Anal. Calcd. for $C_{15}H_{21}ON$: C, 77.88; H, 9.15; N, 6.05. Found: C, 77.69; H, 9.32; N, 5.77; ultraviolet spectrum in dioxane: 2590 Å (ε 9400).

1,5-Bis(dimethylamino)-2,4-diphenyl-3-(3-hydroxybutyl)-3-pentanol (XIX), prepared from 0.075 mole of XIVb and 0.02 mole of lithium aluminum hydride, was a viscous material which could not be distilled or crystallized.

The dimethiodide was prepared in methanol; m.p. 248–249° dec. after recrystallization from methanol.

Anal. Calcd. for $C_{27}H_{44}O_2N_2I_2$: C, 47.52; H, 6.50; N, 4.11; I, 37.19. Found: C, 47.32; H, 6.56; N, 4.37; I, 37.37.

Hydrolysis of glutaramides XIVa *and* XIVb *to glutaric acids* XVII *and* XX, *respectively.* The amide (0.01 mole), suspended in a mixture of 80 ml. of water and 12 ml. of concd. sulfuric acid, was refluxed and stirred frequently for 3 hr. The precipitate was removed from the cooled mixture by filtration and was dissolved in an aqueous solution of potassium bicarbonate. After filtration, the alkaline solution was made acidic, filtered, and the precipitate was allowed to dry thoroughly.

2,4-Diphenyl-3-hydroxy-3-(3-hydroxypropyl)glutaric acid (XVII) was obtained in 80% crude yield; m.p. 198–199° recrystallization from ethanol.

Anal. Calcd. for $C_{20}H_{22}O_6$: C, 67.02; H. 6.19; neut. equiv. 179.2. Found: C, 67.04; H, 6.27; neut. equiv., 179.3.

2,4-Diphenyl-3-hydroxy-3-(3-hydroxybutyl)glutaric acid (XX) was obtained in 85% crude yield; m.p. 204–205° after recrystallization from acetic acid.

Anal. Calcd. for $C_{21}H_{24}O_6 \cdot \frac{1}{2}H_2O$: C, 66.13; H, 6.61; neut. equiv., 190.7. Found: C, 66.12; H, 6.40; neut. equiv., 190.1.

ANN ARBOR, MICH.

[CONTRIBUTION FROM ORGANIC CHEMISTRY BRANCH, CHEMISTRY DIVISION, U. S. NAVAL ORDNANCE TEST STATION]

The Base-Catalyzed Self-Condensation of α,β-Unsaturated Ketones. Condensation of Cyclopropyl Methyl Ketone with 2-Methylpropanal to Isomeric Diketones, $C_{18}H_{28}O_2$[1]

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The base-catalyzed self-condensation reactions of α,β-unsaturated ketones have been examined. It is suggested that each example may be pictured as an initial Michael condensation to an acyclic monoolefinic diketone, followed, in many instances, by a second, intramolecular Michael condensation or an aldol condensation. In the present study, cyclopropyl methyl ketone and 2-methylpropanal condense (through self-condensation of 1-cyclopropyl-4-methyl-2-penten-1-one, V) to epimeric, unconjugated, monoolefinic diketones, $C_{18}H_{28}O_2$ (X). Evidence supporting the structural assignments for these compounds is presented and discussed.

The mild base-catalyzed condensation of aldehydes with ketones, or the self-condensation of ketones, in an aldol condensation leads to ketols, or the derived α,β-unsaturated ketones. If forcing conditions, such as increased base concentration, a stronger base, elevated temperatures or prolonged reaction times are applied to this condensation, several other reactions may occur. For example, side reactions involving the aldehyde are especially favorable if the ketone is unreactive and the aldehyde has two alpha hydrogens.[2] Knoevenagel condensations leading to saturated acyclic 1,5-diketones may result when two or more mole-equivalents of ketone are employed.[3]

A less familiar possible occurrence in an aldehyde-ketone or ketone-ketone condensation under forcing conditions is the self-condensation of the initially formed α,β-unsaturated ketone itself. Several examples of the base-catalyzed self-condensation of various α,β-unsaturated ketones are now known where the structure of the (dimeric) product has been established.[4] In each case the self-condensation may be pictured as an initial Michael condensation at the α′-, α-, or γ-position (*e.g.*,

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(1) Presented at the Pacific Southwest Regional American Chemical Society Meeting, Los Angeles, Calif., December 3, 1960.

(2) α,β-Unsaturated aldehydes or polymers thereof are the products most frequently encountered. (a) S. G. Powell and A. T. Nielsen, *J. Am. Chem. Soc.*, **70**, 3627 (1948); (b) J. E. Dubois, *Ann. chim.* (*Paris*), (12), **6**, 406 (1951); (c) G. de Gaudemaris and P. Arnaud, *Compt. rend.*, **241**, 1311 (1955); (d) R. Heilmann, G. de Gaudemaris, P. Arnaud, and G. Scheuerbrandt, *Bull. soc. chim. France*, 112 (1957).

(3) These most often occur with aromatic ketones and aromatic aldehydes or alicyclic ketones and formaldehyde. They probably arise by a Michael addition of a ketone molecule to the initially formed α,β-unsaturated ketone. (a) The formation of benzamaron is an example; E. Knoevenagel and R. Weissgerber, *Ber.*, **26**, 436 (1893). For other examples see (b) W. Dilthey, *J. prakt. Chem.*, (2), **101**, 177 (1921), (c) St. v. Kostanecki and G. Rossbach, *Ber.*, **29**, 2245 (1896) and (d) J. Colonge, J. Dreux, and H. Delplace, *Bull. soc. chim. France*, 1635 (1956).

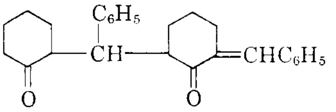
(4)(a) R. Dickinson, I. M. Heilbron, and F. Irving, *J. Chem. Soc.*, 1888 (1927); (b) E. R. H. Jones and H. P. Koch, *J. Chem. Soc.*, 393 (1942); (c) D. Iwanow and T. Iwanow, *Ber.*, **77**, 173 (1944); (d) H. Meerwein, *Ber.*, **77**, 227 (1944); (e) W. A. Ayer and W. I. Taylor, *J. Chem. Soc.*, 2227 (1955); (f) E. A. Braude, B. F. Gofton, G. Lowe, and E. S. Waight, *J. Chem. Soc.*, 4054 (1956); (g) D. B. Bright, *J. Am. Chem. Soc.*, **79**, 3200 (1957); (h) G. Büchi, J. H. Hansen, D. Knutson, and E. Koller, *J. Am. Chem. Soc.*, **80**, 5517 (1958); (i) M. N. Tilichenko and V. G. Kharchenko, *J. Gen. Chem.* (*U. S. S. R.*), **29**, 1909 (1959); (j) K. Kulka, R. J. Eiserle, J. A. Rogers, Jr., and F. W. Richter, *J. Org. Chem.*, **25**, 270 (1960); (k) R. Anet, *J. Org. Chem.*, **26**, 246 (1961). The products described in refs. (a), (i), (j), and k are derived from aldehyde-ketone condensations and those in (c), (d), and (f) from ketone-ketone condensations. Those in (b), (f), (g), and (h) are formed from various α,β-unsaturated alicyclic ketones.

in $\mathrm{R\overset{\alpha'}{C}H_2CO\overset{\alpha}{C}H{=}\overset{\beta}{C}H\overset{\gamma}{C}H_2R'}$) to form an acyclic monoolefinic 1,5- or 1,7-diketone. Three possible fates of this primary product could be predicted and examples of each type have been reported:

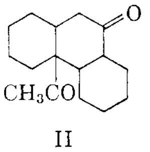
(1) The reaction may stop at the acyclic monoolefinic diketone stage (refs. 4g, i, k, and the example described in the present report).

(2) The unsaturated diketone may undergo an intramolecular Michael condensation to form a cyclic saturated diketone.[4b,h,5]

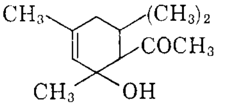
(3) The unsaturated diketone may undergo an intramolecular aldol condensation to yield a cyclic monoolefinic ketol[4c–f,h] or a cyclic diolefinic monoketone[4a,b] (the latter substances often readily derive from their ketol precursor[4c,d,f]). Reported examples of products illustrating each of these three types of behavior are compounds I (from benzylidenecyclohexanone[4i]), II (from 1-acetylcyclohexene[4b,5]), and III (from mesityl oxide[4f]).



I

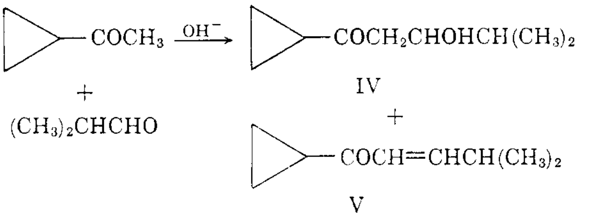


II



III

An interesting example of diketone formation resulting from a base-catalyzed aldehyde-ketone condensation has been described by Smith and Rogier.[6] These workers found that relatively mild reaction conditions (*N* ethanolic potassium hydroxide, two hours, 40° to room temperature) favored the condensation of cyclopropyl methyl ketone with 2-methylpropanal to the ketol (IV) and α,β-unsaturated ketone (V). Prolonging the reaction time under slightly more vigorous conditions (1.8*N* aqueous ethanolic potassium hydroxide, twenty-four hours, 45° to room temperature) led principally to a liquid (b.p. 140–147° at 1 mm.), part of which crystallized (compound *A*, m.p. 58°). Smith and Rogier found *A* to be an unsaturated diketone, $C_{18}H_{28}O_2$, but suggested no possible structures for this substance.



The experiments of Smith and Rogier have been reexamined and extended. They reported that the products formed under mild conditions (IV and V) were difficult to separate. We have found the purification of IV and V to be complicated by the presence of a third component in the mixture. Careful fractional distillation enabled us to produce rather pure V, but not pure IV. [Quantitative hydrogenation of V (platinum catalyst, one atmosphere) led to absorption of one mole-equivalent of hydrogen to form 1-cyclopropyl-4-methyl-1-pentanone (VI), which was isolated as its 2,4-dinitrophenylhydrazone derivative.] The contaminant in IV was separated and purified by distillation and found not to be V, but a material having no strong ultraviolet absorption and a relatively lower refractive index; strong carbon-oxygen single bond stretching absorption was noted in its infrared spectrum (1080 cm.$^{-1}$). On the basis of spectral and quantitative hydrogenation data the contaminant was found to be a ketone-ether having no hydroxyl group or olefinic unsaturation. The substance is believed to be 1-cyclopropyl-3-ethoxy-4-methyl-1-pentanone (VII), formed by addition of ethoxide ion to V. Elemental analysis supports this formula, and heating the crude VII with *p*-toluenesulfonic acid produced only V.

We have confirmed the formation of a high boiling liquid (b.p. 133–138°, 0.7 mm.) under vigorous reaction conditions similar to those described by Smith and Rogier (44% yield calculated as $C_{18}H_{28}O_2$). By careful fractional crystallization from methanol nearly one half of this liquid was crystallized as compound *A*. From the mother liquors remaining there was isolated a second compound (*B*), m.p. 16–18°; no other substances appeared to be present in the mixture.

Attention was first directed to the problem of establishing the structure of highly crystalline compound *A*. Elemental analysis and a molecular weight determination affirmed the molecular formula, $C_{18}H_{28}O_2$. The formation of a bis-2,4-dinitrophenylhydrazone derivative, m.p. 223–224°, reported by Smith and Rogier, was confirmed. In carbon tetrachloride solution the infrared spectrum of *A* revealed a single carbonyl stretching band at 1695 cm.$^{-1}$; in potassium bromide this band was

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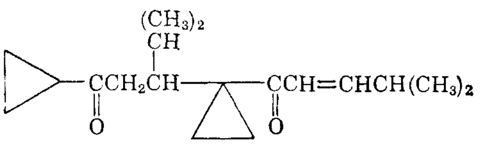
(5) A large number of saturated dimers of α,β-unsaturated ketones, derived from benzaldehyde or substituted benzaldehydes and methyl alkyl ketones by basic catalysts, have been prepared. Ref. 4h and (a) M. Scholtz and W. Meyer, *Ber.*, **43,** 1861 (1910); (b) I. M. Heilbron and F. Irving, *J. Chem. Soc.*, 2323 (1928); (c) I. M. Heilbron and F. Irving, *J. Chem. Soc.*, 931 (1929); (d) C. V. Gheorghiu and B. Arwentiew, *Bull. soc. chim. France* (4), **47,** 195 (1930); (e) C. V. Gheorghiu, *Bull. soc. chim. France* (4), **53,** 1442 (1933); (f) M. Metayer, *Rec. trav. chim.*, **71,** 153 (1952). In none of these examples has the structure of any dimeric product been established, although it has been stated by Heilbron that they are cyclobutane derivatives (refs. 5b,c). Jones and Koch (ref. 4b) have suggested, more reasonably, that the dimers are probably structurally similar to compound II. A dimer of 4-methyl-1-phenyl-2-penten-1-one, claimed to have a cyclobutane structure (ref. 4j), has recently been shown to be a monoolefinic diketone (ref. 4k).

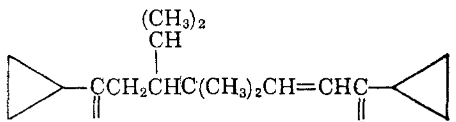
(6) L. I. Smith and E. R. Rogier, *J. Am. Chem. Soc.*, **73,** 3840 (1951).

split slightly (1695 and 1680 cm.$^{-1}$); hydroxyl stretching absorption was absent. [By comparison, a carbonyl stretching band at 1695 cm.$^{-1}$ was found in cyclopropyl methyl ketone (neat).] No strong ultraviolet absorption was found in the region of 210–260 mμ, although maxima were observed at 204.5 mμ (ϵ 14,500) and 286 mμ (ϵ 475). The substance decolorized potassium permanganate in acetone solution. On quantitative hydrogenation with platinum catalyst at one atmosphere one mole-equivalent of hydrogen was absorbed rapidly to yield a saturated diketone; additional hydrogenation proceeded very slowly. These preliminary findings indicate compound *A* to have two carbonyl groups (each attached to a cyclopropane ring) and one nonconjugated olefinic double bond.

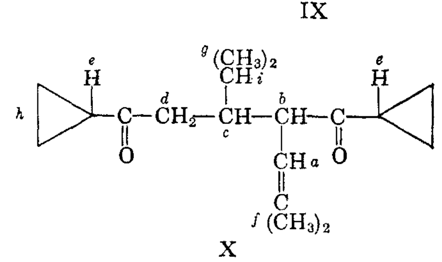
By considering the product (*A*) to form by a Michael addition of the anion of V to V itself, three structures of type 1, discussed above, are possible, depending on the position of attack by V anion. Attack of the cyclopropyl position to form VIII (or the β,γ-olefinic isomer) would be most unfavorable in view of the instability of the required anion intermediate.[7] Attack by the gamma position would lead to IX. Structure IX, as well as VIII, should be eliminated from consideration since the spectral data indicate no olefinic conjugation; the double bond in IX, it is noted, cannot shift to the β,γ-position. Structure X, formed by attack by the alpha position of V anion, agrees with all the above preliminary data.



VIII



IX



X

Structure X is clearly supported by the proton magnetic resonance spectrum (Fig. 1). The chemical shifts are referred to benzene (internal standard). Integrated peak heights and splitting patterns, as well as chemical shifts, were of assistance in making the line-group assignments shown (letters refer to protons labeled in structure X). Of the twenty-eight protons, all but three (types *e* and *i*) appear to be clearly defined in the spectrum. Of significance are the single vinyl proton (*a*), split by coupling with a single adjacent proton (*b*), and the six isopropylidene methyl protons (*f*). The cyclopropyl protons (*h*) are clearly at higher field than those of the isopropyl methyls (*g*), although some overlap is noted.[8,9]

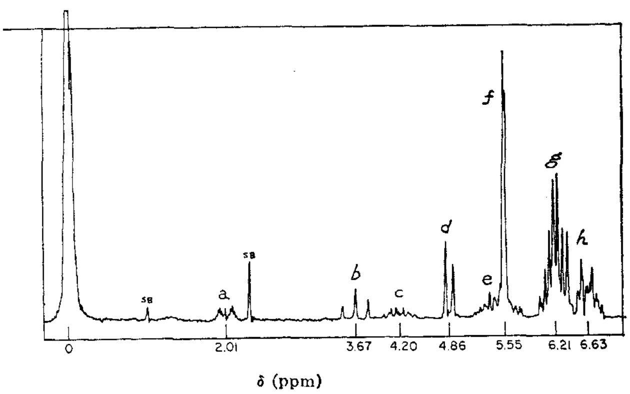
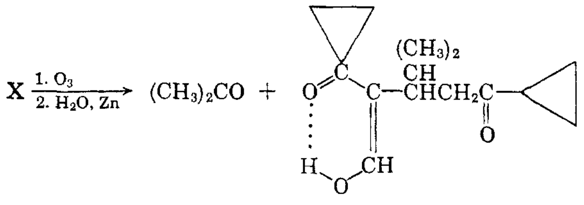


Fig. 1 Proton magnetic resonance spectrum of $C_{18}H_{28}O_2$, compound *A*, at 60 Mc. (benzene solvent and internal reference). Letters refer to hydrogens labeled in formula X; SB, side bands of benzene.

Chemical evidence for structure X was supplied by ozonolysis experiments. Decomposition of the ozonide by refluxing with water and zinc dust led to acetone (isolated as its 2,4-dinitrophenylhydrazone derivative) and an oil which produced a deep red color with ferric chloride. The enolic nature of the oil was affirmed by its infrared spectrum (OH stretching, 3500 cm.$^{-1}$); also evident were strong carbonyl absorption (1680 cm.$^{-1}$) and conjugated olefinic unsaturation (1620 cm.$^{-1}$). The enolic β-ketoaldehyde structure (XI) is suggested for this compound which, with acetone, is an expected ozonolysis product of X; an elemental analysis is in agreement with the formula, $C_{15}H_{22}O_3$. On quantitative hydrogenation XI readily absorbed one mole-equivalent of hydrogen before hydrogen



XI

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[7] The instability may be compared with that of the nitronate ion of nitrocyclopropane which does not form in basic solution; *cf.* H. B. Hass and H. Shechter, *J. Am. Chem. Soc.*, **75**, 1382 (1953).

[8] A phenyl analog of X (phenyl groups replacing cyclopropyls) has been described recently; structure assignment was made principally on the basis of magnetic resonance spectral evidence (refs. (4)(j,k)).

[9] We wish to thank Mr. Don Davis for obtaining some of our preliminary NMR spectra at the California Institute of Technology.

uptake ceased. When the ozonide of X was decomposed with refluxing aqueous hydrogen peroxide the products were acetone, carbon dioxide, cyclopropanecarboxylic acid, and an unidentified keto acid (not 4-cyclopropyl-2-isopropyl-4-ketobutanoic acid, the synthesis of which is described in the Experimental section).

The structure of the above-mentioned isomeric compound *B*, m.p. 16–18°, was next considered; its elemental analysis also agreed with the molecular formula $C_{18}H_{28}O_2$. Its proton magnetic resonance spectrum and infrared spectrum were essentially identical with those obtained for compound *A*. The ultraviolet absorption spectrum revealed no absorption in the 210–250 mμ region; maxima at 205 mμ (ϵ 9500) and 255 mμ (ϵ 1910). Compound *B* was characterized by mono and *bis*-2,4-dinitrophenylhydrazone derivatives, m.p. 128–130° and 222–223°, respectively. Ozonolysis of *B*, under conditions comparable to those used for *A*, led to the same products (acetone and compound XI). Compounds *A* and *B* could be interconverted with aqueous ethanolic potassium hydroxide without concurrent retrogression to V, or formation of a conjugated double bond. It was not possible to isomerize the β,γ-olefinic double bond in *A* or *B* (X) to the α,β-position with acid or basic catalysts. These results indicate the interconversion of *A* and *B* to result by epimerization at the reactive position *b* (X); the remaining asymmetric center at *c* would be expected to be insensitive to basic catalysts.

The observed formation of epimeric diketones having nonconjugated olefinic unsaturation to the apparent complete exclusion of other C_{18} products deserves comment.[8] It is known from the extensive investigations of Linstead and co-workers[10] that gamma dimethyl substitution and alpha alkyl substitution in olefinic ketones strongly favor the β,γ-position of the double bond. The failure of X to undergo further condensation to a diketone or ketol (reaction of types 2 and 3, above) may be explained by the unreactivity of the required cyclopropyl positions[7] and the unfavorable possibility of cyclobutane ring formation in a Michael condensation.[5,11]

EXPERIMENTAL[12]

Condensation of cyclopropyl methyl ketone with 2-methylpropanol (*Procedure A*). To 30 ml. of a solution of ethanolic potassium hydroxide (1*N*) and cyclopropyl methyl ketone (14.3 g., 0.17 mole) was added, dropwise, with stirring 8.8 g. (0.12 mole) of freshly distilled 2-methylpropanal. During the addition (15 min.) the temperature rose from 25 to 40°; stirring was continued for an additional 20 min. (temperature 30–40°). Dilute acetic acid was added and the mixture extracted twice with ether. The extracts were dried and distilled at 10 mm. to yield fractions (*a*) 2.4 g., b.p. 80–90° and (*b*) 9.18 g., b.p. 90–123°. The residue was distilled at 2 mm. to yield fraction *c*, 2 g., b.p. 140–151° and 0.5 g. of residue (*d*). Fractions *c* and *d*, dissolved in methanol and chilled, gave 0.36 g. of crystals, m.p. 35–45°, which on recrystallization melted at 54–55°.

Fractions *a* and *b* were combined and distilled through a 4-ft. center-rod column at 8 mm. to yield the following fractions: (*e*) b.p. 70–76°, n_D^{25} 1.4643, 2.6 g.; (*f*) b.p. 76–85°, n_D^{24} 1.4653, 2.5 g.; (*g*) b.p. 85–96°, n_D^{25} 1.4480, 1.8 g.; and (*h*) b.p. 96–100°, n_D^{25} 1.4582, 2.7 g. Fractions *e* and *f* contain mainly 1-cyclopropyl-4-methyl-2-penten-1-one (V) (31% yield) λ_{max} 223 mμ, ϵ 6900 and 8240, respectively (assumed mol. wt. 138); infrared bands (cm.$^{-1}$) at 1660 (C $=$ O), 1680 (C $=$ O) and 1620 (C $=$ C). Fraction *f*, b.p. mainly 79–81° (8 mm.), was used for analysis.

Anal. Calcd. for $C_9H_{14}O$: C, 78.21; H, 10.21. Found: C, 78.81; H, 10.43.

Fraction *g*, b.p. mainly 90–91° (8 mm.) was found to have no infrared OH stretching absorption; C $=$ O band at 1690 and shoulder at 1660 cm.$^{-1}$, weak C $=$ C band at 1620 cm.$^{-1}$; λ_{max} 223 mμ, ϵ 2560; found: C, 73.50; H, 11.47. A small sample of fraction *g* distilled at 1 atm. with a trace of *p*-toluenesulfonic acid gave V, n_D^{25} 1.4695, λ_{max} 223 mμ, ϵ 8050 (assumed mol. wt., 138). Hydrogenation of 0.173 g. of fraction *g* under conditions identical to those described below for reduction of V resulted in rapid absorption of 0.25 mole-equiv. of hydrogen during 2 min., after which time hydrogenation uptake proceeded very slowly. Absorption of 1 mole-equiv. of hydrogen gave an oil having a strong OH band (3500 cm.$^{-1}$) and very weak carbonyl absorption (1680 cm.$^{-1}$); the reduction product failed to yield a 2,4-dinitrophenylhydrazone. Fraction *g* is believed to contain about three-fourths 1-cyclopropyl-3-ethoxy-4-methyl-1-pentanone (VII) and approximately one-fourth V. A portion of fraction *g* was redistilled to yield a sample b.p. 86° (7 mm.), n_D^{25} 1.4442 which is believed to contain mainly compound VII; infrared absorption bands at 1620 and 1660 cm.$^{-1}$ were extremely weak and strong bands were observed at 1690 (C $=$ O) and 1080 (C—O) cm.$^{-1}$

Anal. Calcd. for $C_{11}H_{20}O_2$: C, 71.69; H, 10.94. Found: C, 71.69; H, 10.27.

Fraction *h* was found to have no ultraviolet absorption maximum at 223 mμ, but a weak band at 259 mμ (ϵ 545; assumed mol. wt., 156); infrared bands (cm.$^{-1}$) at 3600 (OH stretching) and 1680 (C $=$ O conjugated with cyclopropyl). Distillation with iodine gave V, as was reported by Smith and Rogier.[6] Fraction *h* is believed to contain mainly the ketol IV in addition to some VII; *anal.* Found: C, 70.63; H, 10.39. A portion of fraction *h* was redistilled to yield a sample, b.p. 101–102° (7 mm.), $n_D^{25.7}$ 1.4611, believed to contain mainly compound IV which was used for analysis.

Anal. Calcd. for $C_9H_{16}O_2$: C, 69.19; H, 10.32. Found: C, 70.14; H, 10.05.[13]

Hydrogenation of 1-cyclopropyl-4-methyl-2-penten-1-one. A 0.1909-g. sample of V (fraction *f*, above) was hydrogenated at 1 atm., 23° (platinum oxide, ethanol solvent, 1 drop of concd. hydrochloric acid). One mole-equivalent of hydrogen was absorbed within 4 min. after which time hydrogen uptake was much slower (0.03 mole-equiv. per min.). After 1.2 mole-equiv. of hydrogen was absorbed, the platinum was filtered and the filtrate concentrated to remove all volatile materials, leaving a sweet smelling oil, n_D^{25} 1.4390; strong

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(10)(a) R. P. Linstead's work on the effect of alkyl substitution on the position of the α,β- β,γ-equilibrium in various systems has been summarized in H. Gilman, *Organic Chemistry. An Advanced Treatise*, Second Edition, Vol. I, pp. 1041–43, John Wiley & Sons, New York, N. Y., 1943. (b) *cf.* G. A. R. Kon and K. S. Nargund, *J. Chem. Soc.*, 623 (1934).

(11) E. D. Bergmann, D. Ginsburg, and R. Pappo, *Org. Reactions*, **10**, 248 (1959).

(12) Melting points were obtained on a Kofler block and are uncorrected. Ultraviolet spectra were measured in 95% ethanol solvent. Infrared spectra of liquid samples were determined with the liquid itself unless otherwise stated.

(13) Reported for a sample of impure IV, b.p. 117–122° (9 mm.), $n_D^{27.2}$ 1.4611: C, 70.19; H, 10.60 (ref. 6).

C = O band at 1680 cm.$^{-1}$ The reduction product, principally *1-cyclopropyl-4-methyl-1-pentanone* (VI), was converted into its *2,4-dinitrophenylhydrazone* derivative; flat prisms from ethanol, m.p. 91–92°.

Anal. Calcd. for $C_{15}H_{20}N_4O_4$: C, 56.24; H, 6.29. Found: C, 55.55; H, 6.21.

Condensation of cyclopropyl methyl ketone with 2-methylpropanol (Procedure B). To a mixture of 24.5 g. (0.292 mole) of cyclopropyl methyl ketone, 30 ml. of ethanol, 10 ml. of water and 4.4 g. of potassium hydroxide (85% assay) was added dropwise, with stirring, 20.5 g. (0.282 mole) of freshly distilled 2-methylpropanal. During the addition (12 min.) the temperature rose from 23° to 53°; stirring was continued at 23–24° for 59.5 hr. The mixture was diluted with water and extracted with ether; the extracts were washed with sodium bicarbonate solution and dried. After removal of the solvent, the residue was distilled at 0.7–0.8 mm. to yield the following fractions: (1) b.p. 56–101°, 6.5 g.; (2) 101–133°, 1 g.; (3) b.p. 133–138°, 17 g. (mainly $C_{18}H_{28}O_2$ isomers, 44% yield); (4) undistilled residue, 1.8 g. Fraction 1 was redistilled at 0.3–0.4 mm. to yield fraction 1a, b.p. 44–84°, n^{25}_D 1.4605, 2.4 g. (λ_{max} 222 mμ); and 1b, b.p. 84–88°, n^{25}_D 1.4610, 3.1 g. (strong OH band at 3500 cm.$^{-1}$ and C=O at 1680 cm.$^{-1}$); found: C, 68.63; H, 11.08.

Fraction 3 was diluted with an equal volume of methanol and chilled to −15° to yield 5.2 g. of white crystals, m.p. 49–52°. By repeated crystallizations of the mother liquor from methanol an additional 2.9 g. of crystals was obtained, m.p. 50–54°; the total yield, 8.1 g., represents 48% of fraction 3. Two recrystallizations of the first crop of crystals from methanol gave long needles of compound *A*, m.p. 56–58° (reported,[6] m.p. 58°); λ_{max} 286 mμ, ϵ 475; 204.5 mμ, ϵ 14,500; shoulders (slight) at 220 and 238 mμ. Infrared absorption (carbon tetrachloride): 1695 (C=O) and 1655 cm.$^{-1}$, weak (C=C); in potassium bromide disk C=O bands at 1680 and 1695, and weak C=C at 1640 cm.$^{-1}$; no absorption in OH stretching region; supercooled liquid, 1685 (C=O); shoulder at 1650 cm.$^{-1}$ Cyclopropyl methyl ketone revealed a C=O stretching band at 1695 cm.$^{-1}$ (neat).

Anal. Calcd. for $C_{18}H_{28}O_2$: C, 78.21; H, 10.21; mol. wt. 276.2. Found: C, 78.26, 78.21; H, 10.11, 10.12; mol. wt. (Rast) 274, 290.

The bis-2,4-dinitrophenylhydrazone described by Smith and Rogier[6] was prepared; bright orange platelets from ethyl acetate, m.p. 223–224° (reported,[6] m.p. 222–223°).

The combined mother liquors remaining from the above crystallizations were distilled twice to yield an oil from which no further crystallization of compound *A* could be realized. This material is compound *B*; b.p. 115–120° (0.13 mm.), m.p. 16–18° (needles), n^{25}_D 1.493 (ultimate yield, 4 g.; much loss resulted during purification). Ultraviolet absorption: λ_{max} 205 mμ, ϵ 9500; 255 mμ, ϵ 1910 (broad); shoulder at 225 mμ; infrared absorption (neat); 1690 cm.$^{-1}$ (C=O); shoulders at 1668 (medium) and 1625 cm.$^{-1}$ (weak); in the liquid state the infrared spectrum resembles very closely that of compound *A*.

Anal. Calcd. for $C_{18}H_{28}O_2$: C, 78.21; H, 10.21. Found: C, 78.14; H, 10.40.

A bis-2,4-dinitrophenylhydrazone was prepared; bright orange platelets from ethyl acetate, m.p. 222–223°; when mixed with the bis-2,4-dinitrophenylhydrazone derivative of compound *A*, above, the melting point was lowered to 198–202°. The infrared spectra of the two derivatives (potassium bromide) revealed slight but significant differences; that from compound *A* had bands at 1020 and 720 cm.$^{-1}$, absent in the derivative of *B*; the derivative of *B* had bands at 1080 and 728 cm.$^{-1}$ not found in the derivative of *A*.

Anal. Calcd. for $C_{30}H_{38}N_8O_8$: C, 56.69; H, 5.70; N, 17.60. Found: C, 56.34; H, 5.99; N, 17.72.

From the mother liquors remaining from the preparation of the bis-2,4-dinitrophenylhydrazone of compound *B*, a mono-2,4-dinitrophenylhydrazone was isolated; yellow needles from ethanol, m.p. 128–130°; infrared bands (potassium bromide), cm.$^{-1}$; 1660 (C=O) and 1610 (C=N).

Anal. Calcd. for $C_{24}H_{32}N_4O_5$: C, 63.14; H, 7.07; N, 12.27. Found: C, 62.85; H, 6.90; N, 12.29.

Compound *B*, above, was partly isomerized to compound *A*. A 1.3-g. sample of *B*, 0.5 g. of potassium hydroxide, 1 ml. of water and 3 ml. of ethanol were mixed, and the mixture stirred at 35° for 7 hr. After standing at room temperature for 68 hr. the dark red mixture was diluted with water and extracted with ether. The ether extracts were washed with sodium bicarbonate solution and dried; evaporation of the ether gave 1.25 g. of yellow oil. By fractional crystallization from methanol, the reaction product gave a total of 0.44 g. of compound *A*, m.p. 53–56°. Distillation of the remainder gave no forerun and only material, b.p. 134–135°, (0.4 mm.), n^{25}_D 1.4928; infrared spectrum identical to compound *B*. Another experiment, employing slightly different conditions, starting with crystalline compound *A*, led to similar results (mixture of compounds *A* and *B* and no other products produced). The ultraviolet spectra of the products obtained in these experiments revealed no absorption maximum near 223 mμ.

Compound *A* (0.25 g.) was refluxed with 0.01 g of *p*-toluenesulfonic acid (no solvent) for a few minutes; the product had infrared and ultraviolet spectra of compound *A* and partly crystallized on standing to yield recovered *A*. In other similar acid-catalyzed experiments no product was found having strong ultraviolet absorption near 225 mμ or infrared absorption indicating a conjugated double bond.

Hydrogenation of $C_{18}H_{28}O_2$ (compound A). A 0.1006-g. sample of compound *A* was dissolved in ethanol containing 1 drop of sulfuric acid and 0.0185 g. of platinum oxide catalyst. The mixture was hydrogenated at 704.4 mm. and 24°. Within 10 min. 13.4 ml. (1 mole-equiv.) of hydrogen was absorbed, after which time hydrogenation ceased. In the absence of sulfuric acid no hydrogenation occurred in ethanol solvent. The reduction product was a colorless oil having strong carbonyl absorption (1690 cm.$^{-1}$) and no OH stretching absorption; it could not be crystallized and was not examined further.

A similar hydrogenation experiment was performed using acetic acid solvent and sulfuric acid promoter; 3 mole-equiv. of hydrogen was absorbed in 20 min. and two more mole-equivalents after 1 hr. of additional reaction time (5 mole-equiv. total) when hydrogen uptake ceased.

Ozonolysis of $C_{18}H_{28}O_2$, (compounds A and B) Procedure A. A 0.77-g. sample of crystalline compound *A* in 25 ml. of chloroform was treated with a stream of ozone (diluted with oxygen) until reaction was complete (as indicated by the rapid liberation of iodine from a potassium iodide solution into which the exit gases were passed). The solvent was removed *in vacuo* at room temperature and the ozonide decomposed by refluxing with water and zinc dust for 3 hr. while a stream of nitrogen was passed through the solution. The exit gases were passed through Johnson's 2,4-dinitrophenylhydrazone reagent to form a precipitate, m.p. 110–118°; it was recrystallized from ethanol and melted at 123–125° (when mixed with authentic acetone 2,4-dinitrophenylhydrazone, m.p. 124–125°, the melting point was not depressed).

After filtering the zinc and washing with ether, the aqueous part was extracted with ether and the combined ether extracts washed with sodium bicarbonate solution. The ether solution was dried and the ether removed to yield 0.56 g. of an orange oil; distillation gave 0.3 g., b.p. 102–103° (0.03 mm.); n^{25}_D 1.486; infrared bands (cm.$^{-1}$), neat: 3500 (OH), 1680 (C=O), 1620 (C=C). The substance (compound XI) produced a deep red color with aqueous ethanolic ferric chloride solution.

Anal. Calcd. for $C_{15}H_{22}O_3$: C, 71.97; H, 8.86. Found: C, 72.50; H, 9.41.

A 0.1065-g. sample of the above oil was hydrogenated by the procedure employed above for compound *A* (platinum catalyst, 1 atm.). One mole-equiv. of hydrogen was absorbed in 20 min., after which time hydrogenation practically ceased.

Compound *B* was also ozonized by the above procedure to produce acetone 2,4-dinitrophenylhydrazone, m.p. 110–116° (crude), and an oil, b.p. 121–125°, (0.5 mm.), which gave a deep red color with ferric chloride solution; its infrared spectrum was identical with the sample of XI obtained from compound *A*.

Ozonolysis of $C_{18}H_{28}O_2$, (compounds A and B) Procedure B. A 2.76-g. sample of compound *A* dissolved in chloroform was ozonized as described above. The ozonide was decomposed, after removal of the chloroform, by refluxing with 250 ml. of water and 2 ml. of 30% hydrogen peroxide for 5 hr., while a stream of nitrogen was passed through the solution. The exit gases were passed first through Johnson's 2,4-dinitrophenylhydrazine reagent followed by *Anhydrone* and *Ascarite* packed tubes. The *Ascarite* tube absorbed 0.33 g. (0.75 mole-equiv.) of carbon dioxide. Acetone 2,4-dinitrophenylhydrazone was isolated from the Johnson's reagent as in procedure A.

The residue remaining after refluxing was extracted with ether and washed with sodium bicarbonate solution. The neutral material, a yellow oil, was recovered from the ether and distilled; 0.25 g., b.p. 112–113° (0.3 mm.). It gave no color with ferric chloride solution; carbonyl absorption bands were observed at 1760, 1720, and 1680 cm.$^{-1}$ Acidification of the sodium bicarbonate extracts with hydrochloric acid, followed by ether extraction, led to 1.17 g. of material, b.p. 122–124° (0.15 mm.), n_D^{25} 1.4706; infrared bands: 2500–3500 cm.$^{-1}$ (OH stretching), 1725 (shoulder) and 1690 cm.$^{-1}$ (C=O stretching); found: C, 65.12; H, 9.96; neut. equiv., 192, 194. A 2,4-dinitrophenylhydrazone was prepared and crystallized (slowly) from methanol, m.p. 131–133°; found: C, 55.04; H, 5.44; N, 15.02. Ozonolysis of compound *B* by the same procedure also gave the above acidic material (infrared spectrum identical). The acid revealed significant differences in the infrared spectrum in the 7–9 μ region, when compared with the spectrum of 4-cyclopropyl-2-isopropyl-4-ketobutanoic acid (preparation described below).

The above aqueous part remaining after extracting with methylene chloride was made alkaline (*p*H 11) with sodium hydroxide and distilled to remove neutral impurities. The residue was diluted with water and made acidic (*p*H 1) with sulfuric acid and distilled. The distillate (1 l.) was neutralized with sodium hydroxide solution (0.011 mole-equiv. required) and concentrated to near dryness. The residue was acidified with sulfuric acid (*p*H 1) and extracted continuously with ether for 3 hr. Removal of the ether from the extract and distillation of the residue gave 0.27 g. of cyclopropanecarboxylic acid, b.p. 177° (699 mm.), m.p. 14–15°, neut. equiv. 85.6 (calcd. for $C_4H_6O_2$, 86). When mixed with an authentic sample of cyclopropanecarboxylic acid, m.p. 15–16°, the melting point was not depressed (reported,[14] 18.1°, b.p. 181.8–182°, 766 mm.). The infrared spectrum of the above acid was found to be identical with that of authentic cyclopropanecarboxylic acid.

4-Cyclopropyl-2-isopropyl-4-ketobutanoic acid. A solution of 2.0 g. of 1-cyclopropyl-4-methyl-2-penten-1-one (V), 6 ml. of ethanol, 2 ml. of water, and 1.1 g. of potassium cyanide was refluxed for 21 hr. Potassium hydroxide (3.0 g., 85% assay) was added and refluxing continued for 8 hr., during which time ammonia was continuously evolved. After cooling and diluting with water the mixture was extracted with ether. The aqueous part was acidified with hydrochloric acid and extracted with ether. The ether solution was extracted with sodium bicarbonate solution, and the aqueous part extracted once with ether before acidifying with dilute hydrochloric acid. After extraction with ether, the ether solution was dried and the ether removed to yield 1.80 g. of the crude acid. Distillation gave 1.4 g. (52% yield), b.p. 126–128° (0.4 mm.), n_D^{25} 1.4714; viscous liquid having a faint pleasant odor; infrared bands, neat, cm.$^{-1}$: 2500–3500, broad OH stretching; 1690 (ketone) and 1725, shoulder (carboxyl), C=O stretching.

Anal. Calcd. for $C_{10}H_{16}O_3$: C, 65.19; H, 8.75; mol. wt., 184. Found: C, 65.45; H, 9.22; neut. equiv., 186 (by direct titration with 0.1*N* sodium hydroxide).

A *2,4-dinitrophenylhydrazone* was readily prepared, needles from ethanol, m.p. 183–184°; infrared (potassium bromide disk) cm.$^{-1}$: broad OH stretching, 2500–3500; C=O, 1690.

Anal. Calcd. for $C_{16}H_{30}N_4O_6$: C, 52.74; H, 5.53; N, 15.38; mol. wt., 364.3. Found: C, 52.41; H, 5.02; N, 15.24; neut. equiv., 364 (by direct titration with 0.1*N* sodium hydroxide).

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[14] P. Bruylants and A. Stassens, *Bull. acad. roy. Belg.*, 702 (1921); *Chem. Abstr.*, 17, 2872 (1923).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, DUKE UNIVERSITY]

Alkylations at the α-Carbon of Phenylacetamide and Phenylacetic Acid Through Their Disodio Salts[1]

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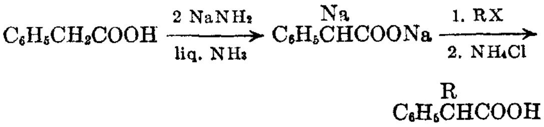
Disodiophenylacetamide, prepared from phenylacetamide and two molecular equivalents of sodium amide in liquid ammonia, was alkylated with alkyl and benzyl halides to give α-alkylphenylacetamides in good yields. α-Phenylethylation produced mainly *erythro*-2,3-diphenylbutyramide. Benzhydrylation was accompanied by self-alkylation of the halide to form tetraphenylethylene. The alkylations of disodio phenylacetate with *n*-butyl bromide and β-phenylethyl chloride are also reported.

Disodio phenylacetate has previously[2] been alkylated with benzyl, benzhydryl, and α-phenylethyl chlorides to form the corresponding α-substituted phenylacetic acids I (Equation 1).



$$C_6H_5CH_2COOH \xrightarrow[\text{liq. NH}_3]{\text{2 NaNH}_2} C_6H_5\overset{\text{Na}}{C}HCOONa \xrightarrow[\text{2. NH}_4\text{Cl}]{\text{1. RX}} C_6H_5\overset{\text{R}}{C}HCOOH \qquad (1)$$

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This method has now been extended to include alkylations with *n*-butyl bromide and β-phenyl-

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[2] C. R. Hauser and W. J. Chambers, *J. Am. Chem. Soc.*, 78, 4942 (1956).