of the 7.88 and 9.01 μ bands of $CHBrF_2$ with the 8.76 and 9.32 μ bands of $CDBrF_2$ in this extract and also in an extract of the starting material and assuming that the starting material was 94% deuterated. Any error in the assumption would result in a proportional error in the same direction in our analyses and would therefore have little effect on our conclusion that hydrolysis is unaccompanied by deuterium exchange.

Acknowledgments.—We wish to acknowledge our indebtedness to the "Kinetic" Chemical Division of E. I. du Pont de Nemours and Company for a sample of bromodifluoromethane.

[22] S. Glasstone, K. J. Laidler and H. Eyring, "The Theory of Rate Processes," McGraw-Hill Book Co., Inc., New York, N. Y., 1941, p. 14.

Atlanta, Georgia

[Contribution from the Department of Chemistry and Chemical Engineering, Stanford University]

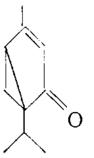
The Synthesis of 4-Isopropyl-1-methylbicyclo[3,1,0]-3-hexenon-2[1] an Isomer of Umbellulone

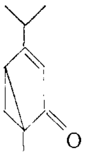
By Howard E. Smith[2] and Richard H. Eastman

Received May 1, 1957

The structure of umbellulone (I) has been confirmed by the unambiguous synthesis of an isomer, 4-isopropyl-1-methylbicyclo[3,1,0]-3-hexenon-2 (II), which contains the same chromophoric system and has an ultraviolet absorption spectrum practically identical with the anomalous absorption spectrum reported for umbellulone.

In conjunction with the current interest in the spectroscopic and chemical properties of the cyclopropane ring[3] and in view of the characteristic ultraviolet absorption spectrum[4] of umbellulone[5] (I)[6] (Fig. 1), described by Gillam and West[4] as anomalous in that it differs from that of any known α,β-unsaturated ketone, the unambiguous synthesis of an isomer, 4-isopropyl-1-methylbicyclo[3,1,0]-3-hexenon-2 (II), of umbellulone was undertaken. Since this isomer contains the same chromophoric system as umbellulone and has an ultraviolet absorption spectrum practically identical with that of umbellulone (compare in Fig. 1), the absorption spectra must be associated with the unique conjugated system present in both substances. The particular isomer was chosen for synthesis rather than umbellulone, since it not only confirms the structure of umbellulone but it is also a convenient intermediate for a projected total synthesis of the ses-


I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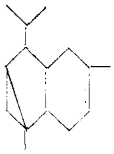
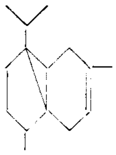

III


IV

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[1] This material is taken from the dissertation of Howard E. Smith offered in partial fulfillment of the requirements for the degree of Doctor of Philosophy at Stanford University. Preliminary reports of this synthesis were presented before the 125th Meeting of the American Chemical Society, Dallas, Texas, March, 1956, and published in *J. Org. Chem.*, **21**, 830 (1956).

[2] Eli Lilly and Co. Fellow 1953–1955.

[3] (a) R. H. Eastman and A. Oken, This Journal, **75**, 1029 (1952); (b) R. H. Eastman, *ibid.*, **76**, 4115 (1954); (c) R. H. Eastman and J. C. Selover, *ibid.*, **76**, 4118 (1954); (d) R. H. Eastman and S. K. Freeman, *ibid.*, **77**, 6642 (1955); (e) R. J. Mohrbacher and N. Cromwell, *ibid.*, **79**, 401 (1957), and earlier papers.

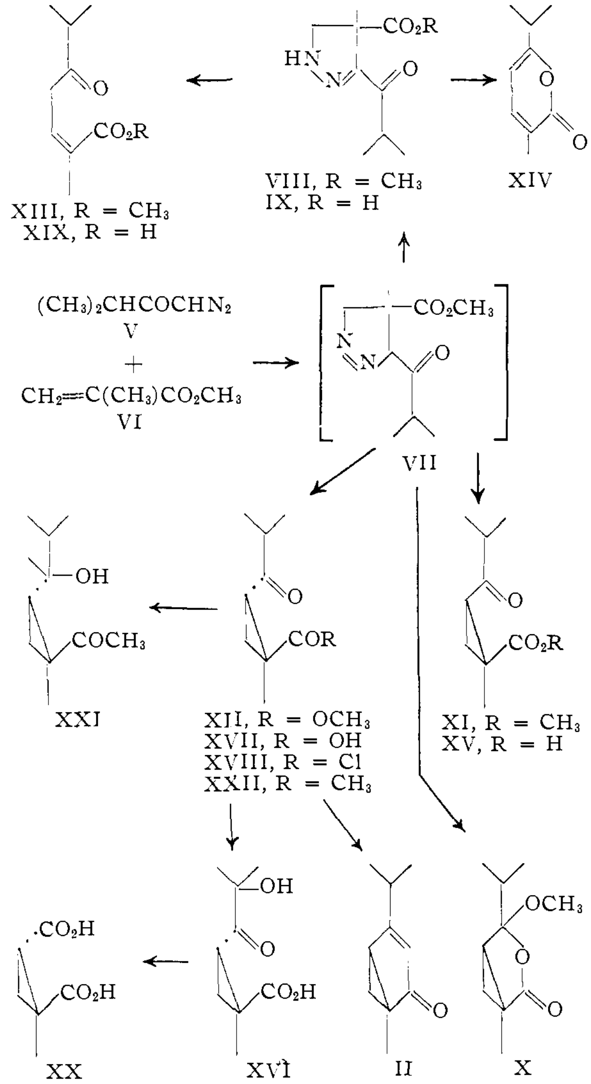
[4] A. E. Gillam and T. F. West, *J. Chem. Soc.*, 95 (1945).

[5] F. B. Power and F. H. Lees, *ibid.*, 629 (1904).

[6] F W. Semmler, *Ber.*, **40**, 5017 (1907).

quiterpene copaene[7] of which the chemical and physical properties do not unambiguously differentiate between the preferred (III) and the alternative (IV) structures.[8]

The synthesis of 4-isopropyl-1-methylbicyclo[3,1,0]-3-hexenon-2 (II) was accomplished through the important intermediate *trans*-2-isobutyryl-1-methylcyclopropanecarboxylic acid[9] (XVII) prepared by the method described by Guha and Muthanna[10] in the synthesis of umbellulonic acid. Isobutyryl chloride was added to an excess of diazomethane[11] and diazomethyl isopropyl ketone (V) was obtained. The latter compound was condensed with methyl methacrylate (VI) and the unisolated product, thought to be 4-carbomethoxy-3-isobutyryl-4-methyl-1-pyrazoline (VII), was pyrolyzed at 85° to a mixture of the *cis*- and *trans*-2-isobutyryl-1-methylcyclopropanecarboxylic acid methyl esters (XI and XII, respectively). Hydrolysis of the methyl esters gave a sirupy mixture of the *cis*- and *trans*-acids from which the *trans* isomer XVII separated as a crystalline solid.



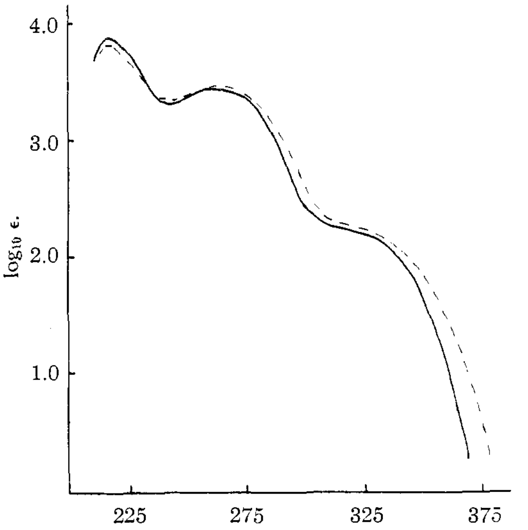


Fig. 1.—The ultraviolet absorption spectra of umbellulone (I), – – – –, and 4-isopropyl-1-methylbicyclo[3.1.0]-3-hexenon-2 (II), ———, in ethyl alcohol.

The infrared absorption spectrum of the mixed esters showed in addition to the expected bands at 5.80 (COOR) and 5.88 μ ($>C{=}O$),[12] an additional band at 5.58 μ. Careful distillation of the mixture gave six fractions with a total boiling range of 4°. Only fraction 1 had an infrared spectrum showing three bands in the 5–6 μ region while the remaining fractions showed only the bands at 5.80 and 5.88 μ. Since both fractions 1 and 5 gave on combustion, data in agreement with the formula $C_{10}H_{16}O_3$ and since both were completely saturated to potassium permanganate, fraction 1 was assumed to contain an appreciable amount of the hemiketal lactone X. When the lactone was removed by distillation from the mixture of esters and the pure esters were passed through a liquid–vapor partition column[13] the resulting curve showed the presence of at least two compounds, but the column was not capable of effecting a clean separation.

In addition to the usual analytical and spectroscopic data, the structure of *trans*-2-isobutyryl-1-methylcyclopropanecarboxylic acid (XVII) was confirmed by oxidation with alkaline potassium permanganate at 100° and chromic acid at room temperature to the known *trans*-1-methyl-1,2-cyclopropanedicarboxylic acid (XX).[14] In the oxidation with potassium permanganate two products were obtained, the known dicarboxylic acid and another crystalline, mono-basic acid, by combustion

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(7) F. W. Semmler and H. Stenzel, *Ber.*, **47**, 2555 (1915).

(8) L. H. Briggs and W. I. Taylor, *J. Chem. Soc.*, 1338 (1947).

(9) In the *trans*-acid the carboxyl and isobutyryl groups are on opposite sides of the cyclopropane ring. The disposition of groups is indicated in the formulas by the use of dashed and solid lines in the usual convention.

(10) P. C. Guha and M. S. Muthanna, *Ber.*, **71**, 2665 (1938); *Cur. Sci.*, **6**, 449 (1938).

(11) A. H. Blatt, "Organic Synthesis," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1954, p. 165; W. E. Bachmann and W. S. Struve, "Organic Reactions," Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1942.

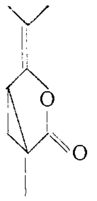
(12) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," John Wiley and Sons, Inc., New York, N. Y., 1954. Subsequent assignments of infrared absorption bands are based on information available in this reference (except where noted).

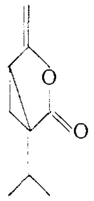
(13) A. T. James and J. P. Martin, *Analyst*, **77**, 915 (1952).

(14) C. K. Ingold, *J. Chem. Soc.*, 395, 398 (1925).

analysis and titration $C_9H_{14}O_4$, which on the basis of its infrared absorption spectrum with bands at 2.94 (OH), 5.87 (C=O) and 5.94 μ (COOH) and its oxidation with periodic acid at room temperature to *trans*-1-methyl-1,2-cyclopropanedicarboxylic acid was assigned the structure *trans*-1-methyl-2-(2-hydroxy-2-methylpropionyl)-cyclopropanecarboxylic acid (XVI).

While the oxidations with potassium permanganate and chromic acid proved conclusively the carbon skeleton of *trans*-2-isobutyryl-1-methylcyclopropanecarboxylic acid, they did not establish the relative orientation of the carbonyl and carboxyl functions attached to the ring. Unambiguous evidence for the *trans* configuration of the acid was obtained through its conversion with thionyl chloride to the corresponding acid chloride XVIII with an infrared absorption spectrum showing bands at 5.66 (COCl) and 5.88 μ (>C=O). Under the conditions of the reaction the *cis*-acid XV would have been expected to form the enol lactone XXIII in analogy to the extremely facile formation of the enol lactone XXIV[15] of umbellulonic acid with infrared bands at 5.58 (γ-lactone) and 5.96 μ (C=C).[16] The expectation was realized when treatment of the oily mixture of the *cis*- and *trans*-acids with thionyl chloride gave a product in whose infrared absorption spectrum appeared the band at 5.99 μ characteristic of the enol lactone system as well as those of the acid chloride. Attempts to separate the enol lactone from the acid chloride by distillation failed because of the proximity of their boiling points.


XXIII


XXIV

An attempt was made to obtain the pure *cis*-2-isobutyryl-1-methylcyclopropanecarboxylic acid by formation of its enol lactone XXIII, and subsequent hydrolysis to the free acid following the work of Tutin[15] with the corresponding enol lactone XXIV of umbellulonic acid. The oily mixture of *cis*- and *trans*-acids was heated with a mixture of acetic anhydride and potassium acetate for periods ranging from a few hours to 52 hours at 85 and 140°. On isolation of the products in the usual way, materials were obtained which had boiling points much lower than the mixture of acids, but which in all cases were complex mixtures of unsaturated substances as indicated by bands in the infrared absorption spectrum at 6.1 to 6.3 μ. The high degree of unsaturation was apparently the result of rupture of the cyclopropane ring, and it was evident that the pure enol lactone could not be obtained using the conditions employed.

Since neither the *cis*-acid nor its enol lactone could be obtained in any satisfactory degree of purity, attention was turned to the utilization in synthesis of the readily obtainable *trans*-2-isobutyryl-1-methylcyclopropanecarboxylic acid chloride (XVIII) which when treated with dimethylcadmium[1,17] gave the diketone, *trans*-1-acetyl-2-isobutyryl-1-methylcyclopropane (XXII). In a number of experiments to increase the yield of diketone the most satisfactory ratio of acid chloride to dimethylcadmium was found to be one mole of the former to 1.16 moles of the latter. If the ratio of acid chloride to dimethylcadmium was higher, the diketone was contaminated with large amounts of acid chloride; if the ratio was lower, two methyl groups were introduced into the acid chloride and only a small amount of diketone was obtained.

The compound formed by the addition of two equivalents of dimethylcadmium to the acid chloride, $(C_{11}H_{20}O_2)_n$ by combustion analysis, had an infrared absorption spectrum which indicated the presence of hydroxyl (2.87 μ) and carbonyl (5.95 μ) groups. The ultraviolet absorption spectrum with a maximum at 285 mμ (ε 79) confirmed the presence of a carbonyl group conjugated with a cyclopropane ring.[1,18] On the basis of these properties and the method of preparation, structures XXI and XXV (*vide infra*) were considered possible for the compound.

Because no corresponding alcohol was isolated from the reaction between dimethylcadmium and *trans*-chrysanthemic acid chloride (XXVI) when the work of Eastman and Freeman[3d] was repeated using a large excess of dimethylcadmium, the structure tentatively assigned to the compound in question is *trans*-1-acetyl-1-methyl-2-(2-hydroxy-1,2-dimethylpropyl)-cyclopropane (XXI). It must be mentioned, however, that the reaction of dimethylcadmium with a ketone was unexpected, since Cason[17] has found that this reagent does not react with aliphatic or cyclic ketones.

The diketone, *trans*-1-acetyl-2-isobutyryl-1-methylcyclopropane (XXII) which had analytical and spectral data in complete agreement with the assigned structure, when treated with 5% aqueous sodium hydroxide formed the α,β-unsaturated ketone, 4-isopropyl-1-methylbicyclo[3,1,0]hexenon-2 (II), by isomerization to the *cis*-diketone followed by intramolecular aldol condensation. The reaction was not quantitative and the product in all circumstances was contaminated with the original diketone. The two compounds could not be separated by fractionating or vapor–liquid partitioning columns, but the α,β-unsaturated ketone was purified by the bisulfite extraction method of Wienhaus and Todenhöfer.[19]

The pure 4-isopropyl-1-methylbicyclo[3,1,0]-3-hexenon-2 had an infrared absorption spectrum which was quite similar to that for umbellulone. There were the anticipated differences in the profile region beyond 7 μ, but in the double bond region there was excellent agreement and the over-all resemblance between the two spectra was striking. The carbonyl and double bond absorption bands of 4-isopropyl-1-methylbicyclo[3,1,0]-3-hexenon-2 oc-

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[15] F. H. Tutin, *J. Chem. Soc.*, 1104 (1906).

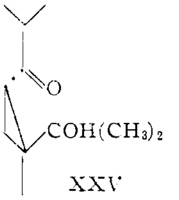
[16] G. I. Fujimoto and J. Prager, THIS JOURNAL, **75**, 3259 (1953).

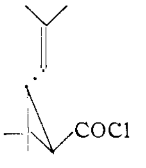
[17] J. Cason, *ibid.*, **68**, 2078 (1946); J. Cason, G. Sumrell and R. S. Mitchell, *J. Org. Chem.*, **15**, 850 (1950).

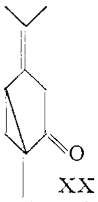
[18] I. M. Klotz, THIS JOURNAL, **66**, 88 (1944).

[19] H. Wienhaus and K. Todenhöfer, *Schimmels Berichte*, 285 (1925).

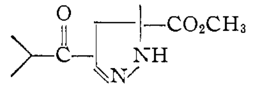
curred at 5.90 and 6.28 μ, respectively, whereas the same bands of umbellulone were at 5.88 and 6.19 μ. One significant difference between the infrared spectrum of the synthetic material and that of umbellulone was that in the spectrum of the former there was a small shoulder at 5.82 μ on the carbonyl absorption band which was assumed to indicate the presence of a small amount of the β,γ-isomer XXVII in which the double bond is exocyclic to the five-membered ring and not in conjugation with the carbonyl group.[20]

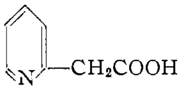

XXV


XXVI


XXVII

Returning now to the pyrolysis reaction by which the mixture of *cis*- and *trans*-2-isobutyryl-1-methylcyclopropanecarboxylic acid methyl esters was obtained, some comment must be made concerning the intermediate pyrazoline. When the condensation product of diazomethyl isopropyl ketone and methyl methacrylate was allowed to stand at room temperature for seven days instead of being decomposed immediately, there was obtained in addition to the mixture of cyclopropane esters, a substantial amount of a nitrogen-containing compound to which has been tentatively assigned the structure of 4-carbomethoxy-3-isobutyryl-4-methyl-2-pyrazoline (VIII). This material was a yellow, viscous oil insoluble in 2 *N* hydrochloric acid and had an infrared absorption spectrum with bands at 2.96 (NH), 5.72 (COOR) and 5.98 and 6.42 μ (COC═NNHR) compatible with the structures 4-carbomethoxy-3-isobutyryl-4-methyl-2-pyrazoline (VIII) and 5-carbomethoxy-3-isobutyryl-5-methyl-2-pyrazoline (XXVIII) both of which may be regarded as vinylogs of amides. When the 2-pyrazoline was subjected to alkaline hydrolysis, a white, crystalline acid was obtained on acidification. Titration and combustion indicated the empirical formula $C_9H_{14}O_3N_2$ for this acid. The structure 4-carboxy-3-isobutyryl-4-methyl-2-pyrazoline (IX) was tentatively assigned to the compound on the basis that it decomposed with loss of carbon dioxide at its melting point in analogy with the behavior of 2-pyridylacetic acid (XXIX) which also readily decarboxylates on heating.[21] The ease of decarboxylation of both compounds may be attributed to the ability of the C═N system to delocalize the anionic charge resident in the transition state on the carbon to which the carboxyl group is attached. The structure 4-carboxy-3-isobutyryl-4-methyl-2-pyrazoline thus inferred requires that the original 2-pyrazoline be 4-carbomethoxy-3-isobutyryl-4-methyl-2-pyrazoline (VIII).


XXVIII


XXIX

The isolation of 4-carbomethoxy-3-isobutyryl-4-methyl-2-pyrazoline in some pyrolysis reactions and not in others is taken to indicate that the initial product of the condensation between diazomethyl isopropyl ketone and methyl methacrylate was 4-carbomethoxy-3-isobutyryl-4-methyl-1-pyrazoline (VII). When the 1-pyrazoline was heated at 85°, it decomposed smoothly and gave a mixture of *cis*- and *trans*-2-isobutyryl-1-methyl-cyclopropanecarboxylic acid methyl esters. As the condensation mixture stood at room temperature, however, the 1-pyrazoline slowly changed by a prototropic shift to the 2-pyrazoline.

Pyrolysis of 5-carbomethoxy-3-isobutyryl-4-methyl-2-pyrazoline (VIII) to the mixture of *cis*- and *trans*-2-isobutyryl-1-methylcyclopropanecarboxylic acid methyl esters was attempted, but all low temperature methods to secure the elimination of nitrogen from the 2-pyrazoline failed. On strong heating, however, some nitrogen was evolved and a complex mixture of substances unsaturated to potassium permanganate was obtained. Saponification of this mixture yielded an acidic oil from which 2,6-dimethyl-5-oxo-2-heptenoic acid (XIX)[22] was obtained as a crystalline solid. The acid was unsaturated to aqueous potassium permanganate and gave combustion and titration data consistent with those calculated for $C_9H_{14}O_3$. Since the ultraviolet absorption spectrum showed only weak absorption in the region 230–250 mμ, the alternative structure with the double bond in conjugation with the keto group was rejected.[23] Because the infrared absorption spectrum of the unhydrolyzed material showed bands at 5.62 (γ-lactone), 5.82–5.88 (COOR) and 6.12 and 6.32 μ (C═C), it was assumed that a lactone XIV was also present in the mixture.

Experimental

Diazomethyl Isopropyl Ketone (V).—To an ice-cold solution of diazomethane (0.58 mole) in 600 ml. of ether was added with stirring 14.0 g. of isobutyryl chloride (0.132 mole) in 50 ml. of dry ether over a period of 0.5 hour.[11] The mixture was stirred for an additional two hours at room temperature. The excess diazomethane was removed and the volume of the solution was reduced to 200 ml. at the steam-plate. The bright yellow solution of diazoketone in which was suspended a small amount of colorless, insoluble material was used in the condensation with methyl methacrylate and the diazoketone usually was not purified further. Since the diazoketone slowly decomposed at room temperature, the solution was stored at −20° for use within 48 hours.

Complete removal of the ether solvent and fractional distillation of the residue gave the diazomethyl isopropyl ketone, a yellow oil with b.p. 72–73° (19 mm.), $n^{20}D$ 1.4721, d^{26}_4 0.973. Decomposition of the oil became rapid at 75° and violent decomposition occurred at 125°. The infrared absorption spectrum, density and refractive index were obtained using freshly distilled material[24]; spectrum, infrared, film: 4.76 μ (diazo), 6.10 μ (C═O).

***cis*- and *trans*-2-Isobutyryl-1-methylcyclopropanecarboxylic Acid Methyl Ester (XI and XII).**—Three portions of diazomethyl isopropyl ketone (0.396 mole total) each in 200 ml. of ether as prepared above were combined, filtered and added dropwise with stirring over a period of two hours to 54.0 g. of freshly distilled, hydroquinone-inhibited,

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(20) H. F. Gray, Jr., R. S. Rasmussen and D. D. Tunnicliff, THIS JOURNAL, **69**, 1630 (1947).

(21) J. L. Bills, "Investigation of the Synthesis of 1-(α-Picolyl)-isoquinolines," Dissertation, Stanford University, 1947.

(22) No conclusions were drawn concerning configuration about the double bond.

(23) R. B. Woodward, THIS JOURNAL, **63**, 1123 (1941); **64**, 76 (1942).

(24) On account of the slow decomposition of the diazoketone at room temperature, combustion analysis of the compound was unreliable.

methyl methacrylate (0.540 mole) at 60°. The ether was removed from the reaction mixture through a Vigreux fractionating column as the addition of the diazoketone solution proceeded. After the addition of the diazoketone was complete the mixture was heated at 60° for an additional two hours. The yellow product was transferred immediately to a 250-cc. modified Claisen distilling flask and a few ceramic chips were added as a catalytic surface. The flask was immersed in an oil-bath and the bath temperature was raised slowly to 85° at which temperature a smooth evolution of nitrogen began. The temperature of the bath was held between 85 and 90° until the evolution of nitrogen had subsided, usually about one hour. The reaction was exothermic and only a small amount of heating was required to maintain the temperature of the oil-bath above 85°. If the temperature was allowed to go above 90°, the evolution of nitrogen became quite rapid and cooling was necessary to maintain control of the reaction.

When the evolution of nitrogen was complete the material remaining in the distilling flask was distilled at reduced pressure and 38.4 g. of a fraction with b.p. 69–88° (2 mm.) was collected. This material was distilled through a 20 TP Fenske fractionating column and there was obtained 25.5 g. of a mixture of *cis*- and *trans*-2-isobutyryl-1-methylcyclopropanecarboxylic acid methyl esters (35.0% based on isobutyryl chloride) with b.p. 67–75° (2 mm.). This material had an infrared absorption spectrum which showed the presence of not only the *cis*- and *trans*-esters but also the lactone of structure X discussed previously. Usually the material was not purified further and hydrolysis gave a mixture of the *cis*- and *trans*-acids from which the *trans* isomer separated as a crystalline solid.

For characterization of the esters a portion of the material with b.p. 67–75° (2 mm.) was subjected to redistillation and a series of six fractions obtained with a total boiling range of 4°. The results of this distillation were discussed previously and two fractions, 1 and 5, were subjected to analysis as follows:

Fraction 1 with b.p. 76° (4 mm.). *Anal.*[25] Calcd. for $C_{10}H_{16}O_3$: C, 65.19; H, 8.75. Found: C, 65.28; H, 8.86. Spectrum, infrared, film: 5.58 μ (γ-lactone), 5.80 μ (COOR), 5.88 μ (∇ C=O).

Fraction 5 with b.p. 80° (4 mm.), n^{20}D 1.4482, d^{23}_4 1.008. *Anal.* Calcd. for $C_{10}H_{16}O_3$: C, 65.19; H, 8.75. Found: C, 65.27; H, 8.82. Spectra, infrared, film: 5.80 μ(COOR), 5.88 μ (∇ C=O); ultraviolet: λ_{max}^{alc} 285 mμ, ϵ_{max} 64.

2-Isobutyryl-1-methylcyclopropanecarboxylic Acid Methyl Ester Semicarbazone.[26]—To 1.0 g. of semicarbazine hydrochloride suspended in 5.0 ml. of methyl alcohol was added 1.0 g. of sodium acetate. This mixture was stirred thoroughly and filtered, and to the clear filtrate was added 1.0 g. of a mixture of *cis* and *trans*-2-isobutyryl-1-methylcyclopropanecarboxylic acid methyl esters (0.0054 mole) with b.p. 80° (4 mm.). After standing at room temperature for 24 hours, 0.7 g. of a white, crystalline solid with m.p. 156–160° was obtained. Recrystallization of this material from water gave 0.2 g. of a sharp-melting, white, crystalline semicarbazone with m.p. 174–175°[27]; spectrum, infrared, Nujol suspension: 2.99 μ (NH); 3.11 μ (NH); 5.80 μ (COOR); 5.92 μ (amide); 6.31 μ (amide).

Anal. Calcd. for $C_{11}H_{19}O_3N_3$: C, 54.75; H, 7.94. Found: C, 55.31; H, 8.04.

***trans*-2-Isobutyryl-1-methylcyclopropanecarboxylic Acid (XVII).**—To 15 g. of sodium hydroxide in 100 ml. of water was added 42.0 g. of a mixture of *cis*- and *trans*-2-isobutyryl-1-methylcyclopropanecarboxylic acid methyl esters (0.228 mole) and the mixture was boiled under reflux for one hour. The homogeneous solution was cooled to room temperature and its acidity adjusted to *p*H 1 with concentrated sulfuric acid. The colorless oil which separated from the aqueous solution was removed with 100 ml. of ether and the remaining aqueous solution was extracted with three 100-ml. portions of ether. After the combined ether solutions were dried and the ether was removed at the steam-plate, there was obtained on distillation of the residue 36.5 g. of a colorless oil with b.p. 125–127° (1 mm.) which on standing at 0° partially crystallized. Removal of the remaining oil by centrifugation gave 15.4 g. of *trans*-2-isobutyryl-1-methylcyclopropanecarboxylic acid, a white, crystalline solid with m.p. 41–53°. Recrystallization of this material from petroleum ether (b.p. 35–58°) yielded the pure *trans*-acid with m.p. 56–57°; spectra, infrared, Nujol suspension: 5.89 μ (COOH and C=O); ultraviolet: λ_{max}^{alc} 288 mμ, ϵ_{max} 70.

Anal. Calcd. for $C_9H_{14}O_3$: C, 63.51; H, 8.29; neut. equiv., 170. Found: C, 63.83; H, 7.84; neut. equiv., 174; pK_a, 3.9.

***trans*-2-Isobutyryl-1-methylcyclopropanecarboxylic Acid Chloride (XVIII).**[18]—To a solution of 13.0 g. of freshly purified thionyl chloride (0.110 mole) in 200 ml. of dry benzene was added 10.0 g. of *trans*-2-isobutyryl-1-methylcyclopropanecarboxylic acid (0.0588 mole), and the mixture was boiled under reflux for 45 minutes. Removal of the solvent at the water-pump and distillation of the residue yielded 7.0 g. of *trans*-2-isobutyryl-1-methylcyclopropanecarboxylic acid chloride (71%), a colorless oil with b.p. 63° (1 mm.), n^{21}D 1.4679; spectra, infrared, liq. film: 5.66 μ (COCl); 5.88 μ (C=O); ultraviolet: λ_{max}^{hex} 212 mμ, ϵ_{max} 3,300; λ_{max}^{hex} 293 mμ, ϵ_{max} 98.

Anal. Calcd. for $C_9H_{13}O_2Cl$: C, 57.14; H, 6.94. Found: C, 57.90, 57.98; H, 7.33, 7.27.

***trans*-1-Methyl-1,2-cyclopropanedicarboxylic Acid (XX) and *trans*-1-Methyl-2-(2-hydroxy-2-methylpropionyl)-cyclopropanecarboxylic Acid (XVI).**—To 5.75 g. of potassium permanganate (0.0364 mole) in 75 ml. of water was added 1.50 g. of *trans*-2-isobutyryl-1-methylcyclopropanecarboxylic acid (0.00882 mole) and the mixture was boiled under reflux for one hour. The mixture was cooled to room temperature and sulfur dioxide passed through the solution until the heavy precipitate of manganese dioxide had completely dissolved. The colorless, clear, aqueous solution of *p*H 1 was then continuously extracted with ether for 13 hours. The ether solution was dried over anhydrous sodium sulfate and evaporated to dryness on the steam-plate. There was obtained 1.30 g. of a white, crystalline solid with m.p. 92–128°. Extraction of this material with chloroform separated it into two fractions. The chloroform-insoluble material was recrystallized from a mixture of benzene and acetone and sublimed at 120° (1 mm.). Final recrystallization from a mixture of ethyl acetate and *n*-hexane gave 0.15 g. of *trans*-1-methyl-1,2-cyclopropanedicarboxylic acid (12%) with m.p. 171–172.5° (reported[14] m.p. 168–169°); spectrum, infrared, KBr disk: 5.94 μ (COOH).

Anal. Calcd. for $C_6H_8O_4$: C, 50.00; H, 5.60; neut. equiv., 72. Found: C, 50.29, 50.23; H, 5.81, 5.67; neut. equiv., 71.

The chloroform solution was washed with 25 ml. of water and dried over anhydrous sodium sulfate. Evaporation at the steam-plate yielded a white, crystalline solid. Recrystallization of this material first from a mixture of benzene and acetone and then from a mixture of *n*-hexane and acetone gave 0.85 g. of *trans*-1-methyl-2-(2-hydroxy-2-methylpropionyl)-cyclopropanecarboxylic acid (52%) with m.p. 110–111°; spectrum, infrared, KBr disk: 2.96 μ (OH), 5.87 μ (C=O), 5.94 μ (COOH).

Anal. Calcd. for $C_9H_{14}O_4$: C, 58.04; H, 7.58; neut. equiv., 186. Found: C, 58.28, 57.88; H, 7.58, 7.68; neut. equiv., 179.

To 1.0 g. of periodic acid dihydrate (0.0044 mole) in 25 ml. of water was added 0.35 g. of *trans*-1-methyl-2-(2-hydroxy-2-methylpropionyl)-cyclopropanecarboxylic acid (0.0019 mole) and the solution was allowed to stand overnight. Continuous extraction with ether and recrystallization as outlined above gave 0.15 g. of *trans*-1-methyl-1,2-cyclopropanedicarboxylic acid (54%) with m.p. 171–172°, identical with material isolated from the potassium permanganate oxidation of *trans*-2-isobutyryl-1-methylcyclopropanecarboxylic acid.

***trans*-1-Acetyl-2-isobutyryl-1-methylcyclopropane (XXII) and *trans*-1-Acetyl-1-methyl-2-(1-hydroxy-1,2-dimethylpropyl)-cyclopropane (XXI).**—In a 125-cc. reaction flask equipped with a mechanical stirrer, dropping funnel and reflux condenser 1.6 g. of magnesium (0.066 mole) was suspended in 47 ml. of dry, peroxide-free ether under an atmosphere of nitrogen. Excess methyl bromide was added to the mixture until all the magnesium had reacted. When solution was complete 6.2 g. of anhydrous cadmium chloride (0.034 mole) was added and the mixture was boiled

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(25) Analyses by Microchemical Specialties Co., Berkeley, California.

(26) It is not known which ester, *cis* or *trans*, formed this derivative, but on the basis of the sharp melting point of the material it was assumed that only one of the isomeric semicarbazones was isolated.

(27) Melting points are not corrected.

under reflux for one hour. The reflux condenser was replaced with a short distilling head and ether was removed from the mixture until only a gray, semi-solid residue remained. To the residue was added 47 ml. of dry benzene and distillation continued until an additional 20 ml. of distillate was collected. The reflux condenser was again put in place and 5.4 g. of *trans*-2-isobutyryl-1-methylcyclopropanecarboxylic acid chloride (0.029 mole) in 10 ml. of dry benzene was added as rapidly as possible. The mixture was finally boiled under reflux for 0.5 hour, cooled to 0° and decomposed with 50 ml. of dilute sulfuric acid. The product was isolated as an aqueous sodium bicarbonate and water-washed benzene solution. After removal of the benzene, distillation separated the residue into two fractions. The first fraction was 3.2 g. of *trans*-1-acetyl-2-isobutyryl-1-methylcyclopropane (66%), a colorless oil with b.p. 74–78° (2 mm.), contaminated with a small amount of the original acid chloride. In practice the impurity was not removed and the material as obtained above was found suitable for further synthetic work.

The second fraction, 0.10 g. of a light yellow oil, was tentatively assigned (*vide supra*) the structure *trans*-1-acetyl-1-methyl-2-(1-hydroxy-1,2-dimethylpropyl)-cyclopropane (19%) and had b.p. 95–97° (2 mm.), $n^{21}\text{D}$ 1.4662; spectra, infrared: 2.87 μ (OH), 5.95 μ (C=O); ultraviolet: $\lambda^{\text{alc}}_{\text{max}}$ 285 mμ, ϵ_{max} 79.

Anal. Calcd. for $C_{11}H_{20}O_2$: C, 71.69; H, 10.94. Found: C, 71.31, 71.44; H, 10.63, 10.76.

For purification of *trans*-1-acetyl-2-isobutyryl-1-methylcyclopropane 2.6 g. of the impure material as obtained above was boiled under reflux with 0.5 g. of sodium hydroxide in 35 ml. of water for one-half hour. The insoluble organic layer which remained after the heating period was removed with ether and the solution dried over anhydrous sodium sulfate. After removal of the ether and distillation of the residue there was obtained 0.5 g. of *trans*-1-acetyl-2-isobutyryl-1-methylcyclopropane (19% based on impure diketone) with b.p. 120–122° (19 mm.), $n^{21}\text{D}$ 1.4670; spectra, infrared, film: 5.94 μ (C=O); ultraviolet: $\lambda^{\text{alc}}_{\text{max}}$ 213 mμ, ϵ_{max} 5,060; $\lambda^{\text{alc}}_{\text{max}}$ 287 mμ, ϵ_{max} 300.

Anal. Calcd. for $C_{10}H_{16}O_2$: C, 71.42; H, 9.52. Found: C, 71.38, 71.46; H, 9.80, 9.81.

4-Isopropyl-1-methylbicyclo[3,1,0]-3-hexenon-2 (II).—To 40 ml. of 5% aqueous sodium hydroxide was added 3.2 g. of *trans*-1-acetyl-2-isobutyryl-1-methylcyclopropane (0.019 mole) and the mixture was boiled under reflux for one hour. The heterogeneous mixture was steam distilled and the organic portion of the distillate removed with ether. The ether solution was dried over anhydrous sodium sulfate and the ether removed through a 14 TP fractionating column. Distillation of the residue yielded 1.8 g. of 4-isopropyl-1-methylbicyclo[3,1,0]-3-hexenon-2, a colorless oil with b.p. 118–122° (19 mm.), $n^{21}\text{D}$ 1.4785, contaminated with the original diketone. A portion of this material, 1.2 g., was suspended in a solution of 3.0 g. of sodium sulfite and 1.5 g. of sodium bicarbonate in 6 ml. of water and the mixture was shaken for 24 hours. After the shaking period the organic material was not completely dissolved and the insoluble layer was removed with *n*-hexane and discarded. To the aqueous solution in which was suspended a small amount of white, crystalline inorganic material was added 9.6 g. of sodium hydroxide and the mixture was steam distilled. The organic oil suspended in the distillate was removed with ether and the ether solution dried over anhydrous sodium sulfate. After removal of the ether and distillation of the residue there was obtained 0.31 g. of 4-isopropyl-1-methylbicyclo[3,1,0]-3-hexenon-2 (11% based on *trans*-1-acetyl-2-isobutyryl-1-methylcyclopropane), a colorless oil with b.p. 54° (1 mm.), $n^{21}\text{D}$ 1.4853; spectra, infrared, film: 5.90 μ (C=O), 6.28 μ (C=C, conj.); ultraviolet: $\lambda^{\text{alc}}_{\text{max}}$ 213 mμ, ϵ_{max} 5,900; $\lambda^{\text{alc}}_{\text{max}}$ 265 mμ, ϵ_{max} 3,200; $\lambda^{\text{alc}}_{\text{sh}}$ 330 mμ, ϵ_{sh} 210.

Anal. Calcd. for $C_{10}H_{14}O$: C, 79.95; H, 9.39. Found: C, 79.57, 79.49; H, 9.52, 9.63.

4-Carbomethoxy-3-isobutyryl-4-methyl-2-pyrazoline (VIII).—After the condensation of diazomethyl isopropyl ketone (0.396 mole) and methyl methacrylate (0.540 mole) (*vide supra*) was complete the yellow product was allowed to stand at room temperature for 7 days rather than being pyrolyzed at 85° immediately. To remove the large amount of polymeric material which had formed on standing the mixture was distilled and a fraction of 52.0 g. with b.p. 70–120° (3 mm.) was collected. Redistillation of this material gave 10.7 g. of a mixture of *cis*- and *trans*-2-isobutyryl-1-methylcyclopropanecarboxylic acid methyl esters (14.7%) with b.p. 59–66° (3 mm.), $n^{20}\text{D}$ 1.4470, and 17.4 g. of 4-carbomethoxy-3-isobutyryl-4-methyl-2-pyrazoline (20.8%) with b.p. 107–110° (2 mm.), $n^{20}\text{D}$ 1.4980. This material was a yellow, viscous oil insoluble in water and 2 *N* hydrochloric acid; spectrum, infrared, film: 2.96 μ (NH), 5.72 μ (COOR); 5.98, 6.42 μ (COC=NNHR).

Anal. Calcd. for $C_{10}H_{16}N_2O_3$: C, 56.59: H, 7.60; N, 13.20. Found: C, 56.60, 56.66; H, 7.48, 7.53; N, 12.95, 13.03.

4-Carboxy-3-isobutyryl-4-methyl-2-pyrazoline (IX).—To 50 ml. of 1.0 *N* aqueous sodium hydroxide was added 3.0 g. of 4-carbomethoxy-3-isobutyryl-4-methyl-2-pyrazoline (0.014 mole) and the mixture was boiled under reflux for one hour. The solution was cooled and extracted with ether. When the acidity of the aqueous layer was adjusted to *p*H 1 with concentrated sulfuric acid a yellow oil separated. The oil was removed with ether and the aqueous layer was discarded. The ether solution was dried over anhydrous sodium sulfate and evaporated at the steam-plate and there was obtained a yellow solid. Crystallization of this material from benzene (charcoal) gave 2.5 g. of 4-carboxy-3-isobutyryl-4-methyl-2-pyrazoline (90%), a white crystalline solid with m.p. 127–128°, which on being heated at its melting point smoothly evolved carbon dioxide.

Anal. Calcd. for $C_9H_{14}O_3N_2$: C, 54.53; H, 7.12; neut. equiv., 198. Found: C, 55.38; H, 7.26; neut. equiv., 200; pK_a, 2.7.

2,6-Dimethyl-5-oxo-2-heptenoic Acid (XIX).[22]—To 24 g. of 4-carbomethoxy-3-isobutyryl-4-methyl-2-pyrazoline was added a ceramic chip and the material was heated slowly to 136° at which temperature a violent evolution of nitrogen occurred and subsided almost immediately. Distillation of the remaining material through a 12 TP helices-packed fractionating column gave as the principal fraction 14.6 g. of a yellow oil with b.p. 102–103° (6 mm.). This material was unsaturated to potassium permanganate and had an infrared absorption spectrum which showed it to be a mixture of unsaturated substances.

To 7.0 g. of this material was added 60 ml. of 1.0 *N* aqueous sodium hydroxide and the mixture was boiled under reflux for two hours. The cooled mixture was extracted with two 50-ml. portions of ether and the ether solutions discarded. The acidity of the aqueous solution was adjusted to *p*H 1 with concentrated sulfuric acid and the oil which separated was removed with two 50-ml. portions of ether. The dried ether solution was reduced at the steam-plate to a brown oil which on standing at 0° partially crystallized. Removal of the remaining oil by centrifugation and recrystallization from *n*-hexane gave 0.5 g. of 2,6-dimethyl-5-oxo-2-heptenoic acid (3% based on 4-carbomethoxy-3-isobutyryl-4-methyl-2-pyrazoline), a white, crystalline solid with m.p. 53.5–54°; spectra, infrared, Nujol suspension: 5.88–5.92 μ (COOH and C=O), 6.12 μ (C=C); ultraviolet: $\lambda^{\text{alc}}_{\text{max}}$ 211 mμ, ϵ_{max} 5,900; $\lambda^{\text{alc}}_{\text{sh}}$ 285 mμ, ϵ_{sh} 42.

Anal. Calcd. for $C_9H_{14}O_3$: C, 63.51; H, 8.29; neut. equiv., 170. Found: C, 63.16; H, 8.38; neut. equiv., 173; pK_a 4.0.

Absorption Spectra.—Ultraviolet absorption spectra were determined with a Beckman Model DU Spectrophotometer and optical density readings were taken at maximum intervals of 5 mμ. The infrared absorption spectra were obtained using a Perkin–Elmer model 21 infrared spectrophotometer with sodium chloride optics. Wave lengths are correct to 0.05 μ.

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