Base Strength of Urea and Thiourea in Methanol

BY RALPH G. PEARSON AND JAMES TUCKER

In some work with solutions containing thiourea and strong acids dissolved in methanol it became apparent that salt formation was appreciable even though thiourea is generally considered too weak a base to form salts stable in solution. The explanation lies in the inherent weak basicity of methanol which causes other bases to appear abnormally strong in this solvent.[1]

The hydrolysis constants for thiourea and urea in dry methanol were determined by a conductimetric method essentially the same as that used by Goldschmidt and Dahlls[1a] to find the base strength of water in methanol. β-Naphthalenesulfonic acid was recrystallized from water and dried to the composition of the monohydrate in a vacuum oven at 60°. Methanol was dried by the use of magnesium turnings.[2] C. P. thiourea and urea were used.

Resistances were measured at 25.0 ± 0.03° on a Jones bridge of solutions containing a fixed amount of acid and varying amounts of base. If R_0 is the resistance of the solution containing only acid and R the resistance of a solution with added base, then $R/(R - R_0)$ plotted against the reciprocal of the base concentration[3] gave straight lines which could be extrapolated to infinite base concentration. From this a value of R_∞ could be found corresponding to the resistance of a solution completely converted to the salt of the base. From R_0, R_∞ and R the fraction of acid converted to salt could be found for each solution and the concentration equilibrium constant, K_h, for the reaction could be determined.

$$BH^+ + CH_3OH \rightleftarrows B + CH_3OH_2^+ \qquad (1)$$

Table I shows the experimental results, the calculated values of R_∞ and the average value of K_h for each base. The effect of urea and thiourea on the resistances of methanolic solutions of lithium acetate and potassium chloride was checked and found to be negligible except for the more concentrated urea solutions. Assuming the effect here to be due to viscosity, an equivalent correction was made on the measured conductances of the acid solutions before any calculations were made.

TABLE I

THIOUREA

Thiourea, molar	Resistance, ohms
0.00556 *M* β-Naphthalene Sulfonic Acid	
0.0000	3111[a]
.0314	3709
.0628	4164
.1257	4643
.2514	5103
∞	5942

$K_h = 5.46 \pm 0.1 \times 10^{-2}$

Urea, 0.00525 *M* Acid

Urea, molar	Resistance, ohms
0.00000	2764[a]
.00271	3552
.00525	4370
.01080	5108
.0314	5331[b]
.0627	5447[b]
∞	5447

$K_h = 4.37 \pm 0.2 \times 10^{-4}$

0.00592 *M* Potassium Chloride

0.0000	3974
.0314	3986
.0627	4002

[a] Different conductivity cells were used. [b] Not corrected for viscosity.

The basic ionization constant can be obtained by dividing the hydrolysis constant into the ion product for methanol, 2.0×10^{-17} at 25°.[1b] The corresponding hydrolysis constants in water are 9.0 for thiourea and 0.67 for urea.[4] The stability of the salts is thus increased several hundred-fold in methanol.

(1) (a) Goldschmidt and Dahlls, *Z. physik. Chem.*, **108**, 121 (1924); (b) Unmack, *ibid.*, **133**, 45 (1928).

(2) Lund and Bjerrum, *Ber.*, **64B**, 210 (1931).

(3) The concentration of free base must be used, correcting for that used up in salt formation. Successive approximations as to the magnitude of K_h are needed to bring the solutions of low base concentration into line.

(4) Walker, *J. Chem. Soc.*, **67**, 576 (1895).

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Isomerization of Saturated Hydrocarbons. VI.[1] Effect of Benzene upon the Isomerization of Methylcyclopentane

BY HERMAN PINES, EUGENE ARISTOFF[2] AND V. N. IPATIEFF

The study of the isomerization of *n*-butane[3] and cyclohexane and methylcyclopentane[1] in the presence of aluminum bromide–hydrogen bromide catalyst using a high vacuum technique and highly purified materials has been reported recently. This work has shown that under certain carefully controlled conditions the isomerization of saturated hydrocarbons does not proceed unless a small amount of an olefin or an alkyl or cycloalkyl halide is present.

In the study of isomerization of methylcyclopentane it was found that small amounts of impurities which are present commonly in this hydrocarbon, such as benzene, have a profound effect upon the rate of isomerization. By fractional distillation it is difficult to eliminate the last traces of benzene; this can, however, be accom-

(1) For paper V of this series see H. Pines, B. M. Abraham and V. N. Ipatieff, THIS JOURNAL, **70**, 1742 (1948).

(2) Universal Oil Products Company Research Fellow 1947–1948.

(3) H. Pines and R. C. Wackher, THIS JOURNAL, **68**, 595 (1946), **68**, 2518 (1946).

plished by passing methylcyclopentane over silica gel.[4]

The following table shows the inhibiting effect of benzene upon the isomerization of methylcyclopentane promoted by *s*-butyl bromide. The experiments were carried out by a general procedure described previously[3]; the reaction temperature was 25° and the duration of each experiment was two hours. On the average about 0.04 mole of methylcyclopentane was used in each experiment.

TABLE I

EFFECT OF BENZENE UPON THE ISOMERIZATION OF METHYLCYCLOPENTANE

Expt.	Reagents used: moles per 100 moles of methylcyclopentane				Cyclohexane formed, mole %
	$AlBr_3$	HBr	*s*-C_4H_9Br	Benzene	
1	2	1.0	0.0	0.000	0
2	2	0.9	.1	.000	51
3	2	.9	.1	.022	22
4	2	.9	.1	.072	5
5	2	.9	.1	.140	3
6	2	1.0	.0	.140	0

The concentration of benzene in methylcyclopentane was determined by ultraviolet analysis. Experiment 4 was made by the addition of benzene to a purified sample of methylcyclopentane.

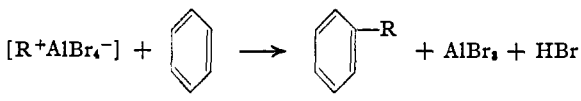
The inhibiting effect of benzene upon the isomerization, which was also observed to occur in the case of *n*-pentane,[5] is probably due to the ease with which the benzene reacts with the chain initiator. The ultraviolet absorption spectra taken of the hydrocarbons obtained from experiment 5 after removal of the catalyst by washing show that probably a mono-alkylbenzene was formed during the reaction. The absorption spectrum of the methylcyclopentane containing 0.14% of benzene and that of the reaction product was taken. The spectrum of the product showed a slight peak at 258.5 mμ where *s*-butylbenzene has a strong absorption band.

In expt. 3 the benzene caused only a partial inhibition of isomerization. This is not surprising since the molal ratio of *s*-butyl bromide to benzene used was over four, and the alkylation usually does not proceed beyond the formation of a tributylbenzene. There was therefore still some *s*-butyl bromide left to act as a chain initiator.

It was also noticed that in the experiments 3, 4, and 5 where benzene and *s*-butyl bromide were used an oily-yellow layer deposited on the walls of the reaction tube; in all the other experiments the product was homogeneous and free of color.[6] It is probable that the alkylbenzenes or cycloalkylbenzenes produced in the reaction formed a complex with the aluminum bromide and hydrogen bromide, similar to the type reported by Norris and Rubinstein.[7]

The inhibition of the isomerization of methylcyclopentane by benzene is in accordance with the proposed chain mechanism of isomerization.[1,8]

In the presence of benzene the chain may break by the reaction



R^+ may correspond to the carbonium ion obtained from the original olefin or from the product resulting from an exchange reaction between methylcyclopentane or cyclohexane formed and the *s*-butylcarbonium ion.

(4) B. J. Mair and A. F. Forziati, *J. Research Natl. Bur. Standards*, **32**, 151, 165 (1944).

(5) J. M. Mavity, H. Pines, R. C. Wackher, and J. A. Brooks, *Ind. Eng. Chem.*, **40**, 2374 (1948).

(6) In the last paper of this series[1] it was reported that the isomerization of methylcyclopentane to cyclohexane was usually accompanied by the formation of an oily layer even though the methylcyclopentane used did not contain any traces of benzene. It was observed now that when methylcyclopentane is further purified by passing it over silica gel certain impurities not detectable by spectrographic analysis and responsible for the formation of an oily layer are removed.

(7) J. F. Norris and D. Rubinstein, THIS JOURNAL, **61**, 1163 (1939).

(8) H. S. Bloch, H. Pines and L. Schmerling, *ibid.*, **68**, 153 (1946).

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Synthesis of 7-Chloro-4-[1-methyl-(1-pyrrolidyl)-butylamino]-quinoline

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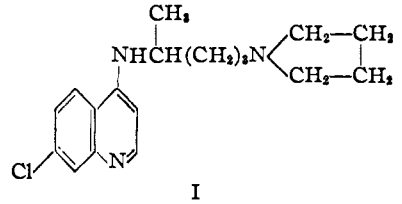
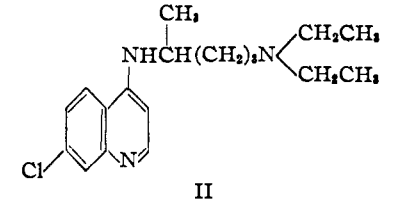
Studies on the effects resulting from an exchange of a pyrrolidyl group for a dialkylamino substituent in various chemotherapeutic agents[1] has now been extended briefly into the field of antimalarials. The synthesis of 7-chloro-4-[1-methyl-4-(1-pyrrolidyl)-butylamino]-quinoline (I), the pyrrolidyl analog of Chloroquine (II) was undertaken in consequence of the utility reported[2] for the latter in the control of malaria.



I



II

(1) (a) Wright, Kolloff and Hunter, THIS JOURNAL, **70**, 3098 (1948); (b) Reid, Wright, Kolloff and Hunter, *ibid.*, **70**, 3100 (1948); (c) Reitsema and Hunter, *ibid.*, in press.

(2) Wiselogle, "A Survey of Antimalarial Drugs," Vol. I, J. W. Edwards, Ann Arbor, 1946, pp. 388–392.