centrated HCl at 180° overnight in sealed tubes, and treated for the isolation of *p*-toluenesulfonylglycine as described.[14] From guanine and xanthine *p*-toluenesulfonylglycine, m.p. 147°, was obtained. From guanine N-oxide and xanthine N-oxide, about 50 mg. of a crystalline compound was obtained which had m.p. 135°. A mixture melting point with *p*-toluenesulfonamide, m.p. 137°, was depressed to 105°. A mixture melting point with an authentic sample of hydroxyglycine, m.p. 135°,[23] showed no depression. Comparison of the infrared spectra of the products obtained with that of hydroxyglycine proved the two to be identical.

Acknowledgment.—We are indebted to Dr. Edward A. Kaczka, Merck & Co., Inc., for a sample of N-hydroxyglycine, and to Marvin J. Olsen for very capable assistance.

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[23] W. Traube, *Ber.*, **28**, 2300 (1895).

Studies toward the Synthesis of the Proposed Structure for the Cockroach Sex Attractant[1]

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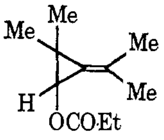
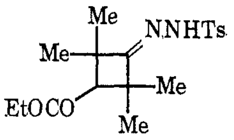
Thermal decomposition of the sodium salt of II has been examined with a view to synthesize I, the proposed structure for the cockroach sex attractant. The decomposition reaction affords a highly complex mixture. Besides the azine VI, two liquid components have been separated by preparative vapor phase chromatography. One of these compounds has been identified as 2,5-dimethylhexatriene (VII). Although the second compound appeared to represent structure I from its spectroscopic properties, it has been shown to possess structure XIII on the basis of chemical evidence. Mechanisms for the formation of VII are amply discussed.

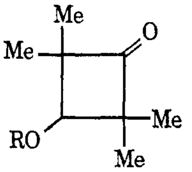
The highly potent sex attractant of the female American cockroach, *Periplaneta americana* L., has aroused considerable interest among several organic chemists. In connection with an earlier structural proposal I for the attractant,[2,3] the thermal decomposition of the sodium salt of the tosylhydrazone II was examined in detail.[4] The method[5] seemed particularly interesting because the desired intermediates III and IV could be readily obtained from the commercially available dimethylketene dimer V. Decomposition of the salt under a mild vacuum gave a sweet-smelling liquid whose vapor phase chromatogram indicated the presence of at least 13 components. Decomposition of the same salt in molten acetamide at 120° under a nitrogen atmosphere yielded a liquid which was found to contain 23 components. A complete separation and identification of this mixture appeared an arduous task. The complexity of this formidable mixture was, however, substantially reduced by partial separation by column chromatography over silica gel. The resulting mixture A was shown to contain 11 components. The residue on the column (mixture B) was discarded.



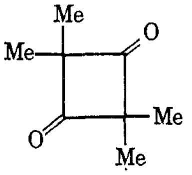
I



II

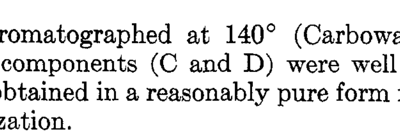


III, R=H
IV, R=CO·Et



V

Occasionally, a solid (m.p. 100–101°) could be separated by careful column chromatography of the crude mixture. The infrared spectrum of the solid in CCl_4 showed, besides other bands, a strong band at 5.75 μ and a medium intensity band at 5.93 μ. The n.m.r. spectrum in $CDCl_3$ showed a three-proton triplet (J = 7 c.p.s.) at τ 8.85, four methyl resonances at τ 8.84, 8.80, 8.69, and 8.59, a two-proton quartet (J = 7 c.p.s.) at τ 7.64, and a sharp one-proton singlet at τ 5.39. The elemental analysis corresponded to the formulation $C_{22}H_{36}N_2O_4$. The solid was soon identified as the azine VI by comparison with an authentic sample.[6] For preparative purposes, the liquid mixture A was chromatographed at 140° (Carbowax 20 M). Only two components (C and D) were well separated and were obtained in a reasonably pure form for further characterization.



VI

Compound C.—The n.m.r. spectrum of this compound was comprised of only three resonance lines: a three-proton signal at τ 8.17 slightly coupled (J = 1 c.p.s.) to a two-proton signal at τ 5.08, and a sharp

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[1] Abstracted from the Ph.D. Thesis (part two) submitted by the author to the Department of Chemistry, Harvard University, April 1965.

[2] M. Jacobson, M. Beroza, and R. T. Yamamoto, *Science*, **137**, 48 (1963).

[3] After the completion of this work, M. Jacobson, M. Beroza, and R. T. Yamamoto [*ibid.*, **147**, 748 (1965)] withdrew their earlier structure[2] for the attractant.

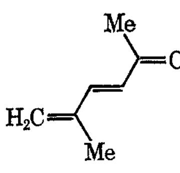
[4] Recently, J. Meinwald, J. W. Wheeler, A. A. Nimetz, and J. S. Liu, [*J. Org. Chem.*, **30**, 1038 (1965)] have reported several interesting attempts to synthesize the attractant. Their study included the approach described in the present article. The results obtained in this laboratory differ sufficiently from those reported by these authors to warrant a separate publication.

[5] Base-catalyzed thermal decomposition of cyclobutanone tosylhydrazone has been reported to yield methylenecyclopropane in an excellent yield: L. Friedman and H. Shechter, *J. Am. Chem. Soc.*, **83**, 1002 (1960).

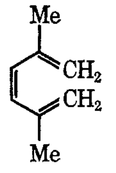
[6] Readily obtained by stirring the keto ester IV with a stoichiometric amount of hydrazine in methanol.

single-proton absorption at τ 3.84.[7] The infrared spectrum of this compound in CCl_4 showed bands at 3.29 (s), 3.40, 5.65 (w), 6.20 (m), 6.90, 7.01, 7.30, 7.65, 8.01, 10.40, and 11.29 μ. (The weak band at 5.65 μ is probably the overtone of the band at 11.29 μ.) The bands at 3.29 and 11.29 μ suggested the presence of $>C{=}CH_2$ unit(s) in this compound. From the position (6.20 μ) and the intensity of the C=C stretch, it was inferred that the system was most probably conjugated. This assumption was further corroborated by its ultraviolet spectrum in cyclohexane which showed strong absorption bands at 271 mμ (ϵ 59,500), 261 (78,500), 251 (61,600), and 242 (33,000). The spectral data seemed to best represent the structure VIIa or VIIb. An authentic sample of 2,5-dimethylhexatriene (VII) prepared from 3-chloro-2-methylpropene by Kharasch's procedure[8] was found to be identical with the compound C. This conclusion was drawn from their superimposible infrared, ultraviolet, and n.m.r. spectra and further substantiated by their failure to separate gas chromatographically on two different columns.

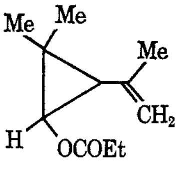
A number of mechanisms could in principle account for the formation of VII in the decomposition of the sodium salt of the tosylhydrazone II. A key feature of one of the most likely schemes involves the labile intermediate VIII. Loss of a molecule of propionic acid (probably through a transition state IXa or IXb) would be expected to yield the triene VII. The process is expected to be facile not only because the relatively strained molecule passes into a strain-free system, but also because of the extra stabilization offered by the resulting molecule in which three double bonds exist in conjugation.



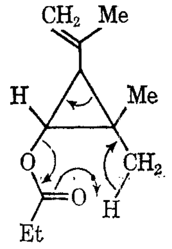
VIIa



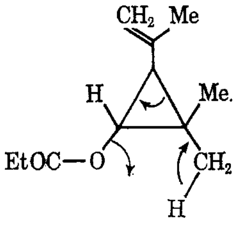
VIIb



VIII

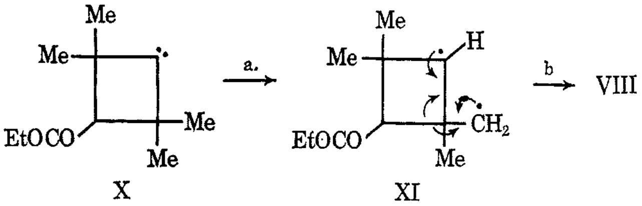


IXa

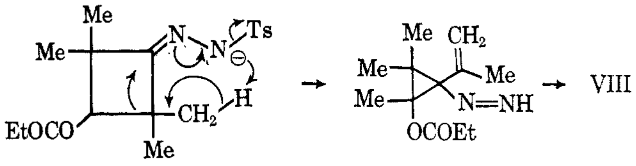


IXb

One of the conceivable paths to account for the formation of VIII may involve an intramolecular hydrogen abstraction by the carbene X from one of the four equivalent methyl groups (step a). The resulting diradical (XI) could undergo an alkyl shift to generate VIII as portrayed below (path b). Such 1,2 alkyl shifts, though not of common occurrence in simple radical reactions, have some parallels in the diradical systems.[9,10] As an alternative, one may consider the possibility of the following concerted pathway.[11]

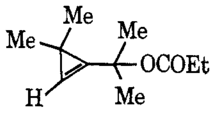


X XI

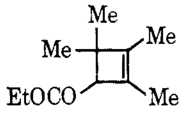


Compound D.—The n.m.r. analysis in $CDCl_3$ showed, besides a triplet and a quartet centered at τ 8.87 and 7.69 (J = 7 c.p.s.), resonance absorptions at τ 9.05, 8.90, 8.46, and 5.17. The relative areas under these peaks were in the ratio 3:2:3:3:6:1. The peaks at τ 8.46 and 5.17 were slightly broad, and it appeared that the protons representing these peaks might be coupled to each other. The infrared spectrum in CCl_4 showed bands at 5.75 and 8.45 μ (propionate group). The region between 5.80 and 6.90 μ was virtually transparent. In addition, two prominent bands were also present at 9.81 and 11.54 μ. A molecular weight of 182 was indicated by its mass spectrum.

The physical data accumulated above were considered in relation to the structures I, XII, and XIII.



XII



XIII

Structure XII could be disregarded immediately because a proton attached directly to a cyclopropene double bond occurs in the range τ 3.0–3.35.[12a] The chemical shift position of the single proton in the compound D lay distinctly outside this range.[12b] Since a clean distinction between I and XIII did not seem possible on the basis of physical data alone, it became necessary to establish the structure of the compound D by alternative means. Considerable evidence is available which shows that cyclopropanols undergo a base-catalyzed isomerization to the corresponding

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[7] A somewhat similar n.m.r. spectrum has been reported (M.I.T. Seminars in Organic Chemistry, Cambridge, Mass., First Semester, 1961–1962, Appendix, Spectrum No. 10) for 2,3-dimethyl-1,3-butadiene; the methyl protons at τ 8.12 are very slightly coupled to each of the two olefinic protons occurring at τ 5.10 and 5.07.

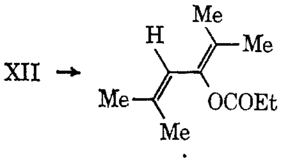
[8] M. S. Kharasch, W. Nudenberg, and E. Sternfeld, *J. Am. Chem. Soc.*, **62**, 2034 (1940).

[9] J. Walker and J. K. Wood, *J. Chem. Soc.*, 598 (1906).

[10] M. C. Flowers and H. M. Frey, *ibid.*, 5550 (1961).

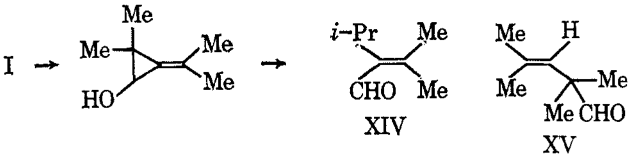
[11] A similar suggestion has been made [R. Hirschmann, C. S. Snoddy, Jr., C. F. Hiskey, and N. L. Wendler, *J. Am. Chem. Soc.*, **76**, 4013 (1954)] to explain the formation of camphene in the base-catalyzed decomposition of camphor tosylhydrazone.

[12] (a) G. L. Closs and L. E. Closs, *ibid.*, **85**, 99 (1963). (b) The compound XII has been prepared by G. L. Closs [Organic Colloquium, Harvard University, March 17, 1964] and shown to rearrange to the diene i on heating to 140°. The compound D was reasonably stable under these conditions.

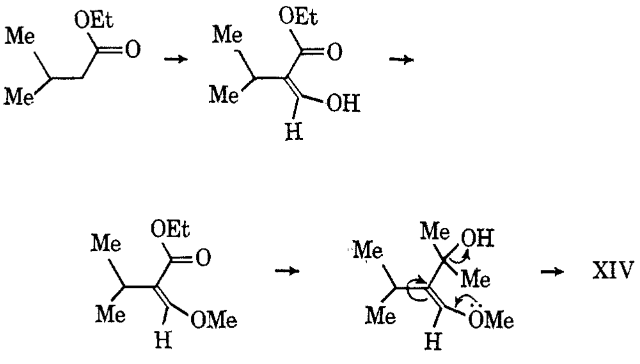


i

aldehydes.[13,14] It was expected that a compound with structure I would be transformed upon hydrolysis to one or both of the possible aldehydes XIV and XV.

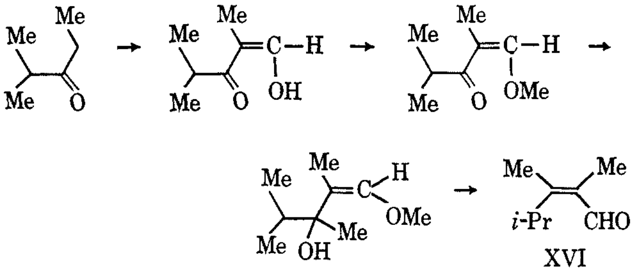


The compound D was successfully hydrolyzed by boiling with oxygen-free water in the presence of catalytic amounts of sodium hydroxide. That the product of hydrolysis was an α,β-unsaturated aldehyde was indicated by its strong absorption at 247 mμ in its ultraviolet spectrum.[15] (The presence of a band at τ 0.05 in the n.m.r. spectrum of the hydrolysis product further suggested the presence of an aldehydic function.) This was further confirmed by the successful transformation of the aldehyde into its 2,4-dinitrophenylhydrazone (m.p. 166–169°). The latter compound was shown to have the expected carbon–hydrogen composition. Its substitution pattern was readily discernible from the ultraviolet spectrum of the 2,4-dinitrophenylhydrazone which showed absorption bands at 385 mμ (ε 26,200), 293 (8000), 259 (14,300), and 220 (12,900), expected for an α,β,β-trisubstituted α,β-unsaturated aldehyde 2,4-dinitrophenylhydrazone.[16] An authentic sample of the expected aldehyde XIV was prepared from the readily available ethyl isovalerate *via* the following sequence of transformations.



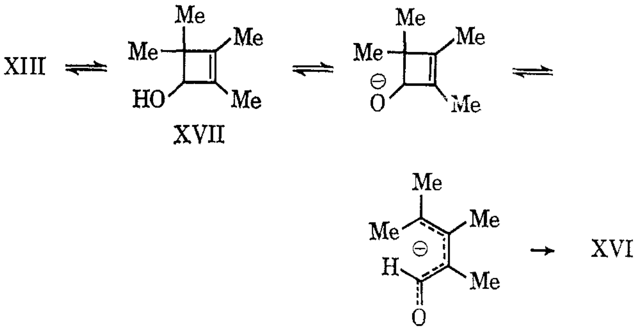
The crystalline 2,4-dinitrophenylhydrazone prepared from the synthetic aldehyde XIV melted at 166–166.5°. The infrared spectra of the two 2,4-dinitrophenylhydrazones were essentially identical (though there were slight differences in their fine details). The ultraviolet spectrum of the latter 2,4-dinitrophenylhydrazone displayed bands at 385 mμ (ε 25,200), 293 (6750), 259 (13,500), and 220 (14,400) and was virtually indistinguishable from that of the first 2,4-dinitrophenylhydrazone. The n.m.r. spectra of the two 2,4-dinitrophenylhydrazones were also very similar (see Experimental Section). The major difference lay in the relative separation of the resonance lines due to the two methyl groups attached to the double bond. The mixture melting point of the two 2,4-dinitrophenylhydrazones, however, showed a considerable depression.

At this stage of the structural elucidation, Day and Whiting[17] reported a synthesis of I by an entirely different procedure. Although no proof was furnished for the carbon skeleton of the synthetic material, the reported n.m.r. data (which differed slightly from that observed for the compound D) seemed to be in good agreement with the structure I. Consequently, the compound D must be different from I. Barring structures I and XII, the evidence thus far pointed strongly toward the structure XIII for the compound D. The α,β-unsaturated aldehyde obtained upon hydrolysis of D must then be represented by the structure XVI. An authentic sample of the aldehyde XVI was prepared from 2-methyl-3-pentanone *via* the scheme outlined below.



The 2,4-dinitrophenylhydrazone of the aldehyde XVI was found to be identical with that obtained from the hydrolysis of the compound D, as indicated by their undepressed mixture melting point and superimposable infrared, ultraviolet, and n.m.r. spectra.

The formation of the α,β-unsaturated aldehyde XVI can be described by several different mechanistic pathways. A likely possibility may involve the hydrolysis of XIII to the cyclobutenol XVII which could rearrange to the observed aldehyde XVI as shown below.[18]



Experimental Section

Melting points were determined on a Kofler block and are corrected. Infrared spectra were taken on a Perkin-Elmer Infracord, Model 137. Ultraviolet spectra were taken on a Cary 14 recording spectrophotometer. N.m.r. spectra were measured on a Varian Associates A-60 spectrometer. Mass spectra were determined by Mr. D. Hoffman on an Associated Electrical Industries MS-9 double-focusing mass spectrometer. Elemental analyses were performed by Scandinavian Microanalytical Laboratories, Copenhagen.

3-Hydroxy-2,2,4,4-tetramethylcyclobutanone (III).—Hydroxy ketone III was readily obtained by the catalytic hydrogenation of 2,2,4,4-tetramethylcyclobutane-1,3-dione in the presence of commercial Raney nickel catalyst. The procedure reported by

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[13] G. W. Stahl and D. L. Cottle, *J. Am. Chem. Soc.*, **65**, 1782 (1943).

[14] C. H. Depuy, G. M. Dappen, and J. W. Hausser, *ibid.*, **83**, 3156 (1961); C. H. DePuy and L. R. Mahoney, *ibid.*, **86**, 2653 (1964).

[15] R. B. Woodward, *ibid.*, **64**, 76 (1942).

[16] E. A. Braude and E. R. H. Jones, *J. Chem. Soc.*, 498 (1945).

[17] A. C. Day and M. C. Whiting, *Proc. Chem. Soc.*, 368 (1964).

[18] Cyclobutenol XVII would be expected to isomerize more readily than the corresponding ester XIII. Temperatures in the vicinity of 200° may be predicted to be necessary to bring about any appreciable isomerization of the latter compound.

Hasek, *et al.*,[19] was essentially followed in this preparation. The yield of the hydroxy ketone (m.p. 115–116°, lit.[19] m.p. 114°) was 65%: λ^{KBr} 2.89 (OH), 5.75 μ (C=O).

Anal. Calcd. for $C_8H_{14}O_2$: C, 67.57; H, 9.93. Found: C, 67.60; H, 9.83.

3-Propionoxy-2,2,4,4-tetramethylcyclobutanone (IV).—Purified ketol III (99.4 g., 0.7 mole) and freshly distilled propionic anhydride (104.0 g., 0.8 mole) were stirred together at 80–85° for a period of 24 hr. The reaction mixture was cooled to room temperature, transferred to a separatory funnel, and shaken with 200 ml. of water. The aqueous layer containing propionic acid was discarded, and the oily residue was shaken with 200 ml. of 0.1 *N* sodium hydroxide. The upper layer was separated, washed with water, and finally dried over anhydrous sodium sulfate. Excess propionic acid and the anhydride were removed under reduced pressure, and the residual keto ester was purified by fractionation. The fraction boiling at 105° (19 mm.) was collected to yield 120.3 g. (88%) of the pure ester [the purity of the material was checked by vapor phase chromatography (retention time 65 min. on a 10-ft. Carbowax 20 M column operated at 94°, helium flow rate 40 cc./min.)]: λ^{neat} 5.61, 5.73, 8.35 μ; n.m.r. ($CDCl_3$) τ 8.90 (singlet), 8.85 (triplet), 8.82 (singlet), 8.75 (singlet), 8.64 (singlet), 7.65 (quartet), 5.28 (singlet) (relative areas 3:3:3:3:3:2:1), consistent with the assigned structure. The compound was analyzed as its tosylhydrazone II.

3-Propionoxy-2,2,4,4-tetramethylcyclobutanone Tosylhydrazone (II).—A portion of 3-propionoxy-2,2,4,4-tetramethylcyclobutanone (115.2 g., 0.6 mole) was dissolved in 220 ml. of methanol. *p*-Toluenesulfonylhydrazine (112.2 g., 0.6 mole) was added to the above solution. A few drops of hydrochloric acid were added and the contents were stirred for 48 hr. Most of the solvent was removed under reduced pressure and the precipitated solid was filtered under suction. The crude material was purified by recrystallization from methanol to afford 167.1 g. (yield 75%) of the desired compound melting at 133–135°: λ^{KBr} 3.06, 5.75, 6.26, 7.50, 8.41, 8.61 μ; n.m.r. ($CDCl_3$), τ 9.05 (singlet), 8.97 (singlet), 8.97 (triplet, central line of this triplet overlaps the singlet at 8.97), 8.93 (singlet), 8.82 (singlet), 7.67 (quartet), 7.64 (singlet), 5.73 (singlet), 2.75 (doublet, J = 8 c.p.s.), 2.58 (singlet), 2.22 (doublet, J = 8 c.p.s.). Relative areas under these signals were in the ratio 3:3:3:3:3:2:3:1:2:1:2.

Anal. Calcd. for $C_{18}H_{26}N_2O_4S$: C, 59.00; H, 7.15; N, 7.65; S, 8.73. Found: C, 58.81; H, 7.12; N, 7.75; S, 8.78.

Sodium Salt of II.—A solution of tosylhydrazone II (151.63 g., 0.42 mole) in 500 ml. of methanol was placed in a 2-l. Pyrex flask. Sodium methoxide powder (22.68 g., 0.42 mole) was added and the contents were warmed in a water bath maintained at 40° for 15 min. Methanol was removed under reduced pressure using a water bath maintained at 40–45°. The sticky solid was freed from the last traces of methanol by evacuation under 0.1 mm. for 18 hr. The solid was scraped off the sides of the flask and was reasonably pure to be used in the next step.

Decomposition of the Sodium Salt of II. Method A. Under Reduced Pressure.—A portion of the sodium salt obtained above (38.8 g., 0.1 mole) was placed in a 250-ml. flask having a side arm. The side tube was connected through a U-tube to a vacuum pump. The flask was mounted on a stand and clamped in such a manner as to allow the side arm to point downwards. The system was evacuated for 0.5 hr., flushed with nitrogen, and re-evacuated. The flask was heated in a hot-air oven at 130–140°, and the U-tube was cooled in liquid nitrogen during the period of decomposition. The products of the decomposition reaction had collected in the U-tube. After the completion of decomposition, the vacuum pump was disconnected and the assembly was allowed to come to room temperature. The inside of the flask was rinsed with *ca.* 15 ml. of *n*-pentane; the pentane extract was concentrated by removal of the solvent under reduced pressure and mixed with the main portion of the liquid in the U-tube. A total of 9.7 g. of a sweet-smelling oil was obtained in this manner. Vapor phase chromatography of this oil (Carbowax 20 M, 140°) indicated the presence of at least 13 components.

Method B. Decomposition in Acetamide.—Acetamide (240 g.) was melted in a flask equipped with a water-cooled condenser, a nitrogen inlet and outlet, and an efficient mechanical stirrer. Powdered sodium salt of the tosylhydrazone II (100.0 g., 0.258 mole) was added to the molten acetamide and the contents were stirred thoroughly. A slow stream of dry nitrogen was maintained over the surface of the reaction mixture. The temperature was raised to 120°; the decomposition proceeded smoothly as indicated by extensive frothing due to the evolution of nitrogen. The reaction was complete in about 4 hr. The reaction mixture was allowed to cool to room temperature, diluted with iced water, and transferred to a separatory funnel. The diluted mixture (*ca.* 700 ml.) was extracted thoroughly with *n*-pentane. The combined pentane extracts were washed with water and dried over anhydrous sodium sulfate. Filtration followed by evaporation of the solvent under reduced pressure (100 mm.) afforded a sweet-smelling oil (30.5 g.). The infrared spectrum of this oil included bands at 5.75 and 8.45 μ. The n.m.r. spectrum was highly complex. Vapor phase chromatography indicated the presence of at least 23 components. A partial separation was effected by column chromatography over silica gel.

Column Chromatography of the Above Mixture.—Silica gel (600 g.) was made into a slurry with hexane–ether (100:3 v./v.) and packed into a 2-ft. column. The oily mixture was diluted with 100 ml. of hexane–ether (100:3) and carefully placed on the column. Elution with the same solvent mixture furnished 9.5 g. of a pale yellow liquid (mixture A) whose vapor phase chromatography (Carbowax 20 M) indicated the presence of 11 components. The remaining material on the column, which was eluted with ether, consisted of *ca.* 20 g. of a thick oil. The components in the thick oil (mixture B) showed very high retention times and were assumed to be high molecular weight compounds and were not investigated further.

Separation of the Components of Mixture A.—For preparative-scale vapor phase chromatography several columns were tried under various conditions. A complete separation could not be effected. A 20-ft. column of Carbowax 20 M on Chromosorb P (60–80 mesh) operated at 140° (helium flow rate 200 cc./min.) was most effective for this mixture. Of the 11 peaks observed under these conditions, only fraction 1 (retention time 17 min.) and fraction 5 (retention time 43 min.) were obtained in a pure state. Fractions 2–4 each formed less than 1% of the total mixture and were not collected. Some fractions were not well separated and were collected together (*e.g.*, fractions 6 and 7). The infrared and n.m.r. spectra of only the pure compounds are listed. **Fraction 1** had retention time 17 min. (20% of mixture A); λ^{CCl_4} 3.29(s), 3.40, 5.65 (w), 6.20 (m), 7.01, 7.30, 7.65, 8.01, 10.40, 11.29 μ; n.m.r. spectrum (CCl_4), τ 8.17 (triplet, J = 1 c.p.s.), 5.08 (quartet, J = 1 c.p.s.), 3.84 (singlet) (relative areas, 3:2:1). **Fraction 5** had retention time 43 min. (18% of mixture A); λ^{CCl_4} 5.75, 8.45, 9.81, 11.54 μ; n.m.r. spectrum (CCl_4), τ 8.87 (triplet, J = 7 c.p.s.), 7.69 (quartet, J = 7 c.p.s.), 9.05 (singlet), 8.90 (singlet), 8.46 (slightly broad singlet), 5.17 (slightly broad singlet) (relative areas, 3:2:3:3:6:1).

Anal. Calcd. for $C_{11}H_{18}O_2$: C, 72.49; H, 9.96. Found: C, 71.68; H, 9.68.

Hydrolysis of Compund D (Fraction 5).—A 42.3-mg. sample of this compound was placed in a small Pyrex tube having a bulb at the bottom. Distilled water (freed from the dissolved gases by boiling for several minutes) (400 μl.) was introduced into the tube. A small drop of 0.1 *N* sodium hydroxide was added and the tube was thoroughly flushed with nitrogen, carefully sealed under a nitrogen atmosphere, and heated in an electric furnace at 150° for 48 hr. The tube was then cooled and the contents were transferred to a 15-ml. centrifuge tube. (This solution absorbed strongly at 247 mμ in the ultraviolet, and a portion of the hydrolyzed mixture showed an absorption signal at τ 0.05 in the n.m.r. spectrum). One milliliter of methanol was added to the contents of the centrifuge tube to obtain a homogeneous solution, followed by a dropwise addition of a 3% solution of 2,4-dinitrophenylhydrazine in 30% perchloric acid until a slight excess of the reagent had been added. An orange solid appeared immediately. The reaction mixture was stored in a refrigerator for several hours. The precipitated 2,4-dinitrophenylhydrazone was scraped off the sides of the tube and freed from the rest of the liquid by centrifuging. The resulting solid was dried under a slow stream of nitrogen and purified by chromatography over silica gel.

Purification of the 2,4-Dinitrophenylhydrazone.—Silica gel was made into a slurry and packed into a small glass column (6 × 0.5 mm.). The red 2,4-dinitrophenylhydrazone obtained above was dissolved in a small volume of dry benzene and introduced

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at the top of the column. Elution with dry benzene afforded a yellow liquid which left *ca.* 20 mg. of an orange-red 2,4-dinitrophenylhydrazone. Further purification was effected by recrystallization from methanol to furnish orange-red needles melting at 166–169°: mol. wt. (mass spectrum) 306; $\lambda_{\max}^{\mathrm{MeOH}}$ 385 mμ (ϵ 26,200), 293 (8000), 259 (14,300), 220 (12,900); n.m.r. spectrum ($CDCl_3$), τ 8.92 (doublet, J = 7 c.p.s.), 8.17 (singlet), 8.04 (singlet), 6.95 (heptet, J = 7 c.p.s.), 2.17 (doublet, J = 10 c.p.s.; each component of this doublet is further split into a doublet, J = 2 c.p.s.), 1.67 (singlet), 1.0 (doublet, J = 2 c.p.s.), −1.55 (singlet) (relative areas under these resonance signals, 6:3:3:1:1:1:1:1:1).

Anal. Calcd. for $C_{14}H_{18}N_4O_4$: C, 54.89; H, 5.92. Found: C, 54.80; H, 6.12.

Preparation of an Authentic Sample of the 2,4-Dinitrophenylhydrazone of α-Isopropyl-β-methylcrotonaldehyde (XIV). A. Ethyl 2-(Hydroxymethylene)-3-methylbutyrate.—To an ice-cooled suspension of sodium hydride (10.0 g., 53.3% mineral oil dispersion) in 45 ml. of anhydrous ether was added freshly distilled ethyl isovalerate (11.0 g., 0.084 mole) followed by ethyl formate (16.5 g., 0.223 mole). Addition of 1 drop of absolute ethanol started a vigorous reaction. A slow stream of nitrogen was maintained over the surface of the reaction which was cooled externally. After 70 hr., the reaction mixture was decomposed by adding crushed ice (100 g.). The aqueous layer was separated and the ether layer was extracted with a 50-ml. portion of 1 *N* sodium hydroxide. The combined aqueous layers were washed with ether and acidified with dilute sulfuric acid. The liberated oil was taken up in ether. The combined ether extracts were washed with water and dried over anhydrous calcium sulfate. Removal of ether yielded 4.8 g. (36%) of a crude oil. Purification by distillation under reduced pressure yielded 4.1 g. of the desired ester boiling at 78–79° (18 mm.). The liquid gave an intense violet color with alcoholic ferric chloride.

B. Methylation of the Above Hydroxymethylene Ester.—To a stirred suspension of freshly ignited potassium carbonate (4.0 g.) in 15 ml. of acetone (dried over potassium carbonate) was added a mixture of the hydroxymethylene ester (4.0 g.) and 3 ml. of methyl iodide dissolved in 5 ml. of acetone. The heterogeneous mixture was heated under reflux for 24 hr. The solid was removed by vacuum filtration. Evaporation of the solvent under reduced pressure afforded a residue (2.0 g.) which was used in the next step without further purification.

C. Treatment of the Methyl Ether from B with Methylmagnesium Iodide.—The crude enol ether obtained above was dissolved in 10 ml. of ether and added dropwise with efficient stirring to a solution of methylmagnesium iodide in ether (prepared from 1.0 g. of magnesium). After the addition was completed, the reaction was refluxed for 15 min. and then cooled. The reaction mixture was added with stirring to a mixture of 100 g. of ice and 5 g. of concentrated sulfuric acid. The resulting mixture was transferred to a separatory funnel and the organic layer was taken up in ether. The aqueous layer was extracted once with ether (10 ml.) and discarded. The ether extracts were combined, and the solution was concentrated by removing the ether under reduced pressure. Methanol (1 ml.) was added to the oily residue; the resulting solution was treated with 1 ml. of 25% aqueous sulfuric acid, and warmed on a water bath for 20 min. The reaction mixture was treated with a 3% solution of 2,4-dinitrophenylhydrazine in 30% perchloric acid. The precipitated red solid was quickly filtered, washed with dilute alcohol, and dried under vacuum at room temperature. Chromatography over silica gel using benzene as the eluent afforded *ca.* 30 mg. of the desired 2,4-dinitrophenylhydrazone. Further purification by recrystallization from methanol furnished orange-red needles melting at 166–166.5°: mol. wt. (mass spectrum) 306; $\lambda_{\max}^{\mathrm{MeOH}}$ 385 mμ (ϵ 25,200), 293 (6750), 259 (13,500), 220 (14,400); n.m.r. spectrum ($CDCl_3$), τ 8.92 (doublet, J = 7 c.p.s.), 8.17 (singlet), 8.14 (singlet), 6.95 (heptet, J = 7 c.p.s.), 2.34 (doublet, J = 10 c.p.s., 2.0 (singlet), 1.89 (doublet, J = 10 c.p.s.; each component of this doublet is further split into a doublet, J = 2 c.p.s.), 1.12 (doublet, J = 2 c.p.s.), −0.2 (singlet) (relative areas, 6:3:3:1:1:1:1).

Preparation of an Authentic Sample of the 2,4-Dinitrophenylhydrazone of α-Methyl-β-isopropylcrotonaldehyde (XVI). A. 1-Hydroxy-2,4-dimethyl-1-penten-3-one.—To an ice-cooled suspension of sodium hydride (20 g., 53.3% mineral oil dispersion) in 125 ml. of anhydrous ether was added a mixture of 2-methyl-3-pentanone (10.0 g., *ca.* 0.1 mole) and ethyl formate (46.4 g., 0.64 mole) (distilled from P_2O_5). One drop of ethanol was added to start the reaction (reaction vessel being cooled externally). A slow stream of nitrogen was maintained over the reaction mixture. After the initial reaction was over, the reaction mixture was allowed to stand at room temperature. The reaction mixture was then decomposed by slow addition of crushed ice and transferred to a separatory funnel. The aqueous layer was withdrawn, and the ether layer was extracted with 50 ml. of 1 *N* NaOH. The combined aqueous layers were washed with ether and acidified with dilute sulfuric acid. The precipitated semisolid was taken up in ether; the ether extract was washed with water and, after a brief drying over calcium sulfate, was stored over molecular sieves. Filtration, followed by evaporation of ether under reduced pressure, yielded a residue which weighed 8.24 g. (64%). The solid gave an intense violet color with alcoholic ferric chloride. Further purification was achieved by distillation under reduced pressure. The fraction boiling at 52–53° (10 mm.) was collected to give a liquid which solidified immediately to a white solid which melted at 45–46° (yield 6.25 g., 49%).

B. Methylation of the Hydroxymethylene Ketone (from Part A).—To a stirred suspension of freshly ignited potassium carbonate (1.5 g.) in 8 ml. of dry acetone was added a solution of 0.9 g. of the above hydroxymethylene ketone in 1 ml. of acetone. Methyl iodide (5 ml.) was added and the heterogeneous mixture was refluxed for 24 hr. The resulting thick paste was shaken with 5 ml. of ether and filtered under suction. Removal of ether yielded 1.1 g. of the crude enol ether which was used in the next step without further purification.

C. Treatment of the Enol Ether with Methylmagnesium Iodide.—An ethereal solution of methyl magnesium iodide, prepared from 0.24 g. of magnesium and 1.5 g. of methyl iodide in 10 ml. of anhydrous ether, was added to a solution of the enol ether (1.1 g.) in 5 ml. of ether. The reaction mixture was refluxed for 15 min., allowed to cool, and then decomposed by pouring into a mixture of 20 g. of ice and 2 g. of concentrated sulfuric acid. The oil solution was transferred to a separatory funnel, the ethereal layer was separated, and the aqueous layer was extracted with ether. The combined ether extracts were placed in a small flask, the ether was removed, and the residue was diluted with 0.5 ml. of methanol followed by treatment with 0.1 ml. of 25% aqueous sulfuric acid. The reaction mixture was heated under reflux for 15 min., cooled to room temperature, and treated with a 3% solution of 2,4-dinitrophenylhydrazine in 30% perchloric acid. An orange-red precipitate appeared almost instantaneously; this was filtered and washed with dilute methanol. The 2,4-dinitrophenylhydrazone was dried under vacuum to yield *ca.* 25 mg. of almost pure material. Further purification was effected by recrystallization from methanol to afford orange-red needles melting at 166–169°. This 2,4-dinitrophenylhydrazone was identical with the one obtained from the hydrolysis of compound D, as indicated by their undepressed mixture melting points and superimposable infrared and ultraviolet spectra: molecular weight (mass spectrum) was 306.

3-Propionoxy-2,2,4,4-tetramethylcyclobutanone Azine (VI).—Silica gel (20 g.) was packed into a column in ether–pentane (1:4 v./v.). The crude oil (from the decomposition of the sodium salt of II in acetamide) (0.9 g.) in 2 ml. of the ether–pentane mixture was placed at the top of the column. The column was eluted with the same solvent mixture. Fractions 1–6 left oily residues and were discarded. Fractions 7–10 gave the solid azine (0.166 g.). Recrystallization from methanol afforded white prisms: m.p. 100–101°; $\lambda^{\mathrm{CCl_4}}$ 5.75, 8.45 (propionate ester), 5.93 μ (C = N); n.m.r. ($CDCl_3$), a three-proton triplet at τ 8.85 (J = 7 c.p.s.), four methyl resonances at τ 8.84, 8.80, 8.69, and 8.59, a two-proton quartet (J = 7 c.p.s.) at τ 7.64, and a sharp one-proton singlet at τ 5.39.

Anal. Calcd. for $C_{22}H_{36}N_2O_4$: C, 67.31; H, 9.24. Found: C, 67.36; H, 9.32.

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