The Synthesis of β-Diketones Containing Chlorodifluoromethyl and Perfluoroethyl Groups and Certain Related Reactions[1]

RICHARD A. MOORE[2] AND ROBERT LEVINE

Department of Chemistry, University of Pittsburgh, Pittsburgh 13, Pennsylvania

Received December 26, 1963

A series of β-diketones of the type $RCOCH_2COR'$, where R = CF_2Cl and C_2F_5, and R′ = alkyl, aryl, and heterocyclic, has been prepared in high yields by the sodium methoxide-effected acylations of the appropriate ketones with methyl chlorodifluoroacetate and methyl pentafluoropropionate. While $CF_2ClCOCH_3$ (I) and $C_2F_5COCH_3$ (VII) may be acylated under basic conditions with the very reactive esters methyl chlorodifluoroacetate and methyl oxalate, respectively, they undergo aldol condensation when treated with sodium methoxide in the presence or absence of methyl benzoate. The reaction of equivalents of I and sodium methoxide for 24 hr. at room temperature gives a mixture of the aldol dimer (II), 1,5-dichloro-4-hydroxy-4-methyl-1,1,5,5-tetrafluoropentan-2-one, and the cyclized aldol trimer (IV), 2,4-dihydroxy-2,4,6-tris(chlorodifluoromethyl)-6-methyltetrahydropyran. Under similar conditions, VII gives a mixture of the aldol product, 1,1,1,2,2,6,6,7,7,7-decafluoro-5-hydroxy-5-methyl-3-heptanone (VIII), its dehydrated derivative, 1,1,1,2,2,6,6,7,7,7-decafluoro-5-methyl-4-hepten-3-one (IX), and 3-hydroxy-3-methyl-4,4,5,5,5-pentafluoropentanoic acid (X), and none of the cyclized aldol trimer (XIII), 2,4-dihydroxy-2,4,6-tris(pentafluoroethyl)-6-methyltetrahydropyran. However, III was obtained by refluxing VII for 72 hr. over barium hydroxide in a Soxhlet apparatus. When a mixture of VII, methyl benzoate, and sodium methoxide in ether was refluxed for 2 days, VII undergoes an unusual type of Claisen condensation to give pentafluoropropionylacetone (XV).

A number of β-diketones containing the trifluoromethyl[3-8] and the perfluoro-*n*-propyl[6,8] groups have been prepared by the sodium methoxide-effected acylations of the appropriate ketones with esters of trifluoroacetic and perfluoro-*n*-butyric acid. Since high yields of products (in some cases up to 90%) were obtained, the perfluorinated esters must be very reactive acylating agents. This is not too surprising since it was shown earlier[9,10] in this laboratory that, when esters of varying structure are subjected to reaction with ketone anions, those esters which have highly electrophilic carbonyl carbon atoms are very active in Claisen condensations. Thus, a highly electronegative perfluoroalkyl group would be expected to make an α-carbonyl carbon atom electron-poor and, therefore, electrophilic, and active in Claisen condensations.

To our knowledge, the synthesis of only one β-diketone containing the perfluoroethyl group, *i.e.*, $C_2F_5COCH_2COCH_3$ (prepared in 84.5% yield by the reaction of acetone with ethyl perfluoropropionate), has been reported[8] and, apparently, the preparation of β-diketones containing the CF_2Cl group are not in the literature. Therefore, a study was made of the synthesis of β-diketones containing the CF_2Cl and the C_2F_5 groups.

Two routes which may be envisioned as leading to the desired β-diketones are indicated.

$$\left.\begin{array}{ll}\text{route 1} & RCO_2CH_3 + CH_3COR' \\ \text{route 2} & R'CO_2CH_3 + CH_3COR\end{array}\right]\xrightarrow{NaOCH_3} RCOCH_2COR' + CH_3OH$$

R = CF_2Cl and C_2F_5
R′ = alkyl, aryl, and heterocyclic

Using route 1 a number of β-diketones containing halogenated alkyl, as well as alkyl, aryl, alicyclic, and heterocyclic, groups were prepared in 55–89% yields (Table I). The synthesis of β-diketones by route 2 involves the acylation of methyl perhaloalkyl ketones with nonhalogenated esters. Apparently the only reported base-catalyzed Claisen condensation involving the acylation of an alkyl perhaloalkyl ketone is the synthesis of hexafluoroacetylacetone by the reaction of 1,1,1-trifluoroacetone with ethyl trifluoroacetate using sodium ethoxide[3] or sodium metal[11] as condensing agent.

Since there are apparently no reported examples of the condensation of alkyl perhaloalkyl ketones with nonfluorinated esters under basic conditions, it was of interest to study the feasibility of using this method (route 2) to prepare β-diketones such as $RCOCH_2COC_6H_5$ (R = CF_2Cl and C_2F_5) which have been prepared in high yield, 89%, by route 1.

First, 1 equiv. of methyl benzoate (in anhydrous ether) was added to 1 equiv. of sodium methoxide (suspended in anhydrous ether) over a 10-min. period followed by the addition of 1 equiv. of CH_3COCF_2Cl (I) over a 5-min. period. The reaction mixture was stirred for 24 hr. at room temperature and processed. None of the desired β-diketone, $C_6H_5COCH_2COCF_2Cl$, was obtained. Instead, the ester was recovered essentially completely, and a 51% yield of 2,4-dihydroxy-2,4,6-tris-(chlorodifluoromethyl)-6-methyltetrahydropyran (IV), the solid, cyclized aldol trimer of I, was obtained. An attempt was made to minimize the formation of IV by adding an excess (1.5 equiv.) of the ester to 1 equiv. of sodium methoxide followed by the addition, over a 5-hr. period, of a dilute ether solution of 1 equiv. of the ketone. After the reaction mixture was allowed to stand at room temperature for 12 hr., it was processed. Again, the ester was almost completely recovered and the only product obtained was IV (43.5%).

To prove that the solid IV can arise from the ketone alone, a sample of I was treated with (a) sodium methoxide and (b) barium hydroxide. From both of these reactions there was obtained a mixture of products

---

(1) This work was performed under Contract No. AT(30-1)-670 between the U. S. Atomic Energy Commission and the University of Pittsburgh.

(2) This paper is based on part of a thesis presented by R. A. M. to the graduate faculty of the University of Pittsburgh in partial fulfillment of the requirements of the Ph.D. degree.

(3) A. L. Henne, M. S. Newman, L. L. Quill and R. A. Staniforth, *J. Am. Chem. Soc.*, **69**, 1819 (1947).

(4) J. C. Reid and M. Calvin, *ibid.*, **72**, 2648 (1950).

(5) R. Levine and J. K. Sneed, *ibid.*, **73**, 4478 (1951).

(6) L. B. Barkley and R. Levine, *ibid.*, **73**, 4625 (1951).

(7) L. B. Barkley and R. Levine, *ibid.*, **75**, 2059 (1953).

(8) J. D. Park, H. A. Brown, and J. R. Larcher, *ibid.*, **75**, 2753 (1953).

(9) J. K. Sneed and R. Levine, *ibid.*, **72**, 5219 (1950).

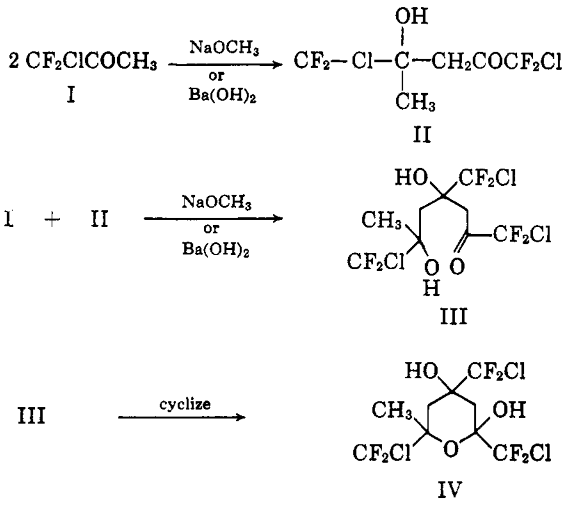
(10) R. Levine and J. K. Sneed, *ibid.*, **73**, 5614 (1951).

(11) R. N. Haszeldine, W. K. R. Musgrave, F. Smith, and L. M. Turton, *J. Chem. Soc.*, 609 (1951).

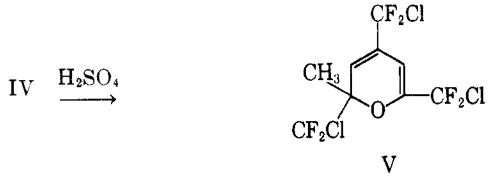
which consisted of the solid tetrahydropyran IV and the liquid aldol dimer (II), 1,5-dichloro-4-hydroxy-4-methyl-1,1,5,5-tetrafluoropentan-2-one.

The solids isolated from the last four reactions were shown to be identical by superimposition of their infrared spectra. The compound does not give an enol test with alcoholic ferric chloride solution and is not oxidized by neutral potassium permanganate at room temperature. On the basis of the above evidence and its elemental analysis, it appears that the compound has structure IV and is structurally analogous to 2,4-dihydroxy-2,4,6-tris(trifluoromethyl)-6-methyltetrahydropyran, which was obtained by Henne and Hinkamp[12] and Simmons and Wiley[13] when 1,1,1-trifluoroacetone was treated with sodium and potassium carbonate, respectively.

It was also found that IV can be obtained in 97% yield by the reaction of I with sodium, employing the procedure used earlier[12] in the analogous reaction with 1,1,1-trifluoroacetone. The tetrahydropyran IV described above may be envisioned as arising according to the following scheme.



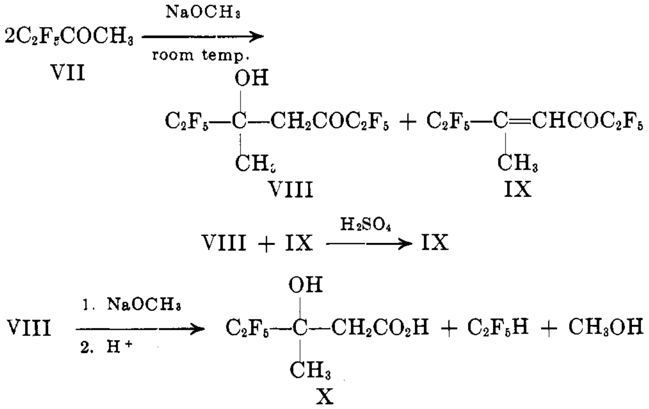
Further proof of the structure of IV was obtained by dehydrating it with concentrated sulfuric acid to form 2,4,6-tris(chlorodifluoromethyl)-2-methyl-2H-pyran (V) in 57.5% yield. The structure of V was elucidated by (a) carbon and hydrogen analysis, (b) its infrared spectrum, and (c) its proton and fluorine magnetic resonance spectra. The infrared spectrum of V showed that it is structurally similar to 2,4,6-tris(trifluoromethyl)-2-methyl-2H-pyran (VI).[12,14] In addition, treatment of a chloroform solution of V with aluminum chloride produces a deep red color while VI gives a magenta color[12] when similarly treated.



V

Since Henne, *et al.*,[3] were able to prepare hexafluoroacetylacetone in 72% yield and obtained none of VI by the sodium ethoxide-effected reaction of 1,1,1-trifluoroacetone with ethyl trifluoroacetate in refluxing ether for 50 hr., it was felt that the interaction of methyl benzoate, I, and sodium methoxide under comparable conditions might give the desired β-diketone, $C_6H_5COCH_2COCF_2Cl$. However, refluxing equivalents of the reactants for 47 hr. gave none of the diketone. Again, the only condensation product isolated was IV (39.0%). To show that a very active acylating ester, such as a fluorinated one, appears to be necessary to compete with the ketone for the anion of the ketone, a reaction was effected between equivalents of I, $CF_2ClCO_2CH_3$, and sodium methoxide at room temperature. There was obtained a 28% yield of what is probably $CF_2ClCOCH_2COCF_2Cl$. This liquid is extremely hygroscopic and changes to a white solid, presumably the dihydrate,[15] when exposed to air.

In general, attempts to effect the acylation of $CH_3COC_2F_5$ (VII) with methyl benzoate in the presence of sodium methoxide led to ketone self-condensation products. However, in contrast with the results obtained with I, VII does not form a cyclic trimer readily. Thus, the interaction of equivalents of VII and sodium methoxide at room temperature for 24 hr. gave what is probably a mixture of the ketone dimer, 1,1,1,2,2,6,6,7,7,7-decafluoro-5-hydroxy-5-methyl-3-heptanone (VIII), and its dehydrated derivative, 1,1,1,2,2,6,6,7,7,7-decafluoro-5-methyl-4-hepten-3-one (IX), and 22.5% of 3-hydroxy-3-methyl-4,4,5,5,5-pentafluoropentanoic acid (X). The mixture of VIII and IX was converted to IX by distilling it from concentrated sulfuric acid. The hydroxy acid X appears to arise by a haloform-type cleavage of the initially formed aldol product (VIII). The origin of X is analogous to the formation of 3-hydroxy-3-methyl-4,4,4-trifluorobutanoic acid which McBee, *et al.*,[16] isolated from the reaction of 1,1,1-trifluoroacetone with aqueous sodium or potassium hydroxide.



$$\underset{\text{VII}}{2C_2F_5COCH_3} \xrightarrow[\text{room temp.}]{NaOCH_3} \underset{\text{VIII}}{C_2F_5-\overset{OH}{\underset{CH_3}{C}}-CH_2COC_2F_5} + \underset{\text{IX}}{C_2F_5-\underset{CH_3}{C}=CHCOC_2F_5}$$

$$\text{VIII} + \text{IX} \xrightarrow{H_2SO_4} \text{IX}$$

$$\text{VIII} \xrightarrow[2.\ H^+]{1.\ NaOCH_3} \underset{\text{X}}{C_2F_5-\overset{OH}{\underset{CH_3}{C}}-CH_2CO_2H} + C_2F_5H + CH_3OH$$

The structure of X was established by (a) elemental analysis, (b) its infrared spectrum, (d) its proton and fluorine magnetic resonance spectra, and (d) its mass spectrum. The mass spectrum, at low ionizing potential, showed two bands at mass numbers 204 and 160, the latter being more intense. These mass numbers correspond to the masses of 3-methyl-4,4,5,5,5-penta-

---

[12] A. L. Henne and P. E. Hinkamp, *J. Am. Chem. Soc.*, **76**, 5147 (1954).

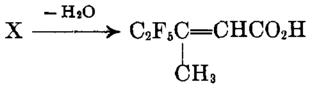
[13] H. E. Simmons and D. W. Wiley, *ibid.*, **82**, 2288 (1960).

[14] A sample of this compound was generously supplied by Professor A. L. Henne.

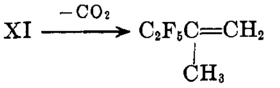
[15] B. G. Schultz and E. M. Larson [*J. Am. Chem. Soc.*, **71**, 3250 (1949)] have reported that $CF_3COCH_2COCF_3$ readily forms a dihydrate.

[16] E. T. McBee, D. H. Campbell, R. J. Kennedy, and C. W. Roberts, *ibid.*, **78**, 4597 (1956).

fluoropenten-2-oic acid (XI) and 2-methyl-3,3,4,4,4-pentafluoro-1-butene (XII) which are the dehydrated and the dehydrated decarboxylated derivatives of X, respectively.

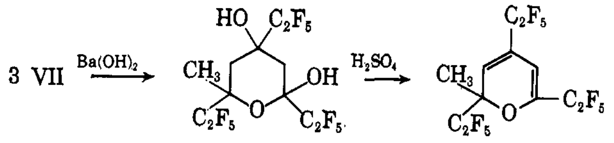

$$X \xrightarrow{-H_2O} C_2F_5\underset{CH_3}{\underset{|}{C}}{=}CHCO_2H$$

XI, mol. wt. 204


$$XI \xrightarrow{-CO_2} C_2F_5\underset{CH_3}{\underset{|}{C}}{=}CH_2$$

XII, mol. wt. 160

Although none of the cyclic trimer of VII was isolated in the previous reaction, refluxing a sample of VII over barium hydroxide in a Soxhlet apparatus for 72 hr. gave a 28% yield of the trimer, 2,4-dihydroxy-2,4,6-tris(pentafluoroethyl)-6-methyltetrahydropyran (XIII) which was dehydrated by concentrated sulfuric acid to 2,4,6-tris(pentafluoroethyl)-2-methyl-2H-pyran, (XIV) in 84% yield.

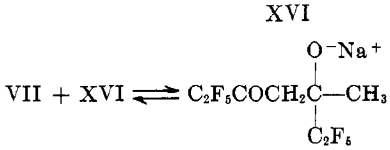


XIII XIV

Since attempts at room temperature (*vide supra*) to acylate I with methyl benzoate failed, it seemed superfluous to attempt the condensation of VII with methyl benzoate under these conditions. However, a condensation was effected at room temperature between VII and methyl oxalate (an ester known to be very reactive in Claisen acylations),[17] using sodium methoxide as the condensing agent, to give a 32% yield of methyl pentafluoropropionylpyruvate, $C_2F_5COCH_2COCO_2CH_3$. It seems, therefore, that as in the acylations of CH_3COCF_2Cl with $CF_2ClCO_2CH_3$ (*vide supra*), and of CF_3COCH_3 with $CF_3CO_2C_2H_5$,[3,11] a Claisen acylation of VII can be effected if a very active acylating agent is used in the reaction.

To determine whether there is any difference in reactivity towards methyl benzoate between I and VII due to the size of the perhaloalkyl group, a condensation was attempted by refluxing equivalents of VII, methyl benzoate, and sodium methoxide in ether for 2 days. Most of the ester (84%) was recovered and although none of the expected β-diketone, $C_6H_5COCH_2COC_2F_5$ was obtained, a small amount (20%) of another β-diketone, pentafluoropropionylacetone, $C_2F_5COCH_2COCH_3$ (XV), was isolated. The identity of XV was established by carbon–hydrogen analysis and by showing that its boiling point, refractive index, infrared spectrum, and the melting point of its copper chelate are identical with the corresponding properties of an authentic sample.[8]

$$\underset{VII}{C_2F_5COCH_3} + Na^+OCH_3^- \rightleftharpoons \underset{XVI}{C_2F_5COCH_2^-Na^+} + CH_3OH$$


$$VII + XVI \rightleftharpoons C_2F_5COCH_2\overset{O^-Na^+}{\overset{|}{\underset{\underset{C_2F_5}{|}}{C}}}{-}CH_3$$

XVII

$$XVII \longrightarrow NaF + CF_2{=}CF_2 + \underset{XV}{C_2F_5COCH_2COCH_3}$$

The formation of XV in this reaction, which involves an unusual type of Claisen condensation, was completely expected, and the mechanism for its formation is not known with certainty. However, a possible route by which its formation may be rationalized follows. The anion (XVI) of the ketone undergoes an aldol condensation with unchanged ketone (VII) to give the anion (XVII) of the aldol product, which may be decomposed at the temperature of refluxing ether to give XV, sodium fluoride, and tetrafluoroethylene. It should be pointed out that the presence of tetrafluoroethylene was not established. It is also possible that XVII decomposes to XV and sodium pentafluoroethide. The loss of perhaloalkyl groups under basic conditions is known. As has been mentioned above, the aldol dimer VIII of the ketone VII is cleaved to the β-hydroxy acid X by reaction with sodium methoxide at room temperature. Bergman[18] has reported that ethyl perfluoropropionate is cleaved in refluxing ethanolic sodium ethoxide to give a mixture of pentafluoroethane and diethyl carbonate. It is also of interest to note that Greene and Zook[19] have observed that methyl trityl ketone (XVI) reacts with sodium triphenylmethide at 210° to give 1,1,1-triphenylacetylacetone, $(C_6H_5)_3COCH_2COCH_3$. This β-diketone appears to arise from a route analogous to that described above for the formation of XV with the difference that the stable triphenylmethyl anion is eliminated from the initially formed aldol dimer of XVI.

Experimental

Halogenated Intermediates. A. Methyl Perfluoropropionate.—A mixture of perfluoropropionic acid (164 g., 1.0 mole), absolute methanol (48 g., 1.5 moles), and 50 ml. of concentrated sulfuric acid was refluxed for 19 hr., and the crude product was distilled from the reaction mixture. The ester was washed with a saturated sodium carbonate solution, a saturated calcium chloride solution, and finally with water. It was distilled from phosphorus pentoxide to give 160 g. (90%) of methyl perfluoropropionate, b.p. 59.5–61° (732 mm.).[20]

B. Methyl Chlorodifluoroacetate.—This ester was prepared by the procedure described above except that a 2.5-hr. reflux period was used. From a mixture of chlorodifluoroacetic acid (261 g., 2.0 moles, supplied through the courtesy of General Chemical Division of Allied Chemical Corporation), absolute methanol (96 g., 3.0 moles), and 100 ml. of concentrated sulfuric acid, there was obtained 261 g. (90%) of methyl chlorodifluoroacetate, b.p. 78.0–78.5° (738 mm.), $n^{25}D$ 1.3474.[21]

C. Methyl Pentafluoroethyl Ketone.—This ketone was prepared by the method of Dishart and Levine.[22] Thus, from the interaction of methylmagnesium iodide (1.8 moles) and pentafluoropropionic acid (98.5 g., 0.6 mole) in *n*-butyl ether at 35°, there was obtained 39.4 g. (40.0%) of methyl pentafluoroethyl ketone, b.p. 38–41° (737 mm.).[22]

D. Methyl Chlorodifluoromethyl Ketone.—This ketone was prepared using the procedure described above for the synthesis of methyl pentafluoroethyl ketone except that ethyl ether was the solvent. From the interaction of methylmagnesium iodide (3.0 moles) and chlorodifluoroacetic acid (130.5 g., 1.0 mole) in 1200 ml. of refluxing ethyl ether, there was obtained 50.0 g.

---

(17) C. R. Hauser, F. W. Swamer, and J. T. Adams, *Org. Reactions*, **8**, 65 (1954).

(18) E. Bergman, *J. Org. Chem.*, **23**, 476 (1958).

(19) J. L. Greene and H. D. Zook, *J. Am. Chem. Soc.*, **80**, 3629 (1958).

(20) D. R. Husted and A. H. Albrecht, *ibid.*, **75**, 1605 (1935).

(21) N. N. Yarovenko, S. P. Motornyi, and L. I. Kirenskaya, *Zh. Obsch. Khim.*, **27**, 2796 (1957); *Chem. Abstr.*, **52**, 8042*b* (1958).

(22) K. T. Dishart and R. Levine, *ibid.*, **78**, 2268 (1956).

(39.0%) of methyl chlorodifluoromethyl ketone, b.p. 54–55° (730 mm.), $n^{25}\text{D}$ 1.3417.[23]

Acylation of Ketones with Methyl Chlorodifluoroacetate and Methyl Perfluoropropionate. A. Procedure I.—This method is patterned after that used by Barkley and Levine[6] for similar reactions with methyl trifluoroacetate and methyl perfluoro-*n*-butyrate. To commercial 95% sodium methoxide[24] (6.0 g., 0.105 mole) suspended in 100 ml. of anhydrous ether, methyl chlorodifluoroacetate (14.4 g., 0.10 mole) of methyl perfluoropropionate (17.8 g., 0.10 mole) dissolved in 15 ml. of anhydrous ether was added in 10 min. To the rapidly stirred mixture (which had usually changed to a pasty consistency about half-way through the addition of the ester), the appropriate ketone (0.10 mole in 15 ml. of anhydrous ether) was added in 5 min. On the addition of the first few drops of the ketone, the gel-like, ester–methoxide–ether mixture changed to a liquid. Stirring was continued for 2 hr. after the addition of the ketone, and then the reaction mixture was allowed to stand at room temperature for the reaction time indicated in Table I. Then, glacial acetic acid (6.8 ml., 7.3 g., 0.12 mole, in 30 ml. of water) was added, followed by copper(II) acetate (14.7 g., 0.07 mole, in 133 ml. of warm water). The ether was distilled and the chelate which precipitated was filtered and washed with cold water and cold petroleum ether (b.p. 30–60°). The chelate was placed in a separatory funnel and was decomposed by shaking with a mixture of ether and 15% sulfuric acid. The ether was separated from the acidic, aqueous layer which was then extracted with several portions of ether. The combined ether extracts were dried over Drierite, the solvent was removed, and the residue was distilled to give the β-diketones which are listed in Table I.

B. Procedure II.—This method is a modification of procedure I. After the reaction times (Table I), 3.0 ml. of concentrated sulfuric acid in 30 ml. of water was added with stirring. The aqueous and ether phases were separated and the aqueous layer was extracted with several portions of ether. The combined ether extracts were treated as described in procedure I.

Attempted Benzoylation of Methyl Chlorodifluoromethyl Ketone (I). A. Interaction of Equivalents of Sodium Methoxide, Methyl Benzoate, and I at 25°.—Reaction of 95% sodium methoxide (6.0 g., 0.105 mole), methyl benzoate (13.6 g., 0.100 mole), and I (12.8 g., 0.100 mole) for 24 hr. according to procedure II gave 13.0 g. (96%) of recovered methyl benzoate, b.p. 84–85° (15–16 mm.), and 6.5 g. (50.8%) of 2,4-dihydroxy-2,4,6-tris-(chlorodifluoromethyl)-6-methyltetrahydropyran (IV), b.p. 83–98° (0.3 mm.), m.p. 91.2–92.2° from *n*-pentane. The infrared spectrum of IV is identical with that of an authentic sample (*vide infra*).

B. Interaction of Equivalents of Sodium Methoxide and I and Excess Methyl Benzoate with the Slow Addition of I at 25°.—Methyl benzoate (14.3 g., 0.105 mole, in 10 ml. of ether) was added in 10 min. to a slurry of 95% sodium methoxide (4.2 g., 0.074 mole, in 20 ml. of ether). Then, I (8.96 g., 0.07 mole, in 35 ml. of ether) was added over a 5-hr. period. The reaction mixture was allowed to stand for 12 hr. more at room temperature and processed by procedure II to give 13.1 g. (92%) of recovered methyl benzoate, b.p. 99–103° (31 mm.), and 3.9 g. (43.5%) of IV, b.p. 86–92° (0.3 mm.).

C. Interaction of Equivalents of Sodium Methoxide, Methyl Benzoate, and I in Refluxing Ether.—Methyl benzoate (13.6 g., 0.10 mole, in 15 ml. of ether) was added in 15 min. to 95% sodium methoxide (6.0 g., 0.105 mole, suspended in 100 ml. of ether). The mixture was heated to refluxing and I (12.8 g., 0.100 mole, in 20 ml. of ether) was added over a 30-min. period. The reaction mixture was refluxed for 47 hr. and processed by procedure II to give 12.6 g. (93%) of recovered methyl benzoate, b.p. 82–97° (13–25 mm.), and 5.0 g. (39.0%) of IV, b.p. 87–110° (0.2–1.0 mm.).

Acylation of Methyl Chlorodifluoromethyl Ketone (I) with Methyl Chlorodifluoroacetate.—Methyl chlorodifluoroacetate 21.7 g., 0.150 mole, in 30 ml. of ether) was added in 15 min. to 95% sodium methoxide (6.0 g., 0.105 mole, suspended in 75 ml. of ether). To the resulting, pasty mass, I (12.8 g., 0.100 mole, in 90 ml. of ether) was added over a period of 4 hr. The reaction mixture was stirred for 1 hr. at room temperature, was allowed to stand for 1 hr. more at room temperature and then was processed according to procedure I to give, after washing with ice–water and cold petroleum ether (b.p. 30–60°), 6.7 g. (33.5%) of the crude copper chelate, m.p. 105–120°, of what is presumably the β-diketone, $CF_2ClCOCH_2COCF_2Cl$. The chelate, which is slightly soluble in both water and petroleum ether, was recrystallized from 95% ethanol and melted at 117.2–120.2°. Decomposition of the chelate and processing according to procedure I gave on distillation 6.8 g. (28.2%) of the crude β-diketone, b.p. 118–128° (735 mm.), which is very hygroscopic and changes to a white solid, presumably the dihydrate,[15] m.p. 127–128° (in a sealed tube) without recrystallization. The crude β-diketone was distilled from phosphorus pentoxide using the method employed with hexafluoroacetylacetone,[15] but decomposition resulted and no isolable products were obtained.

Self-Condensation of Methyl Chlorodifluoromethyl Ketone (I). A. By Sodium Methoxide.—Ketone I (12.8 g., 0.10 mole in 15 ml. of ether) was added in 15 min. to 95% sodium methoxide (6.0 g., 0.105 mole suspended in 100 ml. of ether). The reaction mixture was stirred for 1 hr. at room temperature, allowed to stand for 24 hr., and processed according to procedure II to give 1.3 g. (10%) of II, 1,5-dichloro-4-hydroxy-4-methyl-1,1,5,5-tetrafluoropentan-2-one, b.p. 52–55° at 4 mm. and 75–77° at 12–13 mm. (*vide infra*), and 5.2 g. (40.5%) of crude 2,4-dihydroxy-2,4,6-tris(chlorodifluoromethyl)-6-methyltetrahydropyran (IV), b.p. 97–120° (1.25 mm.), m.p. 91.2–92.2° from *n*-pentane. The solid gave neither an enol test with alcoholic ferric chloride solution nor did it react with neutral potassium permanganate at room temperature. Its infrared spectrum, which was identical by superimposition with the spectra of the samples of IV obtained in attempted benzoylation expt. A–C, showed bands characteristic of OH (3500 cm.$^{-1}$),[25a] aliphatic C–H (2920 and 2980 cm.$^{-1}$),[25b] and aliphatic C–F (1400–1000 cm.$^{-1}$).[25c]

Anal. Calcd. for $C_9H_9Cl_3F_6O_3$: C, 28.04; H, 2.35; Cl, 27.59; F, 29.57. Found: C, 27.92; H, 2.23; Cl, 28.04; F, 30.03.

B. By Barium Hydroxide.—Using the employed method by Conant and Tuttle[26] for the self-condensation of acetone, a sample of I (25.7 g., 0.20 mole) was refluxed over barium hydroxide in a Soxhlet assembly using an oil bath as the heat source. After 6 hr. the bath temperature was 130° and heating was stopped. The liquid products were decanted and the apparatus was rinsed with *n*-pentane. The rinsings were added to the products and the combined organic material was distilled to give 9.8 g. (38%) of recovered I, b.p. 56–58° (735 mm.), and 7.0 g. (27.2%) of II, 1,5-dichloro-4-hydroxy-4-methyl-1,1,5,5-tetrafluoropentan-2-one, b.p. 75–77° (12–13 mm.) and 79.5° (24 mm.), $n^{25}\text{D}$ 1.4026.

Anal. Calcd. for $C_6H_6Cl_2F_4O_2$: C, 28.04; H, 2.35. Found: C, 27.70; H, 2.29.

The infrared spectrum of II showed bands characteristic of OH (3500 cm.$^{-1}$),[25a] aliphatic C–H (2900 and 3000 cm.$^{-1}$),[25b] aliphatic C–F (1400–1000 cm.$^{-1}$),[25c] and C=O adjacent to a perhaloalkyl group (1760 cm.$^{-1}$).[27]

In addition there was obtained 5.1 g. (20%) of IV, m.p. 89–91°.

C. By Sodium.—This reaction was effected by a modification of the procedure used by Henne and Hinkamp[12] for the cyclic trimerization of 1,1,1-trifluoroacetone. Ketone I (12.8 g., 0.10 mole) was added over 15 min. to sodium (2.3 g., 0.10 g.-atom, covered with 100 ml. of anhydrous ether) and the mixture was stirred intermittently for 24 hr. Then, 100 ml. of 20% hydrochloric acid was added cautiously to the vigorously stirred, thick, pasty reaction mixture which was kept at 0° with an ice bath. The phases were separated and the water phase was extracted with several portions of ether. The combined organic phases were dried over Drierite, the solvent was removed, and the residue was distilled to give 12.4 g. (97%) of IV, b.p. 97–101° (0.5 mm.), m.p. 89.6–92° (crude) and 91.2–92.2° from *n*-pentane. The infrared spectrum of this sample of IV is identical with the spectra of the samples of IV which are described above.

Dehydration of IV to 2,4,6-Tris(chlorodifluoromethyl)-2-methyl-2H-pyran (V).—Heating a sample of IV (5.0 g., 0.013 mole) at 150° for 12 hr. with 25 g. or concentrated sulfuric acid followed by distillation gave 2.6 g. (57.5%) of 2,4,6-tris(chloro-

---

[23] K. T. Dishart and R. Levine, unpublished observations.

[24] The sodium methoxide was purchased from Olin Mathieson Corp., Niagara Falls, N. Y.

[25] (a) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," 2nd Ed., John Wiley and Sons, Inc., New York, N. Y., 1958, p. 96; (b) p. 13; (c) p. 329.

[26] J. B. Conant and N. Tuttle, "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1941, p. 199.

[27] C. E. Griffin, *Spectrochimica Acta*, **16**, 1464 (1960).

TABLE I

SYNTHESIS OF β-DIKETONES, $RCOCH_2COR'$, CONTAINING CF_2Cl AND C_2F_5 GROUPS BY ACYLATING KETONES, CH_3COR', WITH HALOGENATED ESTERS, RCO_2CH_3

R	R′	Reaction hr.	Procedure	Yield, %	B.p. °C.	B.p. mm.	$n^{25}D$	Copper salt, m.p., °C.	Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found
CF_2Cl	C_6H_5	20	I	89	130–131 32.4–33.4 (m.p.)[a]	12		268–269.5[a]	$C_{10}H_7ClF_2O_2$	51.63	51.80	3.03	2.81
	CH_3	19	I	76	141	736	1.4347	148.2–148.8[a]	$C_5H_5ClF_2O_2$	35.21	35.02	2.96	2.71
	C_2H_5	20	I	73	158.5	735	1.4376	125.6–126.6[a]	$C_6H_7ClF_2O_2$	39.04	38.68	3.82	3.83
	n-C_3H_7	23	II	64	82	28	1.4406	76.4–77.8[a]	$C_7H_9ClF_2O_2$	42.33	42.39	4.57	5.00
	i-C_3H_7	41	II	69	72	22	1.4394	42–43[a]			41.96		4.49
	i-C_4H_9	17	II	82	91	32	1.4419	103–104[a]	$C_8H_{11}ClF_2O_2$	45.19	45.13	5.22	4.96
	t-C_4H_9	18	II	59	80	26	1.4411	103.2–104.8[a]			44.98		5.14
	n-C_5H_{11}	31	II	81	114.5	29	1.4455	*b*	$C_9H_{13}ClF_2O_2$	47.69	47.77	5.78	5.92
	n-C_6H_{13}	31	II	84	129.5	29	1.4468	*b*	$C_{11}H_{15}ClF_2O_2$	49.90	50.37	6.28	6.44
	2-C_4H_3S[c]	19	I	49	120.5	5	1.5995	253–256[a]	$C_8H_5ClF_2O_2S$	40.26	40.49	2.11	1.92
	2-C_4H_3O[c]	19	I	49	133	36	1.5665	237–239[a]	$C_8H_5ClF_2O_5$	43.17	43.35	2.26	2.17
	C_5H_8O[d]	17	II	70	102.5	32	1.4721	157–158[a]	$C_7H_7ClF_2O_2$	42.76	42.50	3.59	3.79
	$C_6H_{10}O$[d]	17	II	62	121	31	1.4781	154.6–155.8[a]	$C_8H_9ClF_2O_2$	45.62	45.92	4.31	4.33
	$C_{10}H_{10}$[d]	19	II	59	73.8–74.4 (m.p.)[e]			222.5–226[a]	$C_{12}H_9ClF_2O_2$	55.72	55.40	3.51	3.49
C_2F_5	C_6H_5	16	I	89	128.5	28	1.5033	260–261.5[a]	$C_{11}H_7F_5O_2$	49.63	49.43	2.65	2.73
	CH_3[f]	16	I	78	116	734	1.3706	111.4–112[e]					
	C_2H_5	18	II	82	133	737	1.3760	53.2–54.2[a]	$C_7H_7F_5O_2$	38.54	38.25	3.24	3.18
	n-C_3H_7	16	II	63	65.5	30	1.3848	*b*	$C_8H_9F_5O_2$	41.39	41.43	3.91	4.09
	i-C_3H_7	19	II	68	140	735	1.3834	63–65[a]			41.67		3.68
	i-C_4H_9	18	II	60	74.5	30	1.3902	67.6–68.4[a]	$C_9H_{11}F_5O_2$	43.91	43.62	4.50	4.53
	t-C_4H_9	19	II	65	65	30	1.3884	104.8–105.6[a]			44.10		4.63
	n-C_5H_{11}	22	II	67	186.5	725	1.3978	*b*	$C_{10}H_{13}F_5O_2$	46.16	46.08	5.03	4.80
	n-C_6H_{13}	18	II	74	89	10	1.4025	*b*	$C_{11}H_{15}F_5O_2$	48.17	48.43	5.51	5.58
	2-C_4H_3S[c]	19	II	68	92	2.8	1.5238	249–252[a]	$C_9H_5F_5O_2S$	39.71	38.85[b]	1.85	1.50
	2-C_4H_3O[c]	19	II	74	95.5	16	1.4939	199–201[a]	$C_9H_5F_5O_3$	42.20	43.09[g]	1.97	2.14
	C_5H_8O[d]	16	I	82	82	30	1.4070	103–105[a]	$C_8H_7F_5O_2$	41.75	41.64	3.07	3.19
	$C_6H_{10}O$[d]	18	II	55	104.5	42	1.4235	130.8–132[a]	$C_9H_9F_5O_2$	44.27	44.44	3.72	3.61
	$C_{10}C_{10}O$[d]	19	II	62	44.6–45.2 (m.p.)[a]			243.5–246[a]	$C_{13}H_9F_5O_2$	53.43	53.44	3.10	3.36

[a] Recrystallized from methanol-water. [b] Copper salt is a liquid at room temperature. [c] 2-C_4H_3S and 2-C_4H_3O are the 2-thienyl and the 2-furyl radical, respectively. [d] C_5H_8O, $C_6H_{10}O$, and $C_{10}H_{10}O$ are cyclopentanone, cyclohexanone, and 1-tetralone, respectively. [e] Recrystallized from methanol. [f] This compound was prepared by Park, *et al.* (see ref. 8). [g] The poor analysis is probably due to the fact that this compound is light sensitive.

difluoromethyl)-2-methyl-2H-pyran (V), b.p. 51.5° (2 mm.), $n^{25}\mathrm{D}$ 1.4205.

Anal. Calcd. for $C_9H_5Cl_3F_6O$: C, 30.92; H, 1.44. Found: C, 31.18; H, 1.14.

A sample of V, when treated with anhydrous aluminum chloride, gives a deep red color.[12,14] The infrared spectrum of V shows bands characteristic of olefinic C–H bonds (3145 cm.$^{-1}$),[28] methyl groups (3010, 2940, and 1449 cm.$^{-1}$),[28,29] and C–F linkages (1400–1000 cm.$^{-1}$).[25c] In addition, two bands, which are probably characteristic of the two differently substituted double bonds of V, were observed at 1684 and 1629 cm.$^{-1}$. The latter band is probably due to the allyl ether carbon–carbon double bond since it is the more intense and appears, due to conjugation, at a lower frequency than the triply substituted ethylene frequency.[30] The band at 1684 cm.$^{-1}$ is probably due to the other carbon–carbon double bond. An infrared spectrum of 2,4,6-tris(trifluoromethyl)-2-methyl-2H-pyran (VI)[12,14] showed that V and VI are the same type of compound.

The proton magnetic resonance spectrum[31] of V, taken at 40 Mc. in carbon tetrachloride, with tetramethylsilane as the internal standard, has bands at $\tau \simeq 4.12$ and $\simeq 8.30$ p.p.m. in the intensity of 2:3. The first band is probably due to the olefinic protons[32a] and the second is presumably due to the methyl protons.[32b] The F^{19} resonance spectrum,[31] at the same frequency and in the same solvent, with fluorotrichloromethane as internal standard, has bands at about $\phi \simeq 58$ and 61 p.p.m., and a doublet centered at 69, with intensity ratios of 1:1:1, which could arise from the two vinylic chlorodifluoromethyl groups and the chlorodifluoromethyl group on the asymmetric carbon atom,[33] respectively.

Self-Condensation of Methyl Perfluoroethyl Ketone (VII). A. **By Sodium Methoxide.**—Treatment of VII (16.2 g., 0.10 mole) with 95% sodium methoxide (6.0 g., 0.105 mole) in the manner described previously (expt. A) in the analogous reaction with I, gave 7.3 g. of liquid, b.p. 70–80° (82 mm.), which is probably a mixture of 1,1,1,2,2,6,6,7,7,7-decafluoro-5-hydroxy-5-methyl-3-heptanone (VIII) and 1,1,1,2,2,6,6,7,7,7-decafluoro-5-methyl-4-hepten-3-one (IX). This mixture was not subjected to elemental analysis. However, its infrared spectrum in carbon tetrachloride showed bands characteristic of hydroxyl groups (3500 cm.$^{-1}$),[25a] olefinic carbon–hydrogen bonds (3030 cm.$^{-1}$),[34a] aliphatic carbon hydrogen bonds (2950 cm.$^{-1}$),[25b] a carbonyl group α to a perfluoroalkyl group (1750 cm.$^{-1}$),[27] a conjugated carbonyl group (1700 cm.$^{-1}$),[34b] a carbon–carbon double bond (1580 cm.$^{-1}$),[34a] and carbon–fluorine bonds (1400–1000 cm.$^{-1}$).[25c]

In addition, 2.5 g. (22.5%) of X, 3-hydroxy-3-methyl-4,4,5,5,5-pentafluoropentanoic acid, m.p. 68.2–69.0° (from *n*-pentane), was isolated.

Anal. Calcd. for $C_6H_7F_5O_3$: C, 32.44; H, 3.18; F, 42.77. Found: C, 32.75; H, 3.49; F, 43.17.

The infrared spectrum of X in carbon tetrachloride has bands characteristic of a saturated carboxylic acid (3400, 3300–2800 cm.$^{-1}$)[35] and carbon–fluorine bonds.[25c] The mass spectrum[36] of X, at low ionizing potential, has two bands at mass numbers 204 and 160 (the latter more intense), corresponding to the mass of 3-methyl-4,4,5,5,5-pentafluoropenten-2-oic acid (XI, mol. wt. 204) and 2-methyl-3,3,4,4,4-pentafluoro-1-butene (XII, mol. wt. 160).

The proton magnetic resonance spectrum[31] of X taken at 60 Mc. in carbon tetrachloride with tetramethylsilane as the internal standard has bands at $\tau \simeq 2.50$ p.p.m. and 8.50 p.p.m. and a quartet centered at $\tau \simeq 7.25$ p.p.m. These data are characteristic of the protons of the hydroxyl groups (both carboxylic and alcoholic),[37] the methyl group,[32b] and a methylene group on an asymmetric carbon atom[32b] with an intensity of 2:3:2, respectively, indicative of two hydroxyl groups, three methyl protons, and two methylene protons. The F^{19} resonance spectrum[31] of X obtained at 40 Mc. from a water solution, with chlorotrifluoromethane as the external standard, has bands at $\phi \simeq 78$ and 124 p.p.m., which are characteristic of a perfluoroethyl group.[38]

Distillation of 4.4 g. of the liquid mixture of VIII and IX described above, from 15 ml. of concentrated sulfuric acid, gave 2.1 g. of material, b.p. 101–102° (737 mm.), $n^{25}\mathrm{D}$ 1.3170. Although an elemental analysis was not obtained on this compound, it is undoubtedly IX as evidenced by comparing its physical constants with those of the structurally closely related, unsaturated ketone, 1,1,1,5,5,5-hexafluoro-4-methyl-5-penten-2-one (b.p. 76°, $n^{20}\mathrm{D}$ 1.3260)[16] and by its infrared spectrum in carbon tetrachloride solution which has bands characteristic of olefinic carbon–hydrogen bonds (3030 cm.$^{-1}$),[34a] a conjugated carbonyl group (1725 and 1640 cm.$^{-1}$),[34b] and carbon–fluorine bonds (1400–1000 cm.$^{-1}$).[25c]

B. **By Barium Hydroxide.**—Treatment of VII (32.4 g., 0.20 mole) with barium hydroxide, as described above (experiment 5b) in the analogous reaction with I except that the reflux period was 72 hours, gave on distillation 12.3 g. (38%) of recovered VII, b.p. 40–41°, and 9.0 g. (28%) of 2,4-dihydroxy-2,4,6-tris(pentafluoroethyl)-6-methyltetrahydropyran (XIII, b.p. 84.5° at 24 mm., $n^{25}\mathrm{D}$ 1.3372). The infrared spectrum of XIII has bands characteristic of hydroxyl groups (3550 cm.$^{-1}$),[25a] aliphatic carbon–hydrogen bonds (2990 cm.$^{-1}$),[25b] and carbon–fluorine bonds (1400–1000 cm.$^{-1}$).[25c]

Anal. Calcd. for $C_{12}H_9F_{15}O_3$: C, 29.64; H, 1.87. Found: C, 29.41; H, 1.72.

Treatment of XIII (5.0 g., 0.01 mole) with 20 ml. of concentrated sulfuric acid for 12 hr. at 150–160° gave 3.8 g. (84%) of 2,4,6-tris(pentafluoroethyl)-2-methyl-2H-pyran [XIV, b.p. 61° (25 mm.), $n^{25}\mathrm{D}$ 1 3275]. Although this compound was not subjected to elemental analysis, from its boiling point and infrared spectrum in carbon tetrachloride solution, which has bands at the same frequencies as exhibited by 2,4,6-tris(chlorodifluoromethyl)2-methyl-2H-pyran (V) and 2,4,6-tris(trifluoromethyl)-2-methyl-2H-pyran (VI) in the 3100–1500-cm.$^{-1}$ region, there is little doubt about the identity of XIV.

Acylation of Methyl Pentafluoroethyl Ketone (VII) with Methyl Oxalate.—Methyl oxalate (11.8 g., 0.100 mole, in 75 ml. of anhydrous ether) was added over 25 min. to 95% sodium methoxide (6.0 g., 0.105 mole, suspended in 40 ml. of ether). Then, VII (16.2 g., 0.10 mole in 30 ml. of ether) was added over 6 hr. to the rapidly stirred reaction mixture. The mixture was allowed to stand at room temperature for 24 hr. and processed according to procedure II to give 8.0 g. (32%) of methyl pentafluoropropionylpyruvate, b.p. 62.5° (9 mm.), $n^{25}\mathrm{D}$ 1.3991.

Anal. Calcd. for $C_7H_5F_5O_4$: C, 33.88; H, 2.03. Found: C, 34.18; H, 2.1

The infrared spectrum of the product in carbon tetrachloride solution has absorption bands characteristic of olefinic carbon–hydrogen bonds (3050 cm.$^{-1}$)[34a]; carbonyl groups adjacent to perfluoroalkyl groups (1750 cm.$^{-1}$),[27] α to an ester function as in methyl pyruvate (1750 cm.$^{-1}$),[39] and in β-diketones (1650 and 1580 cm.$^{-1}$)[40]; and carbon–fluorine bands (1400–1000 cm.$^{-1}$).[25c] This compound gave a positive enol test with alcoholic ferric chloride solution and formed a green copper chelate, m.p. 232–235° dec. (from aqueous methanol).

Attempted Benzoylation of Methyl Perfluoroethyl Ketone (VII).—Methyl benzoate (13.6 g., 0.10 mole, in 15 ml. of ether) was added in 10 min. to 95% sodium methoxide (6.0 g., 0.105 mole, suspended in 100 ml. of ether). The mixture was heated to refluxing and VII (16.2 g., 0.100 mole, in 15 ml. of ether) was added in 10 min. Refluxing was continued for an additional 48 hr. and the reaction was processed according to procedure II to give (a) recovered methyl benzoate (11.4 g., 84%, b.p. 95–103° at 28 mm.), (b) 2.0 g. (20%) of pentafluoropropionylacetone [XV, b.p. 116.5° at 737 mm., $n^{25}\mathrm{D}$ 1.3693, blue-grey copper chelate, m.p. 111–112° from aqueous methanol,[8] infrared spectrum superimposable on that of an authentic sample (Table I)], and (c) 2.0 g. of material (b.p. 133–170° at 24 mm. and m.p 109–110° from *n*-pentane).

Anal. Calcd. for $C_6H_5F_5O_2$: C, 35.31; H, 2.47. Found: C, 35.61; H, 2.37.

To date, attempts to elucidate the structure of the solid, m.p. 109–110°, by chemical and physical methods, have failed.

---

(28) G. D. Meakins, *J. Chem. Soc.*, 4170 (1953).

(29) See ref. 25, p. 13.

(30) See ref. 25, p. 36, 40.

(31) We are indebted to Mr. J. J. Burke of Mellon Institute for the n.m.r. spectra and their interpretation. The spectra were obtained on a Varian Associates Model A-60 Proton Magnetic Resonance Spectrometer.

(32) (a) L. M. Jackman, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press, New York, N. Y., 1959, p. 61; (b) p. 53.

(33) See ref. 32, p. 101.

(34) (a) See ref. 25, p. 34; (b) ref. 25, p. 133.

(35) See ref. 25, p. 162.

(36) We are indebted to Mr. A. G. Sharkey and Miss J. Schultz of the Bureau of Mines Experiment Station, Bruceton, Pa., for running and interpreting this spectrum on a Consolidated Mass Spectrometer, Model 21-103.

(37) See ref. 32, p. 66.

(38) See ref. 32, p. 76.

(39) See ref. 25, p. 141, 184.

(40) See ref. 25, p. 142.