305, 313, 318 mμ (ε 34,200, 35,000, 5800, 5640, 9340, respectively); $\nu_{max}$ 1620 (C=N), 1560 cm.$^{-1}$, 785 cm.$^{-1}$, 752 cm.$^{-1}$.

**Acknowledgment.**—We are indebted to the National Institutes of Health (Grant CY-4474) to the University of Colorado Council on Research, and to Research Corporation for financial support of this work.

---

# The Acid-Catalyzed Conversion of Diethyl Ketone to Methyl Propyl Ketone—A Reinvestigation[1]

ARTHUR FRY, IKUO OOKUNI, GERASIMOS J. KARABATSOS, JOHN D. GRAHAM, AND FLOIE VANE

*Department of Chemistry, University of Arkansas, Fayetteville, Ark., and Kedzie Chemical Laboratory, Michigan State University, East Lansing, Mich.*

*Received December 11, 1961*

In a previous note,[2] Fry, Eberhardt, and Ookuni reported that diethyl ketone (3-pentanone) rearranged to the extent of 63% to methyl propyl ketone (2-pentanone) upon treatment with 70% perchloric acid for three hours at steam bath temperature. We have been unable to demonstrate such extensive rearrangement in more recent experiments at Michigan State University and at the University of Arkansas. 3-Pentanone is converted to 2-pentanone upon treatment with acid but not to as great an extent as previously reported.

When 3-pentanone is treated with perchloric acid, concentrated sulfuric acid, or benzenesulfonic acid under conditions which allow a reasonably large recovery (~20% or more) of nonpolymeric ketonic material, only a trace of 2-pentanone could be detected by NMR or gas chromatographic analysis of the pentanone fraction.

Under more drastic conditions in which the recovered ketonic fraction amounts to only a few per cent, up to 15% of the recovered pentanone fraction is 2-pentanone. The results of a series of experiments of this type are summarized in Table I.

It is clear that 2-pentanone is formed from 3-pentanone and that its concentration relative to that of 3-pentanone increases with time.[3] The extensive condensation to polymeric material prevents longer time studies. The possibility that the 2-pentanone did not come from the 3-pentanone at all, but that it might have been present as a trace impurity in the starting material and have been concentrated by undergoing a much slower condensation to polymeric material than the 3-pentanone was considered. This possibility was eliminated by showing that the pentanone fraction recovered from treatment of a 50:50 mixture of 2- and 3-pentanones with 70% perchloric acid at 100° for nine hours contained ~25% 2-pentanone and ~75% 3-pentanone. That the conversion is reversible was shown by treatment of 2-pentanone with ~70% perchloric acid at 75° for twenty-four hours. 3-Pentanone was shown to be present by NMR analysis, and the amount was estimated to be ~1% by gas chromatography.

TABLE I

PERCHLORIC ACID-CATALYZED CONVERSION OF 3-PENTANONE TO 2-PENTANONE$^a$

| Temp. | Time, Hr. | Recovered Material, B.P. 50–110°, % | Recovered Pentanone Fraction, % | 2-Pentanone in Recovered Pentanone Fraction,$^b$ % |
|---|---|---|---|---|
| 75 | 24 | $^c$ | $^c$ | 2 |
| 75 | 48 | $^c$ | 1.8 | 5$^d$ |
| 100 | 3 | 12.0 | $^c$ | 3 |
| 100 | 6 | 10.4 | 2.4 | 5 |
| 100 | 9 | 7.0 | 1.5 | 7 |
| 100 | 12 | 9.1 | 1.9 | 12$^e$ |
| 100 | 15 | 5.2 | 0.6 | 11 |
| 100 | 24 | 3.4 | 0.2 | 14 |

$^a$ Three milliliters of ~70% perchloric acid per gram of 3-pentanone. $^b$ Determined by gas chromatography (see Experimental). $^c$ Not determined. $^d$ Infrared analysis shows 6% 2-pentanone; NMR analysis shows 3–5% 2-pentanone. $^e$ Infrared analysis shows 14% 2-pentanone; NMR analysis shows 15.0% 2-pentanone. We are indebted to Dr. Harold F. Smith of Continental Oil Co. for this NMR analysis.

It is interesting to note that the iodoform reaction used in the identification of 2-pentanone in the previous report[2] is not completely reliable in characterizing the methyl ketone. Both 2- and 3-pentanones give iodoform under our usual conditions, although at greatly different rates. This type of behavior has been noted before by Cullis and Hashmi.[4]

## Experimental

**Conversion of 3-Pentanone to 2-Pentanone.**—A typical experiment is described here. Other experiments differed in the relative concentrations of acid and ketone used, the temperature, the time, and the acid used. These variables were changed over a wide range. Much less decomposition takes place in perchloric acid than in sulfuric acid, so perchloric acid was used in most cases. A mixture of 100 g. of 3-pentanone and 300 ml. of 71.7% perchloric acid was heated with stirring for 48 hr. in an oil bath at 75.0 ± 0.2°. The reaction mixture, initially light yellow, gradually turned almost black. The solution was poured into ice and neutralized with sodium hydroxide. The aqueous phase was saturated with sodium chloride and extracted with ether. The ether layer was distilled and several fractions were collected. Most of the organic material remained as a brown, viscous residue. Gas chromatography

---

[1] Supported in part by the U. S. Atomic Energy Commission.

[2] A. Fry, M. Eberhardt, and I. Ookuni, *J. Org. Chem.*, **25**, 1252 (1960).

[3] That this type of behavior is not restricted to this case is clear from the observation that treatment of 2-butanone-1-C$^{14}$ with perchloric acid results in the distribution of the label between the methyl and ethyl groups (I. Ookuni and A. Fry, unpublished data).

[4] C. F. Cullis and M. H. Hashmi, *J. Chem. Soc.*, 1548 (1957).

of the volatile fractions revealed the presence of several low boiling components in addition to 2- and 3-pentanone.[5]

The pentanone fraction was separated by preparative gas chromatography (10-ft. by $^1/_2$-in. column of butanediol succinate on chromosorb) and was shown to contain about 5% 2-pentanone and 95% 3-pentanone by gas chromatography on a 10-ft. by $^1/_8$-in. column of 20% triethylene glycol on firebrick. This sample was also analyzed by infrared, which revealed 6% of 2-pentanone in 3-pentanone, and by NMR, which showed 2-pentanone to be present to the extent of 3–5% in the 3-pentanone.

**Gas Chromatographic Separation of 2- and 3-Pentanone.**—2-Pentanone and 3-pentanone are difficult to separate by gas chromatography on many columns, especially when one component is present in small concentration. The quantitative analyses reported in Table I were taken on the triethylene glycol column mentioned above. When only small amounts are present, the 2-pentanone appears as a shoulder or small peak on the trailing edge of the 3-pentanone peak. For quantitative analysis, samples of known mixtures of 2- and 3-pentanone were run, and the ratio of the 3-pentanone peak height to the 2-pentanone peak height (corrected for the 3-pentanone tail) was plotted against the known concentration of 2-pentanone, giving a linear plot. The unknown samples were run and calculated in the same manner, and the composition was read from the graph. Less than 1% of 2-pentanone could be detected easily, and the error in the measurement at about 10–15% of 2-pentanone is estimated as $< \pm 1\%$ of 2-pentanone. One particular silicone column (but not a number of other silicone columns) also gives a separation of 2- and 3-pentanone, and in this case, in contrast to the triethylene glycol column, the 2-pentanone has the shorter retention time. A poly *m*-phenyl ether column also gives reasonable separation when the percentage of either ketone in the other is large.[6,7]

**NMR Analysis.**—The NMR spectra were taken at 60 Mc. with a Model V4300D Varian Associates spectrometer. The $\alpha$-methyl hydrogens (8.11 $\tau$) of 2-pentanone appear as a singlet with no interference from either the methylene (7.61 $\tau$) or methyl (8.96 $\tau$) hydrogens of 3-pentanone, or from the $\alpha$-methylene (7.62 $\tau$), $\beta$-methylene (8.82 $\tau$), or $\gamma$-methyl (8.96 $\tau$) hydrogens of 2-pentanone. One can easily detect 0.5% of 2-pentanone in 99.5% 3-pentanone.

**Infrared Analyses.**—The infrared analyses were run on a Perkin-Elmer Model 21 instrument. Preliminary work using 4% solutions of the ketone in carbon tetrachloride made use of the bands at 8.60 and 8.95 $\mu$. Later work utilized the 13.78-$\mu$ region where 2-pentanone shows a medium absorption band and the 3-pentanone spectrum is flat. Using the baseline density method, a straight line was obtained by plotting the absorbance *vs.* the % of 2-pentanone in known solutions. The compositions of the unknown mixtures were read from this graph.

**Derivatives of 2-Pentanone.**—It was thought to be desirable to furnish chemical proof of the presence of 2-pentanone in addition to the evidence from gas chromatography, infrared, and NMR spectra. Part of the pentanone fraction (4.0 g., containing ~2% 2-pentanone by gas chromatographic analysis) from a large scale reaction (250 g. of 3-pentanone, 36 hr., 75°) was subjected to the iodoform reaction. The iodoform collected amounted to 1.2 g. (nearly three times the theoretical amount from the 2-pentanone present—upon longer standing, even more iodoform is produced). The sodium salts of the acids produced were isolated in the usual fashion, and the *p*-toluidides were made. Fractional crystallization yielded the *p*-toluidides of butyric acid, m.p. 72–74°, reported[8] m.p. 72°, and of propionic acid (presumably from the 2-pentanone) m.p. 120–124°, reported[8] m.p. 124°.

Several 2-pentanone-rich samples of the pentanone fraction recovered from the acid treatment were combined and the 2-pentanone contained was concentrated by treatment with semicarbazide and fractional crystallization of the semicarbazone mixture. The ketone was regenerated from the enriched 2-pentanone semicarbazone by treatment with acid, and the 2-pentanone was further concentrated by gas chromatography using the analytical column. A sample of ~20 $\mu$g. of highly enriched 2-pentanone was obtained. The semicarbazone was prepared and subjected to fractional crystallization to the extent possible with the small amount of material present. The purest sample of the semicarbazone of 2-pentanone obtained had a m.p. of 108–109°, reported[9] m.p. 110°, mixed melting point with an authentic sample, 106–109°. (The melting point for the semicarbazone of 3-pentanone[9] is 139°).

---

(5) The nature and source of these other components will be the subject of a forthcoming communication.

(6) We are indebted to the Wilkins Instrument and Research Co. for suggesting this column.

(7) Since the completion of the major part of this work, Dr. E. Smith, University of Arkansas, Graduate Institute of Technology, has found that a firebrick column coated with 0.5% adiponitrile gives excellent separation of 2- and 3-pentanone. We wish to thank Dr. Smith for this information and for his helpful discussions of the separation problem. Very recently we have found that 0.5% $\beta,\beta'$-oxydipropionitrile on firebrick gives even better results.

(8) R. L. Shriner, R. C. Fuson, and D. Y. Curtin, "The Systematic Identification of Organic Compounds," 4th ed., J. Wiley and Sons, Inc., New York, 1956, p. 276.

(9) Ref. 7, p. 316.

---

# Methylation Studies of the 2-Methylindole–Methyl Isobutyl Ketone Condensation Product[1]

WAYLAND E. NOLAND AND H. S. DESAI[1a]

*School of Chemistry, University of Minnesota, Minneapolis, Minn.*

*Received December 11, 1961*

Condensation of 2-methylindole with methyl isobutyl ketone in ethanolic hydrochloric acid has recently been reported to give a monobasic 2:1 condensation product, isolated in dimorphic forms, m.p. 150–151° and 185–187°, in 11% yield.[2] The monobasic character and the ultraviolet spectrum of the condensation product indicate that both an indoline and an indole nucleus are present, and led to the suggestion of structure Ia, a product of a rather remarkable double bond shift, as a reasonable possibility.[2] We now wish to report methylation studies, analogous to those employed with the monobasic 2:2 cyclizative condensation product of 2-methylindole and acetone,[3] which confirm the presence of both a basic secondary nitrogen and a secondary nitrogen of the indole type in the molecule.

The preparation has been described[2] of an *N*-(in-

---

(1) It is a pleasure to acknowledge support of this research from the U. S. Public Health Service, through Research Grant CY-4073(C2) from the National Cancer Institute; (a) H. S. D., postdoctoral fellow 1960–1961.

(2) W. E. Noland, M. R. Venkiteswaran, and R. A. Lovald, *J. Org. Chem.*, **26**, 4249 (1961).

(3) W. E. Noland, M. R. Venkiteswaran, and C. G. Richards, *J. Org. Chem.*, **26**, 4241 (1961).