[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NORTHWESTERN UNIVERSITY]

Elimination Reactions in Cyclic Systems. V. General Base Catalysis of *cis* and *trans* Eliminations in the Cyclohexane and Cyclopentane Series[1]

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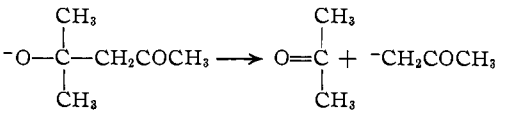
Both the *cis* and *trans* eliminations from 2-*p*-tolylsulfonylcyclohexyl and 2-*p*-tolylsulfonylcyclopentyl *p*-toluenesulfonates have been shown to be subject to general base catalysis. This demonstrates the absence of a stable carbanion intermediate in any of these reactions. Eliminations with triethylamine are all slower than those with the weaker base trimethylamine indicating the operation of a steric effect in these reactions. The smaller ratio of rates, k_{OH^-}/k_{Me_3N} and k_{Et_3N}/k_{Me_3N}, for *cis* eliminations than for *trans* eliminations establishes the importance of steric and electrostatic repulsions in favoring *trans* over *cis* eliminations in these systems. The fact that *cis* and *trans* eliminations in the cyclopentane series with trimethylamine proceed at comparable rates, indicates that the ability to undergo *trans* elimination *via* a planar four-centered transition state is not a factor of primary importance in influencing the rates of these reactions.

At least three factors have been mentioned to explain the more rapid E2 elimination of *trans* than *cis* groupings in cyclohexane derivatives. These are (1) *trans* eliminations are concerted whereas *cis* eliminations proceed by an energetically unfavorable two-stage mechanism involving a carbanion intermediate,[2] (2) steric and electrostatic repulsions between the base and the reacting molecule are less for *trans* than for *cis* eliminations,[3] and (3) planar four-centered transition states with a *trans* arrangement of the groups to be eliminated are energetically favored.[4]

Cristol originally suggested the carbanion intermediate mechanism (labeled ElcB by Ingold) to account for the relative slowness of *cis* elimination of hydrogen chloride from the β-isomer of benzene hexachloride.[2] Cristol and Fix[5] investigated the possibility of deuterium exchange during this reaction. They interpreted the very small amount of deuterium exchange observed as supporting a carbanion mechanism, but Hughes, Ingold and Pasternak[6] have interpreted the same results as evidence for the absence of a carbanion intermediate.

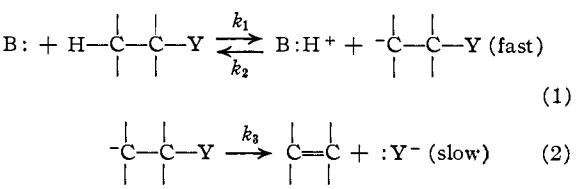
Although no clear-cut example of the operation of the ElcB mechanism in eliminations from a saturated system to form a carbon to carbon double bond appears to have been reported at this writing, there is good reason to believe that a reaction course of this type will be followed in a system, H–C–C–Y, where H–C is sufficiently acidic. This mechanism is apparently operative in the base-initiated elimination of hydrogen chloride from $ClCH{=}CCl_2$, since extensive deuterium exchange has been observed under conditions milder than those used to promote eliminations.[7] In elimination reactions from systems such as H–O–C–Y and H–N–C–Y the reaction course must be frequently that of a two-stage elimination, since the H–O and H–N bonds are relatively acidic. This mechanistic path has been established for the reverse aldol reaction of diacetone alcohol.[8]



It seems certain that the ElcB reaction course will be observed in H–C–C–Y systems when H–C is made sufficiently weak and C–Y is sufficiently strong.

In the previous paper in this series[9] it was shown that *trans* eliminations from *cis*-2-(*p*-tolylsulfonyl)-cyclohexyl and cyclopentyl *p*-toluenesulfonates (II and IV, respectively) were favored over *cis* eliminations from the corresponding *trans* isomers (I and III) by factors of 435 and 20. Since the H–C bond in these compounds has been rendered acidic by the presence of an α-sulfonyl group the likelihood of the formation of a carbanion intermediate appeared to be greater than in the benzene hexachloride case.[2,5,6] A test for the presence of a stable carbanion intermediate was therefore made using a kinetic approach.[10]

In base-catalyzed elimination reactions of the ElcB type



(1)

(2)

the reaction will involve an initial ionization of the substrate which comes to equilibrium, followed by a rate-controlling reaction of the resulting anion. The rate will be a function of the concentration of the anion, $^-C\text{-}C\text{-}Y$, and the anion concentration will be in turn a function of the ratio of the concentration of the base, B, and its conjugate acid,

(1) This investigation was supported by the Office of Naval Research under Contract No. N7 onr-45007. The results were reported in a preliminary fashion in THIS JOURNAL, **76**, 4748 (1954).

(2) (a) S. J. Cristol, THIS JOURNAL, **69**, 338 (1947); (b) S. J. Cristol, N. L. Hause and J. S. Meek, *ibid.*, **73**, 674 (1951); (c) S. J. Cristol and W. P. Norris, *ibid.*, **76**, 3005 (1954).

(3) W. Hückel, W. Tappe and G. Legutke, *Ann.*, **543**, 191 (1940).

(4) D. H. R. Barton and E. Miller, THIS JOURNAL, **72**, 1066 (1950).

(5) S. J. Cristol and D. D. Fix, *ibid.*, **75**, 2647 (1953).

(6) E. D. Hughes, C. K. Ingold and R. Pasternak, *J. Chem. Soc.*, 3832 (1953).

(7) L. C. Leitch and H. J. Berstein, *Can. J. Research*, **28B**, 35 1950); S. I. Miller and R. M. Noyes, Jr., THIS JOURNAL, **74**, 636 1952).

(8) L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, p. 344.

(9) J. Weinstock, R. G. Pearson and F. G. Bordwell, THIS JOURNAL, **78**, 3468 (1956).

(10) A. A. Frost and R. G. Pearson, "Kinetics and Mechanism," John Wiley and Sons, Inc., New York, N. Y., 1953, pp. 207–208.

$B:H^+$. Since in aqueous solution this ratio depends on the hydroxide ion concentration

$$B: + HOH \rightleftharpoons B:H^+ + OH^-$$

such reactions appear to be catalyzed only by hydroxide ions (specific hydroxide ion catalysis).

On the other hand, if the reaction proceeds by way of a concerted path, or a rate-controlling ionization followed by a rapid reaction of the anion, the reaction rate will be the sum of the reactions of all bases present (general base catalysis). From a mechanistic standpoint general base catalysis means that removal of a proton is involved in the rate controlling step.

In order to determine whether the *cis* and *trans* eliminations of I-IV previously described[9] were subject to specific hydroxide or general base catalysis, the rates were studied with trimethylamine and triethylamine in the presence of varying concentrations of the corresponding salt.

Results

The rates of reaction of I, II, III, IV and V[9] with the amines were measured conductometrically in 50% aqueous dioxane solutions buffered by the presence of some of the amine salt. The base was used in large excess so that pseudo first-order kinetics were observed. The rates were obtained by plotting log $R/(R - R_\infty)$ against time,[11] and multiplying the slope by 2.303. The second-order rate constants (k_1) were obtained by plotting the observed first-order rate constants, obtained from at least three different dilutions of the buffer stock solution, against amine concentration. According to the equation

$$k_{obsd} = k_1(\text{amine}) + k_2(OH^-)$$

the slope of such a plot is equal to the second-order rate constant. The data used to obtain a typical first-order rate constant are given in Table I for the reaction between trimethylamine and IV.

TABLE I

RATE OF THE REACTION OF TRIMETHYLAMINE[a] WITH IV IN 50% AQUEOUS DIOXANE AT 25°

Time (sec.)	Resistance (ohms)	log $(R/R - R)$	Time (sec.)	Resistance (ohms)	log $(R/R - R)$
31	1730	0.7612	300	1540	1.1461
50	1710	.7853	350	1520	1.2279
75	1690	.8159	400	1510	1.2758
100	1660	.8579	450	1495	1.3617
125	1645	.8837	500	1490	1.3950
150	1620	.9309	600	1475	1.5159
200	1590	.9969	3500[b]	1430	
250	1560	1.0792			

[a] Trimethylamine concentration equals 0.1914 M. [b] Infinity reading. Rate constant, k_1, is 3.20×10^{-3} sec.$^{-1}$.

The above method of obtaining the rate constants assumes a negligible salt effect. This was tested by determining the rate of elimination of III with and without added lithium nitrate with a constant amount of trimethylamine buffer. The *total* salt concentrations and second-order rate constants were: 0.05 N salt, $k = 1.31 \times 10^{-2}$ l. mole^{-1} sec.$^{-1}$; 0.10 N salt, $k = 1.25 \times 10^{-2}$ l. mole^{-1} sec.$^{-1}$; 0.15 N salt, $k = 1.28 \times 10^{-2}$ l. mole^{-1} sec.$^{-1}$. The variation is well within the experimental error.

(11) Reference 10, p. 35.

Discussion

The fact that observed rates increased in every instance with an increased concentration of amine, even though the concentration of hydroxide ion (or the ratio of concentrations $[B:]/[B:\dot{H}]$) remained constant, shows that these reactions are general base catalyzed. This was further tested for I, where the slower rate caused a greater error in determining the rate constant,[12] by runs in which the amine concentration was kept constant and the amine salt concentration was varied. The relative constancy of the observed rates under these conditions is brought out in Table III.

TABLE III

RATES OBSERVED FOR THE REACTION OF I WITH PIPERIDINE IN THE PRESENCE OF VARIED AMOUNTS OF BH^+

Piperidine hydrochloride concn. (moles/l.)[a]	$k_{obsd.} \times 10^5$
0.020	6.38
.015	6.57
.010	6.55
.005	6.37

[a] In every run the concentration of free piperidine used was 0.1200 M.

These results show that no stable carbanion intermediate is formed in any of these elimination reactions. Since the sulfonyl group stabilizes a carbanion alpha to it, it seems extremely unlikely that a stable carbanion is present in systems where such a stabilizing influence is smaller or altogether absent.[13] On this basis, in our opinion, the *cis* eliminations we have called attention to[14] and that of the β-isomer of benzene hexachloride are best classified as E2 reactions rather than ElcB reactions.

It must be borne in mind, however, that the distinction between an ElcB mechanism and an E2 mechanism vanishes as the life-time of the carbanion intermediate becomes infinitely small. Thus experimentally all one can demonstrate is an upper limit to the life-time of the carbanion. In the reactions reported here a crude estimate of the life-time can be made in the following way. The acid ionization constant of dimethyl sulfone in water has been estimated[15] to be 10^{-23}. Since the rate of deuterium exchange of dimethyl sulfone is only slightly less than the rate of *cis* elimination from compound I when hydroxide ion is the base,[16]

(12) In unpublished work (with T. A. Sullivan) examples of *cis* eliminations of analogs of I have also been shown to undergo general base catalysis.

(13) C. K. Ingold, "Structure and Mechanism of Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, p. 423, has predicted that when the hydrogen atom eliminated is the ionizing hydrogen of a pseudo-acid, the compound would undergo unimolecular conjugations from its conjugate anion, that is, by an ElcB mechanism. This is not what we have found when the pseudo-acid is a sulfone, but may hold for stronger pseudo-acids such as ketones, nitroalkanes and is highly probable in compounds where the hydrogen being eliminated is activated by two such functional groups.

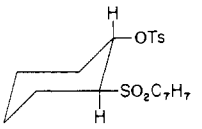
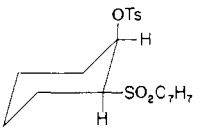
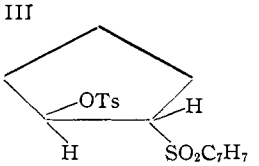
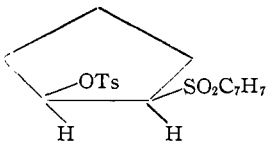
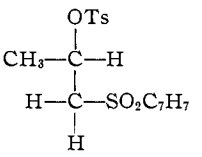
(14) See the earlier papers in this series for several further examples.

(15) R. G. Pearson and R. L. Dillon, THIS JOURNAL, **75**, 2439 (1953).

(16) K. F. Bonhoeffer and J. Hochberg, *Z. physik. Chem.*, **A184**, 419 (1939).

TABLE II

RATES OF AMINE REACTIONS WITH I–V IN 50% AQUEOUS DIOXANE AT 25°

Compound	Amine	Initial amine concn.	$k_{obsd.}$ (sec.$^{-1}$)	k_1 (l. mole^{-1} sec.$^{-1}$)
I	Me_3N	0.0846	9.58×10^{-6}	
		.169	1.95×10^{-5}	
		.254	2.78×10^{-5}	
				1.13×10^{-4}
	Et_3N	0.0628	1.179×10^{-6}	
		.1255	1.396×10^{-6}	
		.1883	2.195×10^{-6}	
				8.0×10^{-6}
trans-isomer (equatorial form)	Piperidine	0.05894	3.895×10^{-5}	
		.1180	6.55×10^{-5}	
		.1768	9.95×10^{-5}	
				5.10×10^{-4}
II	Me_3N	0.06522	2.57×10^{-4}	
		.1304	4.53×10^{-4}	
		.1957	6.16×10^{-4}	
				2.87×10^{-3}
cis-isomer	Et_3N	0.06277	3.96×10^{-4}	
		.1255	4.76×10^{-4}	
		.1883	5.15×10^{-4}	
				9.3×10^{-4}
III	Me_3N	0.06404	8.42×10^{-4}	
		.1281	16.25×10^{-4}	
		.1921	25.3×10^{-4}	
				1.30×10^{-2}
	Et_3N	0.06273	8.80×10^{-5}	
		.09394	12.60×10^{-5}	
		.1255	14.33×10^{-5}	
		.1566	17.60×10^{-5}	
		.1882	21.62×10^{-5}	
				10.1×10^{-4}
IV	Me_3N	0.0638	1.21×10^{-3}	
		.0957	1.79×10^{-3}	
		.1276	2.30×10^{-3}	
				1.56×10^{-2}
		.1914	3.20×10^{-3}	
	Et_3N	0.06273	8.77×10^{-4}	
		.1255	13.07×10^{-4}	
		.1882	17.20×10^{-4}	
				6.77×10^{-3}
V	Me_3N	0.0512	6.56×10^{-3}	
		.0640	8.65×10^{-3}	
		.0768	9.78×10^{-3}	
		.0896	1.22×10^{-2}	
				1.32×10^{-1}
	Et_3N	0.06273	4.86×10^{-3}	
		.08155	5.82×10^{-3}	
		.1004	6.93×10^{-3}	
				5.93×10^{-2}
	NH_3	0.0604	7.04×10^{-4}	
		.1208	1.11×10^{-3}	
		.1812	1.55×10^{-3}	
				7.10×10^{-3}

the same ionization constant may be assumed for I. Considering trimethylamine as the base, the condition for general base catalysis is that $k_2(BH^+) << k_3$.

$$B: + HA \underset{k_2}{\overset{k_1}{\rightleftharpoons}} B:H^+ + A^-$$

$$A^- \xrightarrow{k_3} \text{products}$$

We may set k_1/k_2 equal to K_aK_b/K_w which is the equilibrium constant for the first step in a two-stage ElcB reaction. The equilibrium constant would be of the order $(10^{-23})(10^{-4})/10^{-14}$ or 10^{-13} in water solution, and in 50% aqueous dioxane a reaction producing two univalent ions from neutral molecules would be less favored by one or two powers of ten. Taking 10^{-14} as the

value, we calculate k_2 for trimethylammonium ion to be 10^{10} l. mole^{-1} sec.$^{-1}$ using the value of k_1 given in Table II. For a solution containing 0.03 *M* trimethylammonium ion then, $k_3 >> 3 \times 10^8$ sec.$^{-1}$, which sets an upper limit on the mean lifetime of the carbanion at about 10^{-9} seconds.

Cristol has preferred to interpret the results of his careful and extensive investigation of elimination reactions in terms of a concerted mechanism for *trans* elimination and a two-stage mechanism for *cis* elimination.[2] It is possible to reconcile our data with this point of view if it is assumed that $k_3 > k_2$. Cristol has pointed out that, as the hydrogen being attacked by the base becomes more acidic, it would be expected that the carbanion mechanism would gain favor relative to the concerted mechanism. While this is true, it does not seem to us necessary or desirable to assume, in the absence of evidence for a stable carbanion, that *cis* eliminations derive no benefit energetically from the formation of the carbon to carbon double bond. It seems preferable to take the more moderate view[6] that higher activation energies for *cis* eliminations are required to force the reaction against an unfavorable steric arrangement of groups.

The relative rates of elimination for I–V with hydroxide ion,[1,2] trimethylamine and triethylamine are summarized in Table IV.

TABLE IV

RELATIVE RATES OF REACTION OF I–V IN 50% DIOXANE AT 25°

Compound	Type of elimination	Relative rates with OH^-	Me_3N	Et_3N	Rate ratios k_{OH^-}/k_{Me_3N}	k_{Et_3N}/k_{Me_3N}
I	*cis*	0.19	0.855	0.135	308	0.068
II	*trans*	81	21.7	15.7	5220	.324
III	*cis*	11.9	98.5	17.4	169	.077
IV	*trans*	235	118	114	2780	.435
V	*trans*	1000[a]	1000[b]	1000[c]	1400	.45

[a] $k = 1.84 \times 10^2$ l. mole^{-1} sec.$^{-1}$. [b] $k = 1.32 \times 10^{-1}$ l. mole^{-1} sec.$^{-1}$. [c] $k = 5.93 \times 10^{-2}$ l. mole^{-1} sec.$^{-1}$.

Comparison of the triethylamine rates with the trimethylamine rates shows that in every instance the triethylamine reacts slower. Since triethylamine is the stronger base, the Brönsted catalysis law would predict that it should react faster than trimethylamine. In the ionization of nitroethane, for example, the rates are 2.05 l. mole^{-1} min.$^{-1}$ for trimethylamine and 3.12 l. mole^{-1} min.$^{-1}$ for triethylamine,[17] the ratio k_{Et_3N}/k_{Me_3N} being 1.52. Since the two amines have different steric requirements, the lower rates in the elimination reactions are probably due to a steric retardation of proton abstraction (F-strain in the transition state) in the reaction with triethylamine. A further indication for this is the variation of k_{Et_3N}/k_{Me_3N} values as shown in Table IV. The values for this ratio for the *cis* eliminations occurring with I and III are about one-fifth as large as for the *trans* eliminations with II and IV. Inspection of molecular models of I and III shows that in these compounds the hydrogens are more shielded than in the other three compounds. The operation of a steric factor for proton abstraction has been demonstrated by Pearson and Williams,[17] and by Brown and Moritani.[18]

The much higher values observed for the hydroxide rates than for the amine rates are expected since hydroxide ion is a much stronger base than the tertiary amines. However, the ratio k_{OH^-}/k_{Me_3N} is not constant, the values for the compounds I and III undergoing *cis* eliminations are about one twentieth those for II and IV. A plausible explanation may be found in a consideration of the electrostatics of the transition state. In I and III the proton which is attacked by the base is much closer to the tosylate group than in II and IV. Since the oxygens of the tosylate group have a negative charge due to the polarity of the sulfur–oxygen bond, a negatively charged base would be repelled and the transition state made less stable. A neutral base would acquire a partial positive charge in the transition state, and electrostatic interaction with the negative oxygens of the tosylate group would tend to stabilize the transition state.

From the above discussion it is clear that in compounds I-V steric and electrostatic repulsive forces play an important part in favoring *trans* over *cis* eliminations. The effects are no doubt considerably larger than the 0.2 to 3.0 kcal./mole in activation energy estimated by Cristol[2] since the steric and electrostatic repulsions between the base and tosylate group are larger than between the base and chlorine atom. It thus appears that a considerable part of the factors of 435, 25 and 116 favoring *trans* over *cis* eliminations in the cyclohexane series (II *vs.* I) with hydroxide ion, trimethylamine and triethylamine, respectively, may be attributed to steric and electrostatic repulsions.[4] Differences in the geometry of the transition state[3] and reaction mechanism,[2] in our opinion, assume a minor role.

It is of interest to note that in the reaction of the cyclopentane derivatives III and IV with triethylamine the factor by which *trans* elimination is favored over *cis* elimination is only 6.5-fold as compared to 20-fold for hydroxide ion; with trimethylamine the factor is 1.2-fold. These data show that when electrostatic and steric repulsive forces are reduced to a minimum by using trimethylamine as the base there is very little preference for *trans* elimination. We interpret this to mean that the planar four-centered transition state is of very little importance in providing a favorable reaction path in this system.

Experimental

Product Isolation.—The reaction mixture used to measure the kinetics of the reaction between ***trans*-2-(*p*-tolylsulfonyl)-cyclopentyl *p*-toluenesulfonate** and triethylamine (see below) was evaporated to dryness under vacuum, water added to the residue and the water insoluble product collected. This gave a 78% yield of crystals, m.p. 110–117°, which on recrystallization once from hexane gave crystals, m.p. 115–117°, undepressed by admixture with an authentic sample[19] of *p*-tolylsulfonylcyclopentene of m.p. 115–116°.

A similar procedure with the reaction mixture of ***cis*-2-(*p*-tolylsulfonylcyclopentyl *p*-toluenesulfonate** and triethylamine buffer gave an 80% yield of *p*-tolylsulfonylcyclopentene, m.p. 112–117° before recrystallization.

(17) R. G. Pearson and F. V. Williams, THIS JOURNAL, **76**, 258 (1954).

(18) H. C. Brown and I. Moritani, *ibid.*, **75**, 4112 (1953).

(19) F. G. Bordwell and R. J. Kern, *ibid.*, **77**, 1141 (1955).

A similar procedure with the reaction mixture of 1-(*p*-tolylsulfonyl)-2-propyl *p*-toluenesulfonate and triethylamine gave a 75% yield of crystals, m.p. 90–97°. Recrystallization from hexane gave crystals, m.p. 93–100°, reported[20] for propenyl-*p*-tolysulfone, m.p. 102–103°. The infrared absorption spectrum of the product isolated was different than that of allyl-*p*-tolylsulfone[20] and had a peak at 10.58 μ corresponding to a *trans* disubstituted double bond.

Other experiments of this type are reported by Bordwell and Kern.[19]

Other Materials.—The trimethylamine used in the buffer solution was Eastman Kodak White Label Anhydrous which was distilled into water to give a concentrated stock solution. The triethylamine used in the buffer solution was a middle constant-boiling fraction obtained by distilling the Matheson, Coleman and Bell product. The *p*-toluenesulfonic acid used in the buffers was prepared by boiling an approximately 2.5 *N* water solution of the Matheson, Coleman and Bell product with a generous quantity of charcoal and filtering. "Baker Analyzed" ammonium hydroxide solution and redistilled Matheson piperidine were also used for the preparation of buffers. The dioxane used as a solvent in the kinetic runs was purified by the method described in Fieser.[21]

Buffer Solutions.—The buffer stock solution used in the kinetic runs were prepared by pipetting the proper quantities of standardized amine and *p*-toluenesulfonic acid stock solution into a volumetric flask, adding an amount of pure dioxane equal in volume to the combined volumes of the acid and amine stock solutions and diluting to the mark with 50% by volume dioxane–water. An aliquot was titrated with standard acid to the methyl orange end-point and the value obtained in this manner taken as the concentration of amine in the buffer. The buffer stock solutions were in general about 0.64 *N* in free amine and about 0.05 *N* in amine salt.

The kinetic solution containing buffers were prepared by diluting aliquots of the buffer stock solution with 50% by volume dioxane–water, pipetting 20 ml. of this solution into one arm of a "Y" tube and pipetting 20 ml. of a 50% by volume dioxane–water solution of the sulfone tosylate into the other arm. The sulfone tosylate solution was always made exactly 0.01 *N* so that the experimental infinity readings could be checked both by calculations from an initial reading and by comparison with other runs.

Kinetic Procedures for Amine Rates.—Resistances were measured using an Industrial Instruments, Inc., Model RC16 Conductivity Bridge set at 1000 cycles per second. A modified Jones and Bollinger[22] conductance cell was used with the electrodes coated with platinum black. The reactions were timed with an electric timer. The constant temperature bath was maintained at 25 ± 0.03°. The conductance cells were always rinsed with water, acetone and methanol in that order, dried in a stream of dry nitrogen and equilibrated in the constant temperature bath for at least 5 minutes before being used. The kinetic solutions prepared as previously described were equilibrated in separate arms of the "Y" tube at least 10 minutes before mixing. To start a run the solutions were mixed as the timer was started and the solution poured into the conductance cell. The first reading could usually be obtained within 30 seconds of mixing. The calculations were made as described earlier.

(20) R. S. Schiefelbein, Ph.D. Thesis, Northwestern University, 1949.

(21) L. F. Fieser, "Experiments in Organic Chemistry," D. C. Heath and Co., New York, N. Y., 1941, p. 368.

(22) F. Daniels, J. H. Mathews and J. W. Williams, "Experimental Physical Chemistry," 3rd. Ed., McGraw-Hill Book Co., Inc., New York, N. Y., 1941, p. 368.

EVANSTON, ILLINOIS

[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF THE UNIVERSITY OF NOTRE DAME]

Chichibabin Reactions with Phenylacetaldehyde. II[1]

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The condensation of phenylacetaldehyde, acetaldehyde and ammonia under pressure is shown to give rise to a mixture of 3,5-diphenylpyridine, 3,5-diphenyl-2-methylpyridine and 2-methyl-5-phenylpyridine. Phenylacetaldehyde, propionaldehyde and ammonia give 3,5-diphenylpyridine, 3,5-diphenyl-2-ethylpyridine, 2-ethyl-3-methyl-5-phenylpyridine and 3-methyl-5-phenylpyridine in addition to a benzyldiphenylpyridine, probably the 2-benzyl-3,5-diphenyl isomer. Phenylacetaldehyde, isobutyraldehyde and ammonia give the same benzyldiphenylpyridine, 3,5-diphenylpyridine and what appears to be 2-isopropyl-3,5-diphenylpyridine. Phenylacetaldehyde, benzaldehyde and ammonia give 3,5-diphenylpyridine, a triphenylpyridine which appears to be the 2,3,5-isomer and another compound of unassigned structure. The course of these condensations is discussed.

Introduction

In a previous publication[1] it was shown that the condensation of phenylacetaldehyde with ammonia under pressure gives mainly 3,5-diphenylpyridine and toluene (Fig. 1, scheme B, R = C_6H_5, R′ = $C_6H_5CH_2$) instead of the expected 3,5-diphenylphenyl-2(or -4)-benzylpyridine (Fig. 1, scheme A or C, R = C_6H_5, R′ = $C_6H_5CH_2$). 3,5-Diphenylpyridine was also the major product isolated from phenylacetaldehyde and ammonia in the presence of isobutyraldehyde, but in the presence of acetaldehyde different bases were obtained.

It was the objective of the present study to condense phenylacetaldehyde and ammonia in the presence of a series of other aldehydes, isolate as many of the products as possible and determine their approximate mole ratios. It was hoped that some correlation could be found between the nature and yield of the products on the one hand and the nature of the added aldehyde on the other.

Results

From the reaction of phenylacetaldehyde, acetaldehyde and ammonia, three products were isolated. One was the previously encountered[1] 3,5-diphenylpyridine. The second one had the correct analysis for a methylphenylpyridine. Condensation with benzaldehyde to the corresponding stilbazole (II) followed by oxidation gave a phenylpyridinecarboxylic acid (III) the carboxyl function of which occupies the α-position, since the acid gave a red coloration with ferrous sulfate.[3] Decarboxylation of the acid yielded 3-phenylpyridine, identified with an authentic specimen prepared by coupling 3-(N-nitrosoacetamido)-pyridine with

(1) First paper in this series: E. L. Eliel, R. T. McBride and S. Kaufmann, THIS JOURNAL, **75**, 4291 (1953).

(2) From the Ph.D. dissertation of Charles P. Farley, National Institutes of Health fellow, 1953–1954, du Pont teaching fellow, 1954–1955.

(3) H. S. Mosher in R. C. Elderfield, "Heterocyclic Compounds," Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1950, p. 569.