[Contribution from the Chemical Laboratories of the University of California]

# Condensation of Acrylonitrile with Unsymmetrical Ketones

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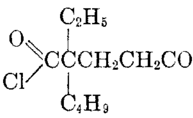
*Received January 3, 1956*

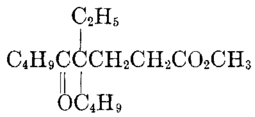
Cyanoethylation of four *n*-butyl *sec*-alkyl ketones has yielded a mixture of isomers in each instance. Each pair of isomers was separated by fractional distillation or converted to a mixture of the corresponding keto esters which was separated by fractional distillation. The isomeric compounds have been shown to result from cyanoethylation on either side of the carbonyl group. The proportion of cyanoethylation at the methinyl carbon decreases as steric hindrance at that position increases. The infrared spectra of two pairs of cyano ketones and four pairs of keto esters have been determined and used for correlations within the series of isomers. The compounds containing a quaternary carbon atom show several characteristic absorption bands in the infrared.

In an earlier investigation[1] in this laboratory, there was developed a method of synthesis of fatty acids with a quaternary carbon in the $\gamma$-position, and with all of the *gamma* substituents larger than methyl. In this synthetic sequence, the chain containing the quaternary carbon was formed by the reaction of a dialkylcadmium reagent with an ester-acid chloride (I) to give a keto ester (II).



$ClC(=O)C(C_2H_5)(C_4H_9)CH_2CH_2CO_2CH_3$

I

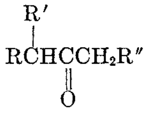


$C_4H_9C(=O)C(C_2H_5)(C_4H_9)CH_2CH_2CO_2CH_3$

II

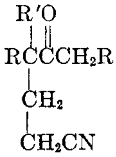
Reduction of the keto ester, II, yielded the desired acid with a quaternary carbon in the $\gamma$-position; however, the utility of the synthesis is decreased by the occurrence of the ester-acid chloride rearrangement[2] which resulted in concurrent formation of the analog of II which has the quaternary carbon in the $\alpha$-position.

The difficulties resulting from occurrence of the ester-acid chloride rearrangement have been avoided in an alternate synthesis published by Slater and co-workers[3] who formed the quaternary carbon atom by condensation of an unsymmetrical ketone (III) with acrylonitrile to give a keto nitrile (IV). Condensation of the acrylonitrile on the methinyl carbon, as shown in IV, rather than with the methylene carbon on the other side of the carbonyl group, was assigned by these authors on the basis of isolation of a solid product melting only slightly below the previously reported melting point for the quaternary carbon isomer. Bruson and Riener[4] had previously reported preferential condensation on methylene rather than methyl, on the basis of characterization of solid products. This synthesis would appear to be a considerable improvement over the earlier one,[1] provided the acrylonitrile condensation does occur exclusively at the methinyl carbon.



$RCH(R')C(=O)CH_2R''$

III

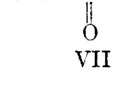


$RC(R')(CH_2CH_2CN)C(=O)CH_2R''$

IV

The earlier investigation[3] of the point of condensation of acrylonitrile was concerned with ketones of the general formula indicated by III, in which R and R′ were methyl; and product analysis consisted only of isolation of a single isomer. In order to evaluate the utility of the Slater method for the synthesis of pure quaternary-carbon acids, the present investigation has been directed to a careful examination of the condensation of acrylonitrile with four ketones of the general formula indicated by III. Unfortunately, condensation has been found to occur on either side of the carbonyl group, and separation of the resultant isomers is so difficult as to render the method of little utility for synthesis of pure compounds.

Ketones selected for the present investigation were 6-ethyl-5-decanone (V), 6-methyl-5-decanone (VI), 3-methyl-4-octanone (VII), and 2-methyl-3-heptanone (VIII). Each of these ketones was conveniently prepared by reaction of the appropriate $\alpha$-alkyl acid chloride with di-*n*-butylcadmium. Ketone V was selected for a study of optimum conditions for the acrylonitrile condensation, and the more significant results have been assembled in Table I. Among the conclusions which may be based on these data are the following:

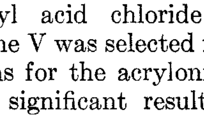


$C_4H_9CH(C_2H_5)C(=O)CH_2C_3H_7$

V

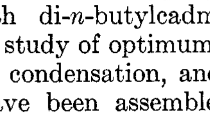
$C_4H_9CH(CH_3)C(=O)CH_2C_3H_7$

VI



$C_2H_5CH(CH_3)C(=O)CH_2C_3H_7$

VII



$CH_3CH(CH_3)C(=O)CH_2C_3H_7$

VIII

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(1) Cason, *J. Org. Chem.*, **13**, 227 (1948).

(2) Cason and Smith, *J. Org. Chem.*, **18**, 1201 (1953).

(3) Campbell, Carter, and Slater, *J. Chem. Soc.*, 1741 (1948).

(4) Bruson and Riener, *J. Am. Chem. Soc.*, **64**, 2850 (1942).

TABLE I
CYANOETHYLATION OF 6-ETHYL-5-DECANONE

| Run No. | Moles[a] of Acrylonitrile | Reaction Time, hrs. (60–65°) | Base[b] (g.) | Solvent[c] (ml.) | Moles of Ketone Recovered | Yield[d] Based on Ketone Consumed, % |
|---|---|---|---|---|---|---|
| 1 | 0.10 | 1 | KOH (1.5) | MeOH (4)<br>*t*-B. (25) | 0.068 | 45 |
| 2 | .10 | 2 | KOH (2.0) | MeOH (6)<br>*t*-B. (6) | .041 | 43 |
| 3 | .10 | 8 | KOH (2.0) | MeOH (6)<br>*t*-B. (6) | .056 | 44 |
| 4 | .21 | 2 | KOH (2.0) | MeOH (6)<br>*t*-B. (6) | .064 | 66[e] |
| 5 | .79 | 8 | KOH (2.0) | MeOH (6)<br>*t*-B. (50) | .016 | 8 |
| 6 | .14 | 2.5 | K (8.0) | *t*-B. (80) | .017 | 14 |
| 7 | .13 | 2.5 | BTA (1.3) | *t*-B. (10) | .060 | 20 |
| 8 | .10 | 5 | KOH (2.2) | *t*-B. (110) | .031 | 39 |
| 9 | .14 | 1.75 | KOH (0.23) | *t*-B. (8) | .061 | 65 |
| 10 | .12 | 2 | KOH (0.23) | *t*-B. (55) | .036 | 57 |
| 11 | .132 | 4.5 | KOH (0.19) | *t*-B. (19) | .071 | 73 |

[a] Calculations are on the basis of 0.1 mole of ketone. All runs were made at the 0.1–0.2 mole level except for run 11, which was a 1.0-mole run. [b] K refers to potassium *tert*-butoxide prepared by dissolving the indicated weight of potassium in *tert*-butyl alcohol. BTA refers to benzyltrimethylammonium hydroxide (Triton B). [c] *t*-B. refers to *tert*-butyl alcohol. [d] Yields are based on the weight of material boiling in the range 150–160° (5 mm.). The two isomeric keto nitriles formed in the reaction are included in this boiling point range, as well as significant amounts of a lower-boiling impurity (*cf.* Table V). [e] In this run, the product collected over the usual boiling point range, as specified in footnote (*d*), contained a considerable quantity of an impurity boiling slightly above the desired cyanoethylation product. Separation of this impurity was extremely difficult.

(1) Potassium hydroxide is the preferred base; stronger bases give very poor yields (Runs 6, 7).

(2) A small excess of acrylonitrile is optimum; a large excess gives lower yields or a product difficult to purify (runs 4,5).

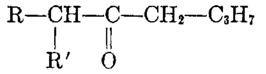
(3) Best results are secured with a relatively small amount of base, and a small amount of solvent is at least as satisfactory as larger amounts (runs 8–11).

(4) Best yields based on ketone consumed are secured when one-third to two-thirds of the starting ketone is recovered.

(5) Duration of reaction at 60–65° beyond 1 hour is of little significance (runs 1–3; 9–11).

Some of these conclusions (*i.e.*, amount of nitrile, amount of base, reaction time) may well be interdependent; however, over-all consideration of them strongly indicates that dicyanoethylation is a major side reaction. This is consistent with the finding that substitution may occur on either side of the carbonyl group.

TABLE II
ISOMER DISTRIBUTION IN CYANOETHYLATION OF KETONES



$\mathrm{R{-}\underset{\underset{R'}{|}}{CH}{-}\underset{\underset{O}{\|}}{C}{-}CH_2{-}C_3H_7}$

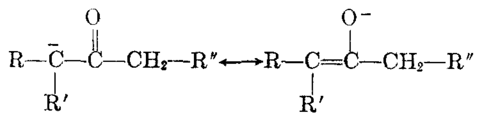
| | | % Substitution[a] on | |
|---|---|---|---|
| R | R' | Methinyl | Methylene |
| $C_4H_9$ | $C_2H_5$ | 25 | 75 |
| $C_4H_9$ | $CH_3$ | 61 | 39 |
| $C_2H_5$ | $CH_3$ | 37 | 63 |
| $CH_3$ | $CH_3$ | 87 | 13 |

[a] Results are based on product analysis by fractional distillation; composition of intermediate fractions was estimated by use of the index of refraction. Data in the first and last rows are based on the results of direct distillation of the keto nitriles resulting from cyanoethylation of the respective ketones. Data in the two middle rows are based on distillation of the keto esters resulting from methanolysis of the cyanoethylation products (*cf.* Experimental). Values are believed to be subject to an uncertainty of about ±10%; however, percentages for a given pair of isomers are more likely to be closer together than shown rather than further apart.

The cyanoethylation products of each of the four ketones, or the corresponding keto esters obtained by methanolysis of the keto nitriles, were subjected to fractional distillation through a four-foot column. In each instance, two isomers were separated, and the approximate isomer distributions are shown in Table II. The precision of the data in this table is seriously limited by difficulty in separating the isomers and the uncertainty of analysis of mixtures by use of the index of refraction. It seems safe to conclude however, that increase of the size of the substituents on the methinyl carbon causes a decrease in the percentage of substitution on that carbon, and the significant shifts in ratio of isomers occur in passing from methyl to a larger group. Even with two methyl groups on the methinyl carbon, about one-fifth of the substitution is on the methylene carbon.

It seems reasonable to regard substitution as occurring more rapidly at the methinyl carbon, except as this substitution is slowed down by steric hindrance. It is to be expected that the more significant differences in isomer distribution would occur when alkyl is changed from methyl to ethyl and that change of ethyl to a larger group would result in no significant difference. These effects are consistent with recorded observations concerning steric factors involved in rates of amide hydrolysis,[5] rates of esterification[6] and rearrangements involving a methyl or ethyl group.[7]

The higher rate of substitution at the methinyl carbon, in absence of steric hindrance, might be ascribed to a higher rate of reaction of the methinyl enolate ion induced by a higher electron density on the reacting carbon in this ion, as compared to that in the methylene enolate ion. It seems probable, however, that a more important factor is the higher concentration of the methinyl enolate ion, which would be expected to have an energy lower than that of the methylene enolate ion. The methinyl enolate ion, IX, receives a contribution from a multiple bond bearing four substituents, in contrast with the methylene enolate ion whose multiple bond bears only three substituents.

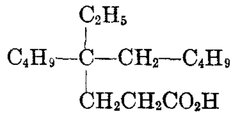


$$R-\underset{\displaystyle R'}{\overset{-}{C}}-\overset{\displaystyle O}{\overset{\|}{C}}-CH_2-R'' \longleftrightarrow R-\underset{\displaystyle R'}{C}=\overset{\displaystyle O^-}{C}-CH_2-R''$$

IXa IXb

Although condensations of large numbers of unsymmetrical ketones have been reported in the literature, there have been relatively few product analyses reported. Most commonly, direction of condensation has been assigned on the basis of isolation of the solid derivative of a single isomer. Such data may indicate the isomer present in larger amount or that yielding the less soluble derivative; however, it does not indicate reliably whether a single isomer is the sole product. In instances where product analyses have been determined, mixtures have been found. In the condensation of methyl $n$-hexyl ketone with methyl formate, Royals and Covington[8] reported about equal amounts of the two isomers. Hauser and Adams[9] reported product analyses for the acid-catalyzed (boron trifluoride) acetylation of a series of unsymmetrical ketones, and in each case except that of methyl ethyl ketone some of each isomer was obtained. It is of interest that the data in this latter investigation may also be well correlated on the basis of steric factors. For example, methyl $n$-butyl ketone gave only 10% substitution on methyl, whereas methyl isobutyl ketone gave 55% substitution on methyl.

There appear to be only two possibilities for isomeric cyanoethylation products such as obtained in the present work: (a) position isomers of the type discussed, (b) diastereoisomers resulting from exclusive substitution on the methylene carbon. For the cyanoethylation products from 6-ethyl-5-decanone (V), the latter possibility has been eliminated by demonstration that one of the two isomers is that resulting from cyanoethylation at the methinyl carbon. The keto nitrile of higher boiling point and higher index of refraction was converted by methanolysis to keto ester II. This keto ester had the same index of refraction and infrared spectrum as the sample previously prepared.[1] Further, it was converted by Wolff-Kishner reduction to the saturated acid X, which had the same index of refraction and infrared spectrum as the previously prepared sample,[1] and gave a $p$-bromoanilide with the melting point previously reported for this compound. Cyanoethylation products from the other ketones were correlated with those from ketone V by use of infrared spectra. In each case, the isomer of higher boiling point and higher index of refraction was that resulting from substitution at the methinyl carbon.



$$C_4H_9-\underset{\displaystyle CH_2CH_2CO_2H}{\overset{\displaystyle C_2H_5}{C}}-CH_2-C_4H_9$$

X

In Fig. 1 are shown the infrared spectra of the two pairs of isomeric keto nitriles which were separated, and in Fig. 2 are shown the infrared spectra of all four pairs of isomeric keto esters. In Table III are recorded the exact positions of certain absorption bands of interest. It may be noted that in both series the spectra for corresponding isomers are quite similar; however, substitution on the opposite side of the carbonyl group leads to several significant differences in the spectra. In general, the spectra of the quaternary carbon compounds are more complex in the 7–11 $\mu$ region.

It is of particular interest that in the series of keto esters, as well as that of the keto nitriles, each of the compounds containing a quaternary carbon shows an infrared band at or near 8.9 $\mu$. Freeman[10] has observed that saturated fatty acids with a quaternary carbon in the *beta*, *gamma*, or *delta* position exhibit an infrared absorption band at about 8.8 $\mu$, and he has suggested that this band may be characteristic of such structures. Our spectra support this conclusion and also extend its generality to include compounds containing a keto group in the $\delta$-position. It may also be noted in Figs. 1 and 2 that each compound having a quaternary carbon exhibits bands at about 7.95 and 10.1 $\mu$, which are absent from the isomeric compounds. It seems reasonable to associate these bands with a quaternary carbon adjacent to a carbonyl group; however,

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(5) Cason, Gastaldo, Glusker, Allinger, and Ash, *J. Org. Chem.*, **18**, 1129 (1953).

(6) Loening, Garrett, and Newman, *J. Am. Chem. Soc.*, **74**, 3929 (1952).

(7) Brown and Kornblum, *J. Am. Chem. Soc.*, **76**, 4510 (1954).

(8) Royals and Covington, *J. Am. Chem. Soc.*, **77**, 3155 (1955).

(9) Hauser and Adams, *J. Am. Chem. Soc.*, **66**, 345 (1944).

(10) Freeman, *J. Am. Chem. Soc.*, **74**, 2523 (1952).

TABLE III

CERTAIN INFRARED BANDS IN KETO NITRILES AND KETO ESTERS

| Curve (*cf.* Figs. 1, 2) | Absorption Bands (μ) | | | | | | |
|---|---|---|---|---|---|---|---|
| | Nitrile | Ester | Keto | | Quaternary Carbon | | |
| 1-1 | 4.45 | | 5.90 | | 7.98 | 8.95 | 10.16 |
| 1-2 | 4.45 | | 5.89 | | 7.94 | 8.93 | 10.21 |
| 1-3 | 4.45 | | 5.88 | | weak | | |
| 1-4 | 4.45 | | 5.89 | | | 8.93 | |
| 2-1 | | 5.75 | 5.89 | 7.64 | 7.98 | 8.93 | 10.10 |
| 2-2 | | 5.75 | 5.88 | 7.68 | 7.94 | 8.92 | 10.10 |
| 2-3 | | 5.75 | 5.88 | 7.66 | 7.94 | 8.93 | 10.10 |
| 2-4 | | 5.75 | 5.88 | 7.69 | 7.94 | 8.94 | 10.16 |
| 2-5 | | 5.74 | 5.86 | | | | |
| 2-6 | | 5.75 | 5.85 | | | | |
| 2-7 | | 5.76 | 5.86 | | | | |
| 2-8 | | 5.74 | 5.85 | | | | |

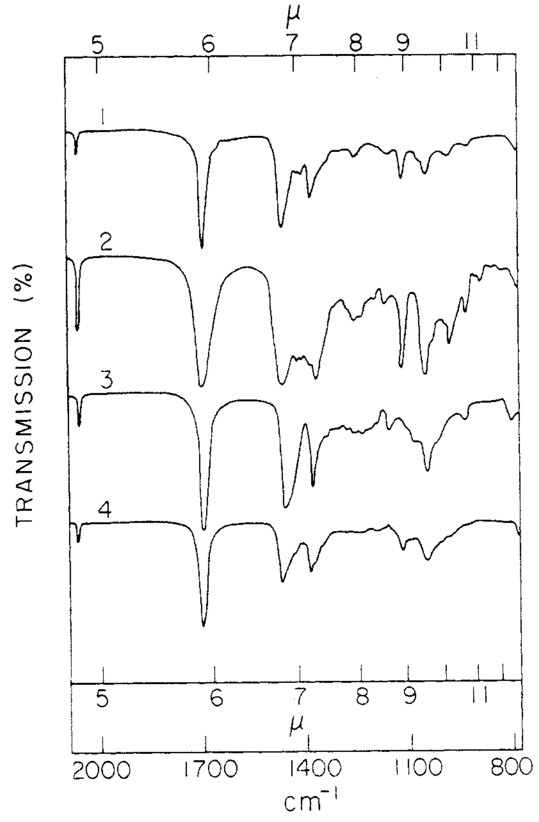

FIG. 1.—INFRARED ABSORPTION SPECTRA OF KETO NITRILES: Curve 1, 4-*n*-butyl-4-ethyl-5-ketononanenitrile; Curve 2, 4,4-dimethyl-5-ketononanenitrile; Curve 3, 4-*n*-propyl-6-ethyl-5-ketodecanenitrile; Curve 4, 4-*n*-propyl-6-methyl-5-ketoheptanenitrile.

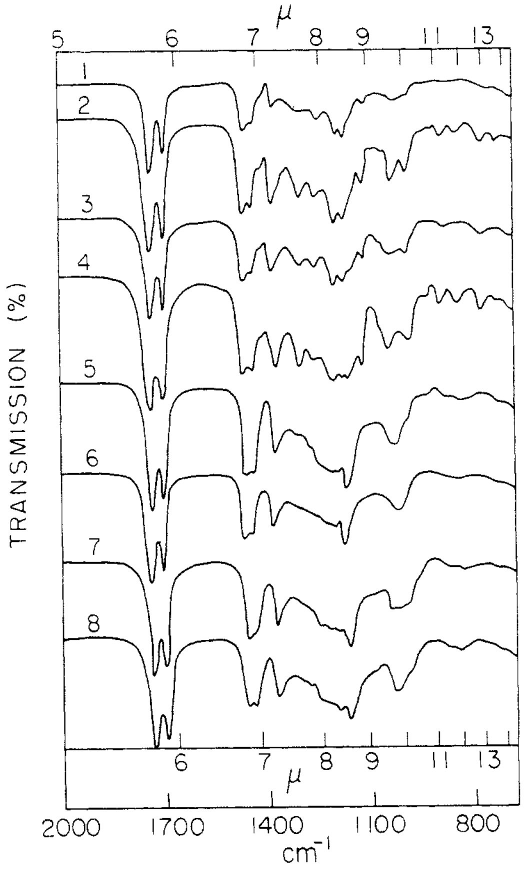

FIG. 2.—INFRARED ABSORPTION SPECTRA OF KETO ESTERS: Curve 1, methyl 4-*n*-butyl-4-ethyl-5-ketononanoate; Curve 2, methyl 4-*n*-butyl-4-methyl-5-ketononanoate; Curve 3, methyl 4-ethyl-4-methyl-5-ketononanoate; Curve 4, methyl 4,4-dimethyl-5-ketononanoate; Curve 5, methyl 4-*n*-propyl-6-ethyl-5-ketodecanoate; Curve 6, methyl 4-*n*-propyl-6-methyl-5-ketodecanoate; Curve 7, methyl 4-*n*-propyl-6-methyl-5-ketooctanoate; Curve 8, methyl 4-*n*-propyl-6-methyl-5-ketoheptanoate.

further confirmation is required to establish the generality of this observation. The four keto esters containing a quaternary carbon atom exhibit a band at about 7.65 μ, which is absent in the isomeric keto esters. This band is shown by none of the keto nitriles, including those containing a quaternary carbon, and is also absent from the spectrum of 4-ethyl-4-*n*-butylnonanoic acid (X). So far as may be concluded from the present work, this band seems to be specifically associated with the structure consisting of a δ-keto ester containing the quaternary carbon in the *gamma* position. Absence of the quaternary carbon bands from the spectra of the other isomers (except that of Curve 4, Fig. 1) indicates a reasonably high degree of purity for the compounds separated by fractional distillation.

TABLE IV

PREPARATION OF *n*-BUTYL *sec*-ALKYL KETONES

| *sec*-Alkyl R | *sec*-Alkyl R′ | Acid Chloride B.P., °C. | Acid Chloride Mm. | Acid Chloride Yield, % | Ketone B.P., °C. | Ketone Mm. | Ketone Yield, % | $n_D^{25}$ | Ketone *Anal.* Found (Calc'd) C | Ketone *Anal.* Found (Calc'd) H |
|---|---|---|---|---|---|---|---|---|---|---|
| $C_4H_9$ | $C_2H_5$ | 78–79 | 19 | 99 | 92.5–94 | 7 | 90 | 1.4284 | 78.00 (78.19) | 13.00 (13.12) |
| $C_4H_9$ | $CH_3$ | 79–80 | 40 | 99 | 103–104 | 30 | 90 | 1.4233 | [a] | [a] |
| $C_2H_5$ | $CH_3$ | 100–101 | 760 | 90 | 74–75 | 30 | 87 | 1.4182 | 75.99 (76.01) | 12.80 (12.75) |
| $CH_3$ | $CH_3$ | 89–90 | 760 | 60[b] | 63–65 | 25 | 95 | 1.4103 | [a] | [a] |

[a] Not analyzed; characterization rests on analyses and infrared spectra of cyanoethylation products. [b] Yield lowered by use of excess acid in order to avoid separation from thionyl chloride.

The infrared spectra show bands characteristic of the structures expected in the compounds being studied. In particular, there may be noted the nitrile band at about 4.45 μ, the keto band at about 5.86 μ, and the ester band at about 5.75 μ.

## EXPERIMENTAL[11]

*2-Alkylalkanoic acids.* 2-Ethylhexanoic, 2-methylbutanoic, and 2-methylpropanoic acids were redistilled commercial products. 2-Methylhexanoic acid was prepared *via* alkylation of diethyl methylmalonate with *n*-butyl bromide in the presence of sodium ethoxide in ethanol. Yield of diethyl methyl-*n*-butylmalonate was 84%, b.p. 84–86° (2 mm.); yield of acid was 89%, b.p. 114–115° (17 mm.).

*Acid chlorides* were prepared by allowing the acid to stand overnight with two molar equivalents of thionyl chloride, except 2-methylpropanoyl chloride, for whose preparation an excess of acid was used. Data on these preparations are included in Table IV.

*n-Butyl sec-alkyl ketones* were prepared by treating the acid chlorides with di-*n*-butylcadmium (prepared *via* the Grignard reagent from 2 moles of butyl bromide per mole of acid chloride) according to the procedure which has been worked out in detail.[12] Data on these preparations are included in Table IV.

*Cyanoethylations.* The procedure regarded as most useful is described for 6-ethyl-5-decanone. Data recorded for this preparation under various other conditions are assembled in Table I.

A solution of 2 g. of potassium hydroxide and 195 g. (1.05 moles) of 6-ethyl-5-decanone in 200 ml. of *tert*-butyl alcohol was warmed with stirring to 60°, then there was added during about ten minutes 74 g. (1.4 moles) of acrylonitrile. A mildly exothermic reaction[13] set in so that cooling was required to keep the temperature at 60–65° during the addition and for a brief interval thereafter. After addition was complete the mixture was stirred for an additional 4–5 hours at 60–65°.

The cooled reaction mixture was acidified with 4 *N* hydrochloric acid; then the organic layer was separated. The organic layer and a subsequent benzene extract were washed in series with water and saturated salt solution, then dried over magnesium sulfate. The solvent was removed and the residue was fractionated to yield 139 g. (72%) of recovered ketone, b.p. 88–90° (5 mm.), and 58.1 g. (73% based upon ketone consumed) of keto nitrile, b.p. 150–160° (5 mm.).

*Separation of keto nitriles.* The cyanoethylation product of 6-ethyl-5-decanone, obtained as described above, consisted of two isomers which were separable by fractional distillation, although with difficulty. A major problem was presented by an impurity distilling at a slightly lower temperature than the lower-boiling keto nitrile. A typical fractionation through the 4-ft. column[14] is presented in Table V.

TABLE V

FRACTIONATION OF ISOMERIC CYANOETHYLATION PRODUCTS OF 6-ETHYL-5-DECANONE

| Frac. No. | Weight, g. | B.P. (5 mm.), °C. | $n_D^{21}$ |
|---|---|---|---|
| 1 | 1.6 | 139.6–142.5 | 1.4466 |
| 2 | 4.3 | 142.5–143.8 | 1.4484 |
| 3 | 11.0 | 143.8–144.9 | 1.4486 |
| 4 | 13.5 | 144.9–149.0 | 1.4500 |
| 5 | 2.5 | 149.0 | 1.4507 |
| 6[a] | 16.0 | 149.0–150.0 | 1.4515 |
| 7 | 2.0 | 150.0–151.6 | 1.4516 |
| 8 | 2.0 | 151.6–159.0 | 1.4538 |
| 9 | 5.0 | 159.0 | 1.4595 |
| 10[a] | 5.6 | 159.0–159.6 | 1.4598 |

[a] Samples used for analysis (*cf.* Table VI) and spectral determinations (*cf.* Fig. 1).

Purification of the cyanoethylation products from 6-methyl-5-decanone and 3-methyl-4-octanone was not accomplished on account of interference of an impurity, presumably the same one encountered in the fractional distillation shown in Table V. This impurity did not seriously interfere with purification of the cyanoethylation products from 2-methyl-3-heptanone; however, the isomeric keto nitriles boiled so close together that entirely pure isomers were not obtained. Absorption curve 4, Fig. 1, shows a band at about 8.9 μ which is characteristic of the isomer containing a quaternary carbon.

Data on the best samples of keto nitriles are assembled in Table VI.

*Methanolysis of keto nitriles.* Most effective purification

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(11) All distillations, except as otherwise specified, were through a 2-foot column of the simple Podbielniak type, with heated jacket and partial reflux head. Analyses are by the Microanalytical Division of the Department of Chemistry, University of California. Infrared spectra were determined on thin films using a Perkin-Elmer Model 21, double-beam, recording spectrophotometer.

(12) Cason and Prout, *Org. Syntheses*, **28**, 75 (1948).

(13) During or shortly after the addition of acrylonitrile to the ketone, a purple-red coloration developed in reactions which had started properly. Occasionally a reaction did not start, even after stirring for a protracted period. Such reactions could sometimes be initiated by addition of more alkali, but at other times reaction could not be induced; work-up yielded starting ketone. Considerable investigation has failed to reveal the cause of this occasional erratic behavior.

(14) The fractionating equipment which was employed was that described earlier by Cason, Allinger, Sumrell, and Williams, *J. Org. Chem.*, **16**, 1170 (1951).

TABLE VI

Cyanoethylation Products of 6-Ethyl-5-Decanone and 2-Methyl-3-Heptanone

| Keto Nitrile | B.P. (5 mm.) °C. | $n^{25}_{D}$ | Analysis Calc'd C | H | N | Found C | H | N |
|---|---|---|---|---|---|---|---|---|
| 4-*n*-Butyl-4-ethyl-5-ketononanenitrile | 159 | 1.4582 | 75.89 | 11.47 | 5.90 | 76.06 | 11.45 | 5.83 |
| 4-*n*-Propyl-6-ethyl-5-ketodecanenitrile | 150 | 1.4499 | 75.89 | 11.47 | 5.90 | 75.91 | 11.20 | 5.95 |
| 4,4-Dimethyl-5-ketononanenitrile | 132 | 1.4460 | 72.93 | 10.56 | 7.72 | 73.40 | 10.82 | 7.67 |
| 4-*n*-Propyl-6-methyl-5-ketoheptanenitrile[a] | 127 | 1.4437 | 72.93 | 10.56 | 7.72 | 73.31 | 10.42 | 7.63 |

[a] The infrared spectrum of this nitrile (*cf.* Fig. 1) indicates presence of significant quantities of the quaternary carbon isomer.

TABLE VII

Analytical Data and Physical Properties of Pairs of Isomeric Keto Esters

| Keto Ester | B.P. (5 mm.) °C. | $n^{25}_{D}$ | Analysis Calc'd C | H | Found C | H |
|---|---|---|---|---|---|---|
| Methyl 4-*n*-butyl-4-ethyl-5-ketononanoate | 160 | 1.4519 | 71.06 | 11.18 | 70.90 | 10.98 |
| Methyl 4-*n*-propyl-6-ethyl-5-ketodecanoate | 152 | 1.4443 | 71.06 | 11.18 | 70.34 | 10.92 |
| Methyl 4-*n*-butyl-4-methyl-5-ketononanoate | 148 | 1.4471 | 70.27 | 11.01 | 70.57 | 11.02 |
| Methyl 4-*n*-propyl-6-methyl-5-ketodecanoate | 141 | 1.4419 | 70.27 | 11.01 | 69.88 | 11.13 |
| Methyl 4-ethyl-4-methyl-5-ketononanoate | 129.8 | 1.4459 | 69.39 | 10.81 | 69.03 | 10.66 |
| Methyl 4-*n*-propyl-6-methyl-5-ketooctanoate | 123.6 | 1.4398 | 69.39 | 10.81 | 68.91 | 10.77 |
| Methyl 4,4-dimethyl-5-ketononanoate | 122 | 1.4407 | 67.24 | 10.35 | 67.09 | 10.55 |
| Methyl 4-*n*-propyl-6-methyl-5-ketoheptanoate | 117 | 1.4360 | 67.24 | 10.35 | 66.91 | 10.31 |

and separation of isomers was accomplished by conversion of the keto nitriles to keto esters. In this way, interference by the aforementioned impurity was eliminated. In a representative procedure, 4.1 g. (0.02 mole) of 4-*n*-butyl-4-ethyl-5-ketononanenitrile, b.p. 154.5° (4.5 mm.), was heated under reflux for 7 hours with 100 ml. of methanol saturated with anhydrous hydrogen chloride. The cooled reaction mixture was diluted with water and worked up to yield 3.7 g. (90%) of keto ester, b.p. 159.5–160° (5 mm.). A center cut was used for analysis and for determination of properties listed for the first item in Table VII. For the previously prepared sample[1] of this keto ester, there was reported $n^{30}_{D}$ 1.4500, or by extrapolation $n^{25}_{D}$ 1.4520.

Data for all four pairs of isomeric keto esters are assembled in Table VII. A typical fractional distillation for separation of isomeric keto esters is shown in Table VIII.

TABLE VIII

Fractionation of Isomeric Keto Esters from Cyanoethylation Products of 6-Methyl-5-Decanone

| Frac. No. | Weight, g. | B.P. (5 mm.), °C. | $n^{26}_{D}$ |
|---|---|---|---|
| 1 | 0.3 | 135.8–139.8 | 1.4410 |
| 2 | 1.1 | 139.8–140.8 | 1.4415 |
| 3[a] | 0.6 | 140.8–141.8 | 1.4415 |
| 4 | 0.3 | 141.8–142.8 | 1.4414 |
| 5 | 3.8 | 142.8–143.5 | 1.4431 |
| 6 | 1.6 | 143.5–147.5 | 1.4453 |
| 7[a] | 3.4 | 147.5–148.0 | 1.4467 |
| 8 | 2.6 | 148.0–148.5 | 1.4470 |

[a] Samples used for analysis (*cf.* Table VII) and spectral determinations (*cf.* Fig. 2).

*4-Ethyl-4-n-butylnonanoic acid* (X). For a further identification of the sample of methyl 4-*n*-butyl-4-ethyl-5-ketononanoate obtained in the present work, the sample was reduced by the Wolff-Kishner method as described previously,[1] to give 4-*n*-butyl-4-ethylnonanoic acid, $n^{25}_{D}$ 1.4550 (previously reported value $n^{25}_{D}$ 1.4552). The infrared spectra of the two samples were identical. The acid obtained in the present work was also converted to the *p*-bromoanilide, m.p. 121.6–122°, which gave no depression in melting point on mixing with the previously prepared sample (m.p. 121.3–121.6°).

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