[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, THE UNIVERSITY OF TEXAS]

Allylic Chlorides. VIII. 1-Chloro-3-methyl-2-butene

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This paper reports the preparation of 1-chloro-3-methyl-2-butene and its reaction with potassium iodide in acetone, sodium ethoxide in ethanol and its catalytic hydrolysis by an acid solution of cuprous chloride. This investigation is an extension of previously reported research[2,3,4] pertaining to the influence of substituents on the reactivity of the allylic chlorine of various allylic chlorides.

Experimental

Potassium Iodide.—C. P. potassium iodide was recrystallized from water and dried for several hours at 120°. It failed to give a positive test for iodate ion.

Acetone.—C. P. acetone was distilled through a 4-foot glass helix-packed column and a fraction with $n^{25}D$ 1.3561 was used for making the potassium iodide solutions. The acetone did not color copper sulfate in thirty minutes.

Sodium Ethoxide in Ethanol.—Approximately 1.2 g. of clean sodium metal was added to about 400 ml. of ethanol and the volume adjusted to 500 ml.

Cuprous Oxide.—J. T. Baker C. P. Analyzed cuprous oxide was used without further purification.

1-Chloro-3-methyl-2-butene.—1-Chloro-3-methyl-2-butene was prepared by the addition of hydrogen chloride to isoprene.[5] The material used in the rate studies had the following physical constants: b. p. 52.5–53.5° (100 mm.); $n^{25}D$ 1.4439; d^{25}_4 0.9264; *MR* (calcd.) 29.69, (obsd.) 29.98.

Reaction with Potassium Iodide in Acetone.—The same procedure was used as previously described.[2] The following data were obtained at 20°.

Time, hours	Reacted, %	k, hr. mole l.
0.10	27.0	7.04
.20	46.8	7.23
.25	49.2	6.23
.30	55.7	6.30
.50	70.0	5.72
.60	72.1	5.07
.80	82.6	5.32
	Average k	6.13

The relative reactivity of 1-chloro-3-methyl-2-butene compared to allyl chloride as 1.00 is 28.1. There is a definite drift in the specific reaction rate constant.

Catalytic Hydrolysis with Cuprous Chloride in Hydrochloric Acid.—The same procedure and apparatus was used as that described in an earlier paper of this series.[6] The hydrolysis was caused to take place in 100 ml. of 1.5% hydrochloric acid using 0.0035 mole of cuprous chloride as a catalyst. Four hundredth (0.04) of a mole of the organic chloride was used in each run. Because of the very high rate of hydrolysis, a temperature of 0° was used. The following data were obtained.

Time, hours	Reacted, %
0.2	39.0
0.5	39.0
1.0	81.8
1.5	86.4
2.0	87.0
2.0	87.1

Reaction with Sodium Ethoxide in Ethanol.—The procedure used for this study was the same as that described by Tamele, *et al.*[7] At 50° the reaction was almost complete within twelve minutes and even at 0° the reaction was too rapid to permit a determination of the specific reaction rate constant. At −50° the reaction was 82.5% complete in twenty-one minutes and 90% complete in thirty minutes. Because a specific reaction rate constant obtained at this temperature would be of questionable value, none was obtained.

Discussion

The effect on the reactivity of an allylic chlorine toward *potassium iodide* of replacing a hydrogen atom on the number 3 carbon atom $\left(\underset{3}{C}=\underset{2}{C}-\underset{1}{C}\right)$ with a methyl group was first noted by Tamele, *et al.*,[7] in a comparison of the reactivity of allyl chloride and crotyl chloride. Their work indicated a 2.4-fold increase in reactivity, but because the crotyl chloride was not characterized as to geometrical configuration and this configuration plays an important role in determining reactivity,[2] their work was more qualitative than quantitative. The present investigation has shown that when both hydrogen atoms on the number 3 carbon atom are replaced with methyl groups there is approximately a 28-fold increase in reactivity.

It has previously been shown[2] that the electronegativity of the substituting group on the number 2 carbon atom could be related to the reactivity of the allylic chlorine toward potassium iodide. There is no similar relationship to be found for substitutions on the number 3 carbon atom, because both a methyl group and a chlorine atom increase the reactivity of the allylic chlorine and this effect is in the same order of magnitude; 1-chloro-3-methyl-2-butene = 28.1; 1,3-dichloro-2-butene[6] = 23.3 (low boiling isomer) and 27.8 (high boiling isomer).

The influence of methyl groups on the number 3 carbon atom on the reaction of allylic chlorides with *sodium ethoxide* offers a striking example of the unpredictability of a seemingly simple reaction. At 35° allyl chloride reacts to the extent of 21% in twenty hours, crotyl chloride reacts to the extent of 50% in twenty hours, while 1-chloro-3-methyl-2-butene reacts to the extent of 90% in thirty minutes at −50°. Be-

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[2] Hatch, Gordon and Russ, THIS JOURNAL, **70**, 1093 (1948).

[3] (a) Andrews and Kepner, *ibid.*, **70**, 3456 (1948); (b) Hatch and Alexander, *ibid.*, **71**, 1037 (1949).

[4] (a) Hatch and Estes, *ibid.*, **67**, 1730 (1945); (b) Hatch and Roberts, *ibid.*, **68**, 1196 (1946); (c) Andrews and Kepner, *ibid.*, **69**, 2230 (1947).

[5] Jones and Chorley, *J. Chem. Soc.*, 832 (1946).

[6] Hatch and Ballin, THIS JOURNAL, **71**, 1041 (1949).

[7] Tamele, Ott, Marple and Hearne, *Ind. Eng. Chem.*, **33**, 115 (1941).

cause of the unusual speed of this reaction, it was thought possible that some product other than the expected 1-ethoxy-3-methyl-2-butene was formed. Only 1-ethoxy-3-methyl-2-butene was found as a product and in good yields. As yet no adequate hypothesis has been developed to explain the unusual reactivity of 1-chloro-3-methyl-2-butene compared to that of crotyl chloride and allyl chloride. These data, however, tend to substantiate a previous observation that the reactions between allylic chlorides and potassium iodide and sodium ethoxide go by different mechanisms.

The effect of replacing one of the methyl groups of 1-chloro-3-methyl-2-butene with a chlorine atom can be determined by comparing the relative reactivity of 1-chloro-3-methyl-2-butene (very fast) with that of 1,3-dichloro-2-butene at 50° (low boiling isomer 4.77, high boiling isomer 6.16). This comparison is possible because geometrical configuration is only a minor factor in determining reactivity in the reaction with sodium ethoxide. Apparently the replacing of one methyl group by a chlorine atom slows down the reaction very markedly. It is also apparent that the high rate of reaction is not associated with the lack of a hydrogen atom on the number 3 carbon. As with the potassium iodide reaction, there is no correlation between the electronegativity of the substituents on the number 3 carbon and the rate of reaction—both chlorine atoms and methyl groups when replacing hydrogen atoms activate the allylic chlorine toward sodium ethoxide.

The activating influence toward *cuprous chloride catalyzed hydrolysis* of methyl groups on the number 3 carbon has been shown by the fact that 1-chloro-3-methyl-2-butene is by far the most reactive of the allylic chlorides which have been studied.[8] This increased reactivity would be expected if the catalytic hydrolysis involves the formation of a complex between the cuprous ion and the carbon-to-carbon double bond of the allylic chloride.[9] The methyl groups would serve as an electron source for the double bond thus causing the double bond to become more neucleophilic and consequently more reactive toward cuprous ion.

Summary

The reactivity of 1-chloro-3-methyl-2-butene was determined with the following reagents: potassium iodide in acetone, sodium ethoxide in ethanol and cuprous chloride in hydrochloric acid.

Methyl groups on the number 3 carbon atom greatly increase the reactivity of the allylic chlorine toward all three of these reagents.

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[8] Paper presented by Hatch, Brown and Bailey before the Southwest Regional Meeting of the American Chemical Society held at Shreveport, La., December 10 and 11, 1948.

[9] Andrews and Keefer, THIS JOURNAL, 70, 3261 (1948).

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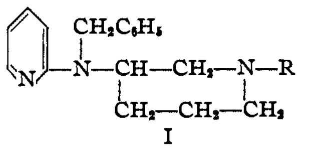
Syntheses of 3-Aminopiperidines

BY ROBERT H. REITSEMA AND JAMES H. HUNTER

A number of physiologically active compounds are known to have an ethylenediamine chain as a part of their structure. Since 3-aminopiperidines can be considered as cyclic ethylenediamines, it was of interest to investigate the effect of replacing the ethylenediamine unit with a 3-aminopiperidine group. Two potential histamine antagonists of type I have been synthesized as examples of such substitution in the antihistamine N,N-dimethyl-N′-benzyl-N′-(α-pyridyl)-ethylenediamine (II).[1]



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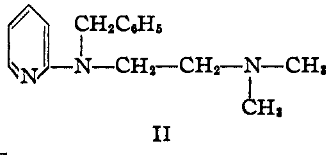

II

The preparation of 3-alkylaminopiperidines was approached three ways. Reductive alkylation of amines with 1-alkyl-3-piperidones was the most successful procedure employed. In this manner 1-alkyl-3-benzylamino- and 1-alkyl-3-(β-dimethylaminoethylamino)-piperidines were obtained. The yields were comparable to those observed in the 4-aminopiperidine series.[2] The Hofmann rearrangement of 1-ethyl-nipecotamide gave the expected 1-ethyl-3-aminopiperidine, but the yield was low. The third synthesis involved selective alkylation of N-3-piperidyl-*p*-toluenesulfonamide. The preparation of N-3-pyridyl-*p*-toluenesulfonamide and its reduction to N-3-piperidyl-*p*-toluenesulfonamide was accomplished; however this approach was abandoned due to the slowness of the reduction. The more difficult selective alkylation of 3-aminopiperidine, prepared by reduction of 3-aminopyridine,[3,4] was not attempted.

1-Methyl- and 1-ethyl-3-piperidone were prepared by the method of Prill and McElvain[5] from

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[1] Huttrer, *et al.*, THIS JOURNAL, 68, 1999 (1946).

[2] Reitsema and Hunter, *ibid.*, 70, 4009 (1948).

[3] Tschitschibabin and Gertschuk, *Ber.*, 63B, 1153 (1930).

[4] Nienburg, *ibid.*, 70B, 635 (1937).

[5] Prill and McElvain, THIS JOURNAL, 55, 1233 (1933).