avian malaria, nor was any detectable difference in toxicity for mice observed.

RESEARCH LABORATORIES
MERCK & CO., INC.
RAHWAY, NEW JERSEY RECEIVED DECEMBER 31, 1946

## Preparation of 3-Cyano-4-piperidone

BY G. BRYANT BACHMAN AND R. S. BARKER

Although N-substituted 4-piperidones have been prepared in satisfactory yields by cyclization procedures from N-alkyl-di-($\beta$-carbethoxyethyl)-amines[1] and from N-alkyl-di-($\beta$-cyanoethyl)-amines,[2] results with the N-unsubstituted analogs have been less gratifying.[3] We have found that di-($\beta$-cyanoethyl)-amine may be converted to 3-cyano-4-piperidone in 70% yield by cyclizing in the presence of sodium, sodium amide or sodium alcoholates, followed by hydrolysis of the intermediate 3-cyano-4-iminopiperidine. When sodium is used as the catalyst it is desirable to use a solvent of the ether class (*e. g.*, dioxane) and to employ a metal carrier (*e. g.*, naphthalene).

**Acknowledgment.**—The authors are indebted to Eli Lilly and Company for financial support.

### Experimental

**3-Cyano-4-iminopiperidine.**—Dioxane, 400 ml., distilled from sodium, was charged into a 3-neck flask equipped with a nitrogen inlet, a reflux condenser and drying tube, and an efficient stirrer. Naphthalene, 25 g., sodium, 2 g., and bis-($\beta$-cyanoethyl)-amine,[4] 50 g., were added and the air was displaced by nitrogen. The mixture was stirred several hours on a steam-bath. The pale yellow solution gradually became cloudy and precipitated an amorphous brown solid. The product was worked up in two different ways.

**Method A.**—The hot reaction mixture was poured into one liter of benzene, cooled and filtered. The uncyclized amine is soluble in benzene, whereas the imine is not. The product was crystallized from ethanol, m. p. 187–188° (dec.). It can also be crystallized readily from acetone or from a mixture of dioxane and alcohol (9:1).

**Method B.**—The hot dioxane mixture was diluted with about 10% by volume of hot alcohol and the product allowed to crystallize. For the hydrolysis to the piperidone either the benzene or dioxane–alcohol precipitate can be used satisfactorily.

*Anal.* Calcd. for $C_6H_5N_3$: C, 58.48; H, 7.35; N, 34.10. Found: C, 58.46, 58.55; H, 7.21, 7.30; N, 34.05, 34.12.

Phenyl isothiocyanate derivative had a m. p. 170–171° (dec.).

*Anal.* Calcd. for $C_{13}H_{14}N_4S$: S, 12.37. Found: S, 12.26, 12.32.

**3-Cyano-4-piperidone.**—3-Cyano-4-iminopiperidine, 50 g., and 150 ml. of 5 *N* hydrochloric acid were heated to 100° for twenty minutes. The solution was cooled and neutralized to *p*H 4–5 with concentrated sodium hydroxide solution, keeping the temperature below 30°. The fine white crystals were filtered, more sodium hydroxide was added to *p*H 6–7, and the product was again filtered. This process was repeated until the filtrate became alkaline to litmus paper. The crystalline product, after washing with water and alcohol, weighed 41 g. (82% yield). To recrystallize the product it was dissolved in aqueous ammonia and vacuum distilled (water pump) on a steam-bath. The first crop of crystals appeared after half the solution had been distilled. It was filtered off and the filtrate was further concentrated to obtain a second and a third crop. The product was washed with water and alcohol. It gave a red-brown color with ferric chloride but showed no definite m. p. It was amphoteric and the titration curve showed a break at *p*H 3.1.

*Anal.* Calcd. for $C_6H_4ON_2$: C, 58.05; H, 6.49; total N, 22.57; amino N, 11.29. Found: C, 57.82, 57.93; H, 6.50, 6.53; total N, 22.53, 22.47; amino N (by potentiometric titration), 11.1, 11.2.

(1) McElvain and Stork, THIS JOURNAL, **68**, 1049 (1946).
(2) Cook and Reed, *J. Chem. Soc.*, 399 (1945).
(3) Kuettel and McElvain, THIS JOURNAL, **53**, 2692 (1931).
(4) Wiedeman and Montgomery, *ibid.*, **67**, 1995 (1945).

DEPARTMENT OF CHEMISTRY
PURDUE UNIVERSITY
LAFAYETTE, INDIANA RECEIVED FEBRUARY 5, 1947

## Cyanoacetal—A Correction

BY WALTER H. HARTUNG AND HOMER ADKINS

We reported in 1927 that we had obtained cyanoacetal[1] through the reaction of bromoacetal with potassium cyanide in an alcohol–water solution containing potassium iodide. Jacob van de Kamp and others have called our attention to the fact that they had been unable to obtain cyanoacetal by following the procedure described by us. Uhle and Jacobs[2] obtained cyanoacetal in 14% yield by carrying out the reaction in a manner similar to that described in our paper. They worked on a larger scale and followed a different procedure in isolating the desired product. Uhle and Jacobs graciously ignored our paper although it is clear from a comparison of the data in the two papers, that we had not isolated cyanoacetal. Since we did not have cyanoacetal in hand, the figure for the equilibrium constant reported in our paper for the reaction

$$CNCH_2CH(OC_2H_5)_2 + H_2O \rightleftarrows CNCH_2CHO + 2C_2H_5OH$$

is not significant. We regret very much our mistake and appreciate the forbearance of our friends.

Robert L. Clarke and S. M. McElvain, of this Laboratory, have obtained the same results as those reported by Uhle and Jacobs. They will publish their results in the near future as well as a description of their preferred procedure whereby cyanoacetal was prepared in excellent yield by a series of reactions through $(C_2H_5O)_2CHCH_2CO_2C_2H_5$.

(1) Hartung and Adkins, THIS JOURNAL, **49**, 2520 (1927).
(2) Uhle and Jacobs, *J. Org. Chem.*, **10**, 81 (1945).

UNIVERSITY OF WISCONSIN
MADISON, WISCONSIN RECEIVED FEBRUARY 17, 1947

## Equilibrium Studies on the Dehydrogenation of Primary and Secondary Alcohols. II. Cyclohexanols

BY ADRIAN H. CUBBERLEY AND MAX B. MUELLER

Free energies, heats and entropies of dehydrogenation of a number of alcohols were recently reported from this Laboratory.[1]

Further results obtained using the same appara-

(1) Cubberley and Mueller, THIS JOURNAL, **68**, 1149 (1946).

tus and technique on cyclohexanol, 2-methylcyclohexanol and 3-methylcyclohexanol are being reported at this time.

The following heat capacity equation[1] was used for the three reactions.

$$\Delta C_p = 7.28 - 0.0118T$$

Values of $\Delta H_0$ and $I$ in the free energy equation

$$\Delta F = \Delta H_0 - 16.77T \log T + 0.0059T^2 + IT$$

calculated from the experimental results by the method of least squares are listed in Table I.

TABLE I

VALUES OF $\Delta H_0$, $I$, $\Delta F_{298}$, $\Delta H_{298}$, $\Delta S_{298}$

| Alcohol | $\Delta H_0$ | $I$ | $\Delta F_{298}$ | $\Delta H_{298}$ | $\Delta S_{298}$ |
|---|---|---|---|---|---|
| Cyclohexanol | 13,588[a] | 17.09 | 6840 | 15,233 | 28.16 ± 0.25 |
| 2-Methylcyclohexanol | 13,465 | 17.05 | 6705 | 15,110 | 28.20 ± .15 |
| 3-Methylcyclohexanol | 13,380 | 17.29 | 6691 | 15,025 | 27.97 ± .20 |

[a] $\Delta H_0$ for cyclohexanol was calculated from Kistiakowsky's value for $\Delta H_{355}$ (Kistiakowsky, *et al.*, THIS JOURNAL, **61**, 1868 (1939)).

It is apparent that the substitution of a single methyl group ortho or meta to the hydroxyl has no appreciable effect on the thermochemistry of the dehydrogenation of cyclohexanols.

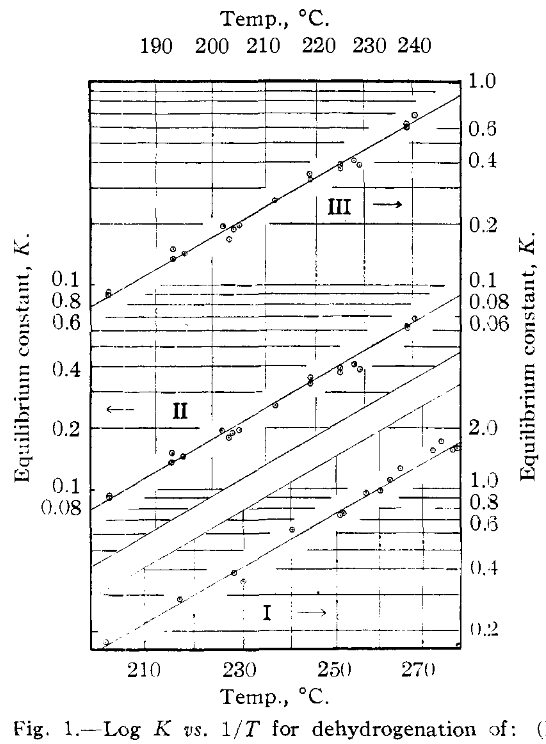


Fig. 1.—Log $K$ *vs.* $1/T$ for dehydrogenation of: (I) cyclohexanol, (II) 2-methylcyclohexanol and (III) 3-methylcyclohexanol.

Experimentally determined values of the equilibrium constants are compared in Fig. 1, with the values calculated from the free energy equations.

RESEARCH LABORATORY
THE BARRETT DIVISION
ALLIED CHEMICAL & DYE CORPORATION
EDGEWATER, N. J. RECEIVED JANUARY 10, 1947

## Numbers of Isomeric Alkylbenzenes

BY ALFRED W. FRANCIS

The exact numbers of structurally isomeric hydrocarbons of the paraffin series,[1,2] olefin series,[3] acetylene series,[4] and of their derivatives, alcohols, etc.[2,5] (or alkyl groups), and more complex derivatives[6] are listed in the literature up to 20 to 40 carbon atoms. Each series shows a progressive increase of about 2.5 fold for each additional carbon atom so that simple equations permit approximate extrapolation to any desired extent. It does not seem to have been noted that there are slight alternations in the ratio, which in the case of paraffin isomers is higher from odd to even number of carbon atoms than from even to odd, analogous to the increments of melting points of normal paraffin hydrocarbons as shown in Fig. 1; and that like the latter, the alternation gradually subsides with increasing carbon content, although it is still detectable at $C_{40}$.[7]

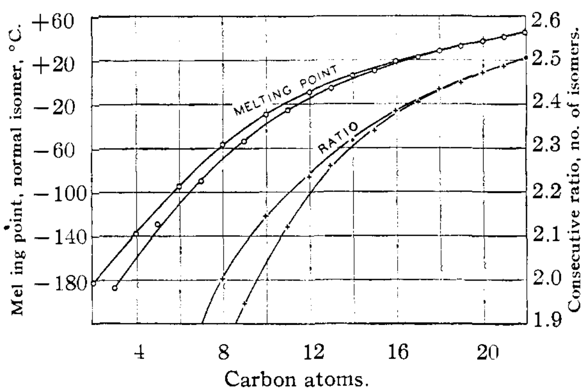


Fig. 1.—Analogy between alternations in melting points of normal paraffin hydrocarbons (physical observations) and in consecutive ratios in number of paraffin isomers (mathematical calculations).

The numbers of structurally isomeric alkylbenzenes are not listed beyond those with twelve carbon atoms[8] although mathematical equations are derived for the calculation of the number of isomers with any combination of substituents (one item in Table I).[8,9] In view of increasing

(1) Henze and Blair, THIS JOURNAL, **53**, 3084 (1931).

(2) Perry, *ibid.*, **54**, 2919 (1932).

(3) Henze and Blair, *ibid.*, **55**, 685 (1933).

(4) Coffman, Blair and Henze, *ibid.*, **55**, 253 (1933).

(5) Henze and Blair, *ibid.*, **53**, 3045 (1931).

(6) Henze and Blair, *ibid.*, **56**, 157 (1934).

(7) Logarithmic interpolation and allowance for the alternation mentioned permitted the detection of trifling errors in the listed numbers of paraffin isomers of 29 and 40 carbon atoms. The former was recalculated by the present author, giving the number, 1,590,507,821; and the latter was recalculated by one of the original authors (H. R. Henze, private communication) giving 62,481,806,147,341. Both numbers are consistent with the logarithmic interpolation, which is accurate to about half of the figures, provided neighboring numbers are correct.

(8) Polya, *Compt. rend.*, **201**, 1169 (1935); *Helv. Chim. Acta*, **19**, 23 (1936).

(9) T. L. Hill, *J. Phys. Chem.*, **47**, 253, 413 (1943); *J. Chem. Phys.*, **11**, 294 (1943).