Diisobutylethylcarbinol (I).—A solution of ethylmagnesium bromide in ether prepared from 218 g. (2.0 moles) of ethyl bromide and 48.6 g. (2.0 moles) of magnesium turnings in a total of 500 ml. of anhydrous ether was refluxed 30 minutes, and treated with a 1:1 ether solution of 142 g. (1.0) mole of diisobutyl ketone added over a period of 1.5 hours. A total of 5.2 l. (S.T.P.) of gas was evolved during this addition. This volume represented a total of approximately 0.2 mole of ethane and ethene. The reaction mixture was slowly hydrolyzed with 600 ml. of 4 *N* HCl during 3.5 hours, 33.5 l. (S.T.P.) of gas being collected. This volume represented 1.5 moles of ethane. The ether and water layers were separated and the aqueous phase extracted three times with 150-ml. portions of ether. The original ether layer and the extracts were combined and dried over anhydrous sodium sulfate. The ether was removed on a water-bath leaving 158 g. of higher boiling material. This liquid was distilled at 16 mm. pressure using a modified Vigreux column, and the following were obtained: (a) unreacted diisobutyl ketone, b.p. 61–67°, d^{25}_4 0.7576, n^{25}D 1.4254, 36.5 g., identified by its 2,4-dinitrophenylhydrazone melting at 92°; (b) diisobutylcarbinol and diisobutyl ketone, b.p. 78–88°, n^{25}D 1.4286–1.4330, 32.5 g., and (c) the tertiary alcohol I, b. 88–93°, n^{25}D 1.4330–1.4353, 65.0 g. A small amount of olefinic material also was detected in a. The physical constants of a selected fraction of the new alcohol I are b.p. 91–93° (16 mm.), d^{25}_4 0.8252 and n^{25}D 1.4347. The gas evolved during hydrolysis of the reaction mixture represented unreacted Grignard reagent, and approximately 0.4 mole of ketone failed to react.

Dehydration of Diisobutylethylcarbinol (I).—The alcohol was heated under reflux in the presence of oxalic acid, and the hydrocarbon layer so obtained was then heated for 2.5 hours over sodium. That portion distilling at 159–162° at 710 mm. had the following properties: d^{25}_4 0.7504, n^{25}D 1.4248.

Anal. Calcd. for $C_{11}H_{22}$: C, 85.25; H, 14.58. Found: C, 85.49; H, 14.51.

Ozonolysis of the Olefins $C_{11}H_{22}$.—The ozone oxidation apparatus was similar to that employed by Henne and Hill.[3] Using the procedure for the preparation of ketones as described by Henne and Hill,[4] a fraction boiling over the range 70–90° was obtained which upon treatment with 2,4-dinitrophenylhydrazine reagent gave a solid melting at 73–74° (uncor.) from ethanol. The 2,4-dinitrophenylhydrazone from ethyl isobutyl ketone melts at 75°.[4] Treatment of the fraction which distilled at 147° with the 2,4-dinitrophenylhydrazine reagent gave a solid which melted at 91–92° (uncor.) from ethanol. A mixed melting point of this compound with a sample of the 2,4-dinitrophenylhydrazone from diisobutyl ketone showed no depression.

[3] A. L. Henne and P. Hill, THIS JOURNAL, **65**, 752 (1943).

[4] C. F. H. Allen, *ibid.*, **52**, 2955 (1930).

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, ILLINOIS INSTITUTE OF TECHNOLOGY]

The Reactions of Silver Nitrate with Some Substituted Neopentyl Bromides

BY MYRON L. BENDER AND HARRY ROBBINS[1]

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The reactions of silver nitrate with 2,2-dimethyl-1,3-dibromopropane, 2,2-dimethyl-3-bromo-1-propanol and 2,2-dimethyl-3-acetoxy-1-bromopropane in 70% aqueous ethanol produced 2-methylbutanal in each case. Kinetic studies indicated that the rate of each reaction was proportional to the halide concentration and to the silver ion concentration. Energies of activation for these reactions have been determined. On the basis of the product analyses and kinetics, mechanisms involving molecular rearrangement and, in one case, an allylic rearrangement are postulated. It appears that no neighboring group reactions take place in these 1,3-systems under the conditions described.

Introduction

The neighboring group reaction, in which an atom or group of atoms is postulated to participate in the reaction of a second functional group on an adjacent carbon atom, has been useful in explaining a number of stereochemical and kinetic results.[2] The neighboring group reaction has been postulated to proceed through cyclic, usually positively charged, intermediates arising from the participation of the neighboring group in the displacement of the leaving group. Such a mechanism adequately explains the stereochemical result of over-all retention of configuration in certain reactions[2a] and also explains the fact that some of the more powerful neighboring groups provide substantial driving forces to the reaction, resulting in enhanced rates of reaction.[2b]

The participation of the neighboring groups cited above pertains to those groups situated on the carbon atom adjacent to the carbon atom containing the displaced group. Several reactions which can be interpreted as involving neighboring groups in the 3-position with respect to the displaced group have been reported with neopentyl derivatives. The neighboring groups in these cases may be the oxide ion,[3] the hydroxyl group,[4,7] the halogen

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[1] Abstracted from the M.S. thesis of H. R.

[2] (a) Much of the stereochemical work is summarized by S. Winstein, H. V. Hess and R. E. Buckles, THIS JOURNAL, **64**, 2796 (1942); (b) much of the kinetic results is summarized by S. Winstein and co-workers, *ibid.*, **70**, 812, 816, 821 and 828 (1948); (c) see also C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell Univ. Press, Ithaca, N. Y., 1953, pp. 381–395, and P. D. Bartlett in H. Gilman, "Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1953, Vol. III, pp. 37–41.

[3] F. Govaert and M. Beyaert, *Natuurw. Tijdschr.*, **22**, 73 (1940) (*C. A.*, **37**, 3054 (1943)); S. Searles, R. G. Nickerson and W. K. Witsiepe, Abstracts of the 123rd Meeting of the A.C.S., p. 31M (1953).

[4] J. Barbiere and J. Matti, *Bull. soc. chim.*, [5] **5**, 1565 (1938).

atom[5,7] and the amino group.[6] The 3-hydroxyl and 3-halogen neighboring groups were involved in reactions consisting in the replacement of a hydroxyl group both with phosphorus tribromide and with hydrogen bromide. The former reagent has been shown to give a normal displacement reaction with neopentyl alcohol in the presence of quinoline,[8] but the latter reagent has been shown to give either no bromide or *t*-amyl bromide with neopentyl alcohol.[9] Of pertinent interest to the consideration of the reactions of 3-substituted neopentyl derivatives is the report of Lindegren and Winstein.[10] They found that in the acetolyses of substituted neopentyl *p*-bromobenzenesulfonates, the 3-methylthio and 3-acetoxy groups exhibited kinetic and structural evidence of neighboring group participation, whereas halogen in the 3-position did not.

This investigation is concerned with the reactions of 3-substituted neopentyl bromides. The products of such systems are usually a reliable criterion of the reaction mechanism: an SN1 reaction[9] is usually accompanied by rearrangement of the carbon skeleton; an SN2[11] or a simple neighboring group reaction[10] usually results in retention of skeletal configuration. The reaction of neopentyl bromide with silver nitrate in 70% aqueous ethanol exhibits second-order kinetics, yielding products with a rearranged carbon skeleton.[11] Investigations of the reactions of 2,2-dimethyl-1,3-dibromopropane, 2,2-dimethyl-3-bromo-1-propanol and 2,2-dimethyl-3-acetoxy-1-bromopropane under similar conditions are reported here.

Experimental

Materials.—1-Bromo-2,2-dimethylpropane was prepared from dimethyl-1-propanol according to the procedure of Sommer,[8] b.p. 104–107°, $n^{20}\text{D}$ 1.4367. 2,2-Dimethyl-1,3-propanediol prepared by the reaction of isobutyraldehyde and formaldehyde[12] was converted to 2,2-dimethyl-1,3-dibromopropane by treatment with phosphorus tribromide,[12] b.p. 63–65° (24 mm.), $n^{20}\text{D}$ 1.5051. 2,2-Dimethyl-3-bromo-1-propanol was prepared by the reaction of fuming hydrobromic acid with 2,2-dimethyl-1,3-propanediol,[7] b.p. 73–74° (8 mm.), $n^{20}\text{D}$ 1.4797. 2,2-Dimethyl-3-acetoxy-1-bromopropane was prepared by the reaction of 2,2-dimethyl-1,3-propanediol with glacial acetic acid and 48% hydrobromic acid according to the method of Searles,[13] b.p. 83° (8 mm.), $n^{20}\text{D}$ 1.4565.

Anal. Calcd. for $C_7H_{13}O_2Br$: C, 40.2; H, 6.27: Br, 38.3. Found: C, 40.2; H, 6.34; Br, 38.6.

Identification of the Reaction Products.—2,2-Dimethyl-3-bromo-1-propanol (1.67 g., 0.010 mole), silver nitrate (17.0 g., 0.100 mole) and 60 ml. of water were introduced into a 100-ml. round-bottom flask. This flask was attached to a 20-cm. column packed with glass helices. The reaction mixture was heated at total reflux for 30 minutes, and then slowly distilled for three hours at the rate of a few drops/min. The distillate consisted of an organic layer and an aqueous layer which was extracted with ether. The ether extract gave a positive Schiff test and a 2,4-dinitrophenylhydrazone, m.p. 127.5°. Authentic 2-methylbutanal was prepared by the oxidation of 2-methylbutanol (Eastman Kodak Co.) with chromic acid. The melting point of a mixture of the 2,4-dinitrophenylhydrazones of authentic 2-methylbutanal and the unknown melted at 127°.

2,2-Dimethyl-3-bromo-1-propanol (3.34 g., 0.020 mole) was refluxed with a tenfold excess of silver nitrate in 70% aqueous ethanol (70% ethanol by volume) for one week. The solvent was partially evaporated and the residue was extracted with ether for 20 hours in a continuous extractor. No 2,2-dimethyl-1,3-propanediol could be isolated from the ether extract although as little as 0.01 g. could be recovered in blank experiments. A further experiment indicated that if 2,2-dimethyl-1,3-propanediol had been formed, it would not have been oxidized by the nitric acid produced. The reaction of silver nitrate with the bromide described above was repeated with provision for the collection of gaseous products in a Dry Ice trap. The contents of the trap gave a negative test when treated with bromine in carbon tetrachloride.

Similar experiments involving 2,2-dimethyl-1,3-dibromopropane and 2,2-dimethyl-3-acetoxy-1-bromopropane indicated that 2-methylbutanal was the sole product of each reaction.

The method of Bennett,[14] as modified by Bryant and Smith,[15] was used for the quantitative estimation of the aldehyde formed in each of the above reactions. The halide (*ca.* 2 ml.), silver nitrate (10 g.) and water (70 ml.) were refluxed for 30 minutes. The reaction mixture was then slowly distilled through a 20-cm. column packed with glass helices for a period of two hours. Since the nitric acid produced in the solvolyses could oxidize the aldehyde, it was essential to minimize the contact time of these materials. This was done by (1) increasing the velocity of the reaction by using excess silver nitrate (see above) and (2) by removing the product from the reaction mixture by fractional distillation as soon as it was formed. The distillate and the liquid phase remaining in the distilling flask were extracted with petroleum ether. The combined extracts were added to the hydroxylamine hydrochloride solution for quantitative estimation of the aldehyde. The weight of the precipitated silver bromide was used for estimation of the halide reacted. *p*-Nitrobenzaldehyde was used to standardize the method.

Kinetics.—For the kinetic determinations the procedure of Dostrovsky and Hughes was followed.[11] Equal volumes of 0.2800 *M* silver nitrate and 0.2000 *M* halide in 70% aqueous ethanol (70% ethanol by volume) (0.5600 *M* silver nitrate was used with 2,2-dimethyl-1,3-dibromopropane) were mixed at room temperature. Five-ml. aliquots were sealed in ampoules taking care to minimize the air space, and placed in the appropriate thermostat. Ampoules were removed at various time intervals and the unreacted silver nitrate was determined by titration with standard ammonium thiocyanate, using ferric alum as indicator.[16] The reactions were followed to approximately 90% completion. The kinetic data, corrected for volume expansion of the solvent, are graphically presented in Figs. 1 and 2. Duplicate runs were made and the average values of the rate constants are shown in Table II.

Results and Discussion

Only one substance, 2-methylbutanal, was isolated from the reactions of silver nitrate with 2,2-dimethyl-1,3-dibromopropane, 2,2-dimethyl-3-bromo-1-propanol and 2,2-dimethyl-3-acetoxy-1-bromopropane in 70% aqueous ethanol. The absence of 2,2-dimethyl-1,3-propanediol and olefins was demonstrated. Table I indicates the yields of aldehyde as determined by the titration method of Bryant and Smith.[15]

The formation of 2-methylbutanal is evidence that the reactions proceeded with rearrangement of the carbon skeleton.

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[5] R. W. Shortridge, R. A. Craig, K. W. Greenlee, J. M. Derfer and C. E. Boord, THIS JOURNAL, **70**, 946 (1948).

[6] W. B. Wheatley and L. C. Cheney, *ibid.*, **74**, 1359 (1952).

[7] G. M. Bennett and W. G. Philip, *J. Chem. Soc.*, 1938 (1928); A. Franke, *Monatsh.*, **34**, 1898 (1913).

[8] L. H. Sommer, H. D. Blankman and P. C. Miller, THIS JOURNAL, **73**, 3542 (1951).

[9] F. C. Whitmore and H. S. Rothrock, *ibid.*, **54**, 3431 (1932).

[10] C. R. Lindegren and S. Winstein, Abstracts of the 123rd Meeting of the Amer. Chem. Society, p. 30 M (1953).

[11] I. Dostrovsky and E. D. Hughes, *J. Chem. Soc.*, 157, 169 (1946).

[12] F. C. Whitmore, A. H. Popkin, J. P. Wilkins and H. I. Bernstein, THIS JOURNAL, **63**, 124 (1941).

[13] S. Searles, private communication.

[14] A. H. Bennett, *Analyst*, **34**, 14 (1909).

[15] W. D. Bryant and D. M. Smith, THIS JOURNAL, **57**, 57 (1935).

[16] W. F. Hillebrand and G. E. F. Lundell, "Applied Inorganic Analysis," 2nd Ed., John Wiley and Sons, Inc., New York, N. Y., 1953, pp. 207–209.

TABLE I

THE SILVER ION SOLVOLYSES OF 3-SUBSTITUTED NEOPENTYL BROMIDES

Reactant	2-Methylbutanal, yield,[a] %
2,2-Dimethyl-1,3-dibromopropane	16
2,2-Dimethyl-3-bromo-1-propanol	46
2,2-Dimethyl-3-acetoxy-1-bromopropane	21

[a] The low yields are probably due to oxidation of the aldehyde by nitric acid formed in the solvolysis as evidenced by the fact that a portion of the organic product was soluble in sodium bicarbonate.

A possible mechanism for the reaction of 2,2-dimethyl-3-bromo-1-propanol is

$$(CH_3)_2(CH_2OH)CCH_2Br \xrightarrow[-AgBr]{Ag^+}$$

$$(CH_3)_2(CH_2OH)CCH_2^+ \longrightarrow$$

$$(CH_3)(CH_2OH)(C_2H_5)C^+ \xrightarrow{-H^+}$$

$$(CH_3)(C_2H_5)C{=}CHOH \longrightarrow (CH_3)(C_2H_5)CHCHO$$

Ionization of the bromo group is followed by a methyl migration to form a tertiary carbonium ion. A proton is then eliminated from the hydroxymethyl group to form the enol of 2-methylbutanal, which then tautomerizes. It is possible that the proton is eliminated from the methylene group producing an allylic alcohol which rearranges to the aldehyde (see below). The reaction of 2,2-dimethyl-3-acetoxy-1-bromopropane would be expected to take an analogous course, except that, at some stage, hydrolysis of the acetoxy group takes place.

In the case of 2,2-dimethyl-1,3-dibromopropane, the product analysis does not permit a decision as to whether the rearrangement occurs during the reaction of the first or second bromine atoms. It is suggested that the rearrangement occurs during the removal of the first bromine atom, leading to the formation of 1-bromo-2-methyl-2-butene. This allylic bromide is then hydrolyzed rapidly under the reaction conditions to form the corresponding allylic alcohol which is known to rearrange under acidic conditions to the aldehyde.[17] The kinetic data discussed below bear out this scheme.

It is assumed that the kinetics of these reactions are of the second order as was shown by Dostrovsky and Hughes for the reaction of neopentyl bromide.[11] The kinetic data for the reactions of the substituted neopentyl bromides at 93 and 109° are shown in Figs. 1 and 2. Linear second-order plots are observed except in the case of 2,2-dimethyl-3-acetoxy-1-bromopropane. In this case deviation from linearity occurs at the beginning of the reaction, but a straight line parallel to that of 2,2-dimethyl-3-bromo-1-propanol occurs at longer times. This has been interpreted to mean that a rapid hydrolysis of the acetoxy group occurs at the beginning of the reaction giving the bromo alcohol which then reacts with silver nitrate as described above. The rate constant for the silver ion reaction of the acetoxy compounds was determined from the initial slope of the curve, indicated by the line C′.

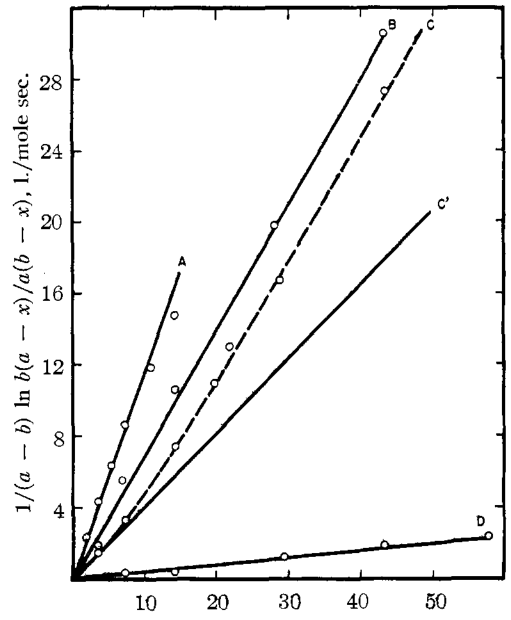

Fig. 1.—Silver ion solvolysis of neopentyl halides at 92.3 ± 0.5°: A, 2,2-dimethyl-3-bromopropane; B, 2,2-dimethyl-3-bromo-1-propanol; C, 2,2-dimethyl-3-acetoxy-1-bromopropane (C′ initial slope); D, 2,2-dimethyl-1,3-dibromopropane (abscissa = $1/(a - 2b) \ln b(a - 2x)/a(b - x)$).

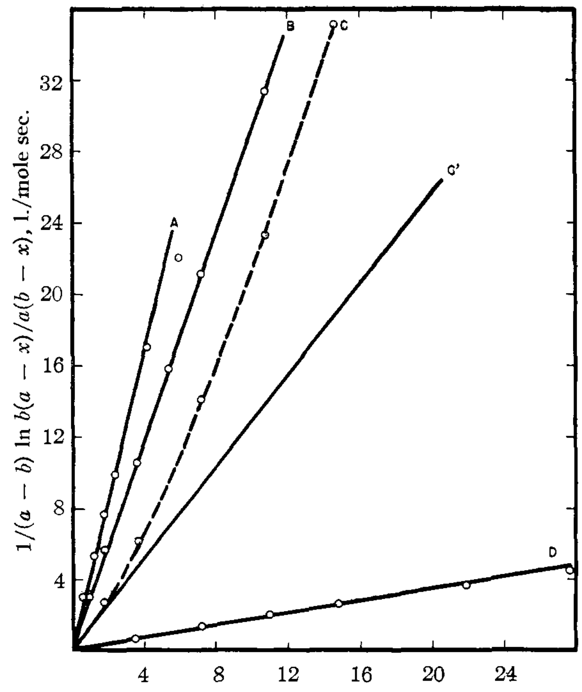

Fig. 2.—Silver ion solvolysis of neopentyl halides at 109.1 ± 0.2°: A, 2,2-dimethyl-1-bromopropane; B, 2,2-dimethyl-3-bromo-1-propanol; C, 2,2-dimethyl-3-acetoxy-1-bromopropane (C′ initial slope); D, 2,2-dimethyl-1,3-dibromopropane (abscissa = $1/(a - 2b) \ln b(a - 2x)/a(b - x)$).

Because the data for the reaction of 2,2-dimethyl-1,3-dibromopropane fit the rate equation, $2.303/(a -$

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(17) S. Hearne, M. Tamele and W. Converse, *Ind. Eng. Chem*, **33**, 805 (1941).

TABLE II

RATE CONSTANTS AND ACTIVATION ENERGIES OF SILVER ION SOLVOLYSES

Compound	$k_2 \times 10^4$, l./mole sec. 63.9°	92.3 ± 0.5°[d]	109.1 ± 0.2°	E_A,[c] kcal./mole
2,2-Dimethyl-1-bromopropane	0.84,[a] 1.01[b]	11.3 ± 1(92.4)	42.5 ± 1	22.5 ± 1.3
2,2-Dimethyl-3-bromo-1-propanol		7.1 ± 0.3(91.9)	30.5 ± 1	23.7 ± 0.7
2,2-Dimethyl-3-acetoxy 1-bromopropane		3.7 ± .4(92.8)	14.9 ± 1	24.0 ± 1.2
2,2-Dimethyl-1,3-dibromopropane		0.42 ± .03(91.9)	1.75 ± 0.1	23.0 ± 0.7

[a] Extrapolated using the energy of activation. [b] Dostrovsky and Hughes, reference 11. [c] The Arrhenius energies of activation were calculated from the rate constants at the two temperatures shown. The uncertainty in the values of the activation energies negates the drawing of conclusions from these values. [d] This range is due to a steady drift of the thermostat. During a single experiment the values in parentheses were good to ±0.1°.

2*b*) $\log [b(a - 2x)/a(b - x)] = kt$, which assumes a slow removal of the first bromine atom and a fast hydrolysis of the second bromine atom, confirmation is obtained for the mechanism of this reaction proposed above.

Conclusions

In the absence of neighboring group participation, it is expected that the electronegative 3-substituents will retard the reaction, and that the magnitude of the retardation will be dependent on the magnitude of the electrostatic effect of the 3-substituent. The order of substituent effects on reaction rates in Table II parallels the effect of these substituents on the dissociation constants of carboxylic acids.[18] The reactions of the compounds containing the 3-bromo- and 3-hydroxy substituents show retardation of rate and rearrangement, results indicating that neighboring group participation by these 3-substituents probably does not occur. In the case of the compound containing the 3-acetoxy substituent, the kinetic result of retardation indicates that it, also, does not participate as a neighboring group. The structural result of rearrangement in this latter case does not necessarily lead to the same conclusion since most of the rearranged product is probably produced *via* the bromo alcohol.

It is interesting to compare these results with those of Lindegren and Winstein.[10] The two sets of data are in agreement concerning the role of halogen but not concerning that of the acetoxy group. The kinetic evidence for participation of the 3-acetoxy group is especially convincing since kinetic criteria are usually less sensitive than structural criteria. It is possible that the discrepancy between the two results with respect to the acetoxy group may be reconciled by a consideration of the reaction conditions employed.[19]

CHICAGO, ILLINOIS

[18] S. Winstein, E. Grunwald and L. L. Ingraham[2b] have calculated the driving force of several neighboring groups including the *trans*-2-bromo and *trans*-2-acetoxy groups after taking into account the electrostatic effect of these groups. Comparison of these calculations with the retardations reported here for the 3-substituents indicates that electrostatic interactions will account for the present results.

[19] The referee has suggested the following possible explanation. A comparison of the solvents used in the two studies indicates that the aqueous ethanol employed in the present investigation is a better nucleophilic solvent than is the acetic acid employed by Lindegren and Winstein. However, if the comparison is made from the point of view of the *Lim.* character of the solvolysis, it is possible to say that the conditions of Lindegren and Winstein are more of the *Lim.* variety than are those of the present investigation (S. Winstein and H. Marshall, THIS JOURNAL, **74**, 1123 (1952)). One would expect that a more limiting solvolysis would favor external solvation over internal solvation and thus reduce the neighboring group participation. If one, however, considers the competition between external and internal solvation from the point of view of the variation in the nucleophilicity of the solvent, one arrives at an opposite conclusion which is in agreement with the data.

[CONTRIBUTION FROM ROHM AND HAAS CO.]

The Aminomethylation of Olefins. V. A New Synthesis of 4-Phenylpyridine and Related Compounds

BY CLAUDE J. SCHMIDLE AND RICHARD C. MANSFIELD

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A new and relatively simple synthesis of 4-phenylpyridine from α-methylstyrene, formaldehyde and ammonium chloride is reported.

Previous methods of synthesis[1-5] of 4-phenylpyridine (III) suffer the disadvantages of low yield, involved and tedious procedures, contamination of the product by isomers and the use of relatively unavailable and expensive starting materials. Melting points for 4-phenylpyridine (III) ranging from 69–78° have been reported by previous investigators.[1-5]

We have found that 4-phenylpyridine (III) can be prepared from α-methylstyrene, formaldehyde and ammonium chloride. Hartough and co-workers[6] have reported the condensation of these materials to give 6-methyl-6-phenyltetrahydro-1,3-oxazine (I). Studies in this Laboratory have shown that the latter material can be converted with ex-

[1] A. Hantzsch, *Ber.*, **17**, 1518 (1884).

[2] R. Möhlau and R. Berger, *ibid.*, **26**, 1994 (1893).

[3] R. Forsyth and F. L. Pyman, *J. Chem. Soc.*, 2922 (1926).

[4] J. Overhoff and G. Tilman, *Rec. trav. chim.*, **48**, 993 (1929).

[5] J. W. Haworth, I. M. Heilbron and D. H. Hey, *J. Chem. Soc.*, 349 (1940).

[6] H. D. Hartough, J. J. Dickert and S. L. Meisel, U. S. Patent 2,647,117 (July 28, 1953); *C. A.*, **48**, 8265 (1954).