Pre-equilibrium in the Schmidt Reaction of Benzhydrols

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Benzhydrol 類의 Schmidt 反應에 있어서의 Pre-equilibrium
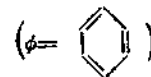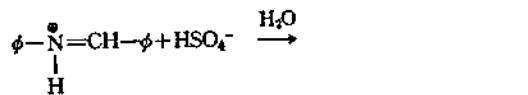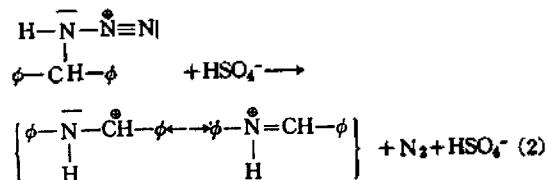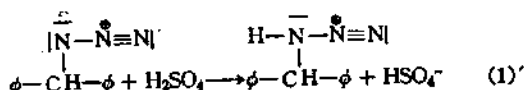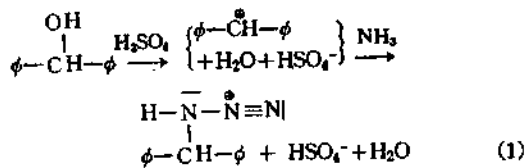
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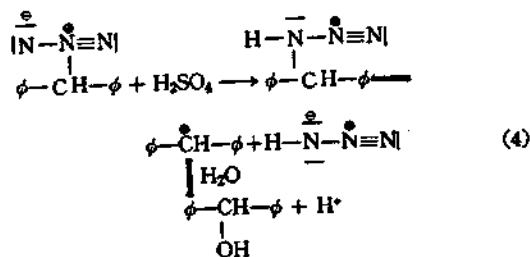
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要　　約

Benzhydryl azide 類에 Benzhydrol 類를 混合하여 Schmidt 反應을 遂行할 때에 Benzhydryl 基 間에 完全한 Radical exchange 現象이 일어남을 알았다. 故로 Benzhydrol 類의 Schmidt 反應에 있어서는 一但 生成된 Benzhydryl azide 가 濃硫酸存在下에서 Benzhydryl cation 과 Hydrazoic acid 로 分離되어 完全平衡狀態에 있음을 確認할 수 있었다.

Introduction

The mechanism for the Schmidt reaction of benzhydrols has been proposed as follows, [1] [2]

$$\phi-\underset{\substack{|\\OH}}{C}H-\phi \xrightarrow{H_2SO_4} \left\{\begin{array}{c}\phi-\overset{\oplus}{C}H-\phi\\+H_2O+HSO_4^-\end{array}\right\} \xrightarrow{NH_3}$$

$$\phi-\underset{\substack{|\\C\\|}}{\overset{H-\overset{-}{N}-\overset{\oplus}{N}\equiv N|}{}}H-\phi + HSO_4^- + H_2O \qquad (1)$$

or

$$|\overset{-}{N}-\overset{\oplus}{N}\equiv N| \qquad H-\overset{-}{N}-\overset{\oplus}{N}\equiv N|$$
$$\phi-CH-\phi + H_2SO_4 \longrightarrow \phi-CH-\phi + HSO_4^- \qquad (1)'$$

$$\phi-\underset{\substack{|\\C}}{\overset{H-\overset{-}{N}-\overset{\oplus}{N}\equiv N|}{}}H-\phi \quad +HSO_4^- \longrightarrow$$

$$\left\{\phi-\underset{\substack{|\\H}}{\overset{-}{N}}-\overset{\oplus}{C}H-\phi \leftrightarrow \phi-\underset{\substack{|\\H}}{\overset{\oplus}{N}}=CH-\phi\right\} +N_2+HSO_4^- \quad (2)$$

$$\phi-\underset{\substack{|\\H}}{\overset{\oplus}{N}}=CH-\phi+HSO_4^- \xrightarrow{H_2O}$$

$$\phi-\overset{\oplus}{N}H_3 + \phi-CHO + HSO_4^- \qquad (3)$$

$$\left(\phi= \hexagon \right)$$

We can consider, however, that the process is probably more complicated than the above. Namely, the conjugated acid of benzhydrylazide may exist as an equilibrium state with the benzhydryl ion and azoic acid before rearrengement of molecule as below,

$$|\overset{\ominus}{N}-\overset{\oplus}{N}\equiv N| \qquad H-\overset{-}{N}-\overset{\oplus}{N}\equiv N|$$
$$\phi-CH-\phi + H_2SO_4 \longrightarrow \phi-CH-\phi$$

$$\phi-\overset{\oplus}{C}H-\phi+H-\overset{\ominus}{N}-\overset{\oplus}{N}\equiv N| \qquad (4)$$
$$\downarrow H_2O$$
$$\phi-\underset{\substack{|\\OH}}{C}H-\phi + H^+$$

If this assumption was true, it can be regarded that some parts of the azide exist as hydrol in the equilibrium mixture and that there will be radical exchange between them before molecular rearrengement when hydrol is added to azide. In order to examine whether radical exchange between bezhydryl azide and benzhydrol occur or not, the following two type of reactions were carried out.

(a) Schmidt reaction of benzhydryl azides in the existence of benzhydrols labeled with chlorine.

(b) Schmidt reaction of benzhydryl azides labeled with chlorine in the existence of benzhydrols.

From the data obtained, it can be concluded that the assumption made above was reasonable.

Experimental

Preparation of benzhydrols: P-chloro benzhydrol, m. p. 60. 5°C—61. 5°C, was prepared by reduction of p-chlorobenzohydrophenone both by zinc dust and alcoholic sodium hydroxide [3] (70. 5% yield) and aluminium isopropoxide [4] (90. 0% yield) ; reported m. p.'s are 60 -61° [5], 62° [6], 60—61° [2]. 4, 4'dichlorobenzhydrol, m. p. 93. 5—94. 0°C was prepared by reduction of 4. 4'-dichlorobenzophenone by sodium borohydride in methanol [7] (60% yield), reported m. p. is 93. 3—93. 9°C [8].

Preparation of azoic acid solution [9] [01] : The paste was prepered from 97. 5gr. (1. 5 mole) of sodium azide and 97 ml. of warm water. To the paste 600 ml. of benzene was added and the mixture was cooled to 0°C while the mixture was stirred and 40 ml. (0. 75 mole) of concentrated sulfuric acid (SG. 1. 84) was added dropwise. The reaction temperature was kept under 10°C. After the addition of acid, the organic layer was decanted and dried by using anhydrous sodium sulfate. The concentration of hydrazoic acid in benzene solution was determined by pipetting 1 ml of the solution into 20 ml of water and titrating with 0. 1 N NaOH solution. The concentrations of azoic acid obtained in the benzene solutions were as follows.

Run No.	Concentration (Mol)
1	1. 43
2	1. 35
3	1. 35
4	1. 00

Preparation of azides: The modified method [11] of the procedure which was proposed by Ege and Sherk [12] was applied in this research. For example, the p-chlorobenzhydrylazide was prepared by the following procedure.

32 gr. (0. 230 mole) of trichloroacetic acid and 21. 8 gr. (0. 10 mole) of p-chlorobenzhydrol were added to 250 ml of anhydrous benzene. To this mixture a total of 300 ml of 1. 0M solution of hydrazoic acid in benzene(0. 30 mole) was then added. The resulting pale yellow solution was allowed to stand at room temperature for 10 days, then poured into water. The benzene layer was washed with water until the water washed did not give an acid reaction with litmus paper. The benzene solution was then dried over anhydrous magnesium sulfate, then the solvent was distilled off under reduced pressure at 20-30°C. The residue was 25. 0 gr. of pale yellow oil. An equal volume of petroleum ether was added to the resulting solution and passed through a 1. 5 × 40 CM-Column of alumina(grade 2, 3% of H_2O). After evaporation at room temperature 14. 9 gr of pale yellow oil was obtained. The purities which were determined from N_2 gas evolved in Schmidt reaction and the yield were follows.

Table 1. Yields and purites of azides.

Run No.	Yield (gr.)		Purity (%)
	crude	final	
Benzhydryl azide			
1	24. 9	6. 9(33. 7%)	—
2	19. 7	11. 4(54. 5%)	99. 2
p-Chlorobenzhydryl azide			
3	25. 0	14. 9(61. 0%)	91. 8
4	25. 0	11. 1(45. 5%)	99. 2
4, 4'-Dichlorobenzhydryl azide			
5*	27. 0	15. 7(62. 2%)	91. 3

* used 0. 5 mole of hydrazoic acid for 0. 1 mole of 4, 4'-Dichlorobenzhydrol.

Schmidt reaction: The procedure which was proposed by McEwen and Gudmundsen [1] was used in this research. A 50-ml flask which contained 0. 002 mole of benzhydrols and 10 ml of 5 M sulfuric acid in

glacial acetic acid was immered in a water-bath maintained at 25 ± 0.05°C, and 0.002 mole of azide was dropped into the flask with sample vial which was already supported over the solution. Shaking was commenced immediately after the introduction of the azide. The evolution of nitrogen was measured by mercury gas burret to determine the end points and the purities of the azides.

Preparation of sample for the determination of product[9]: The reaction mixture was diluted to three times its volume with water and exhaustively extracted with 75ml of n-pentane(three times with 25 ml each). The aqueous phase was then made basic with 45% sodium hydroxide solution and again extracted by the same method. The pentane extracts then dried over anhydrous magnesium sulfate, filtered, and most of pentane was evaporated under vacuum. The residues were made up to 5-ml of n-pentane solution using 5ml volumetric flask.

The determinaion of product ratio: Two types of gas chromatograph machine were used for the analysis of products.

For Run No. 3 and 4

　Perkin-Elmer Model 154B, Column 154-0012C,
　Column temperature 175°C, Column pressure 20 lb/in,

Volts between filaments 7.95 v, Recorder range 1, sample injected 0.1 ml.
Recorder Speedomax Type G Model S.

For Run No. 6—13

　Aerograph model A-90-P, Column Silicone GESF-96,
　Column Temperature 242~255° C,
　Column Pressure 60 lb/in,
　Current of Filament 200 map,
　Sample injected 0.005 ml.

The retention times of the products at above condition were

For Model 154B

　Benzaldehyde 4.4 min.,
　p-chlorbenzaldehyde 8.1 min.
　Aniline 4.5 min., p-chloroaniline 10.8 min.

For Model A-90-P

　Benzaldehyde 2.76 min.,
　p-chlorobenzaldehyde 4.1 min.
　Aniline 2.76 min., p-chloroaniline 4.9 min.

Although there was no difference between benzaldehyde and aniline in retention time, the p-chloro compounds gave complete separation into benzaldehydes and anilines.
The determination of quantities of products was performed by using peak height(except #3 & #4, these were determined by using peak areas). More

Table 2. Molar fractions and recoveries of products in schmidt reactions.

React No.	% of Azide	Benzaldehyde	p-chloro-Benzaldehyde	Aniline	p-chloro-aniline	Total Products (mole)	Total Recovery (%)
Benzhydryl azide+p-chlorobenzhydrol							
3	99.2	0.52	0.13	0.32	0.03	0.001987	50.2
6	99.8	0.53	0.18	0.25	0.05	0.001924	48.2
9	95.0	0.43	0.15	0.36	0.05	0.001777	44.4
10	97.3	0.51	0.15	0.29	0.05	0.002202	55.0
p-chlorohydryl azide+Benzhydrol							
4	91.8	0.50	0.13	0.29	0.08	0.002049	55.5
8*	91.5	0.53	0.13	0.30	0.04	0.001805	51.2
44'-Dichlorobenzhydryl azide+Benzhydrol							
11	91.3	0.50	0.12	0 32	0.06	0.001932	52.8
12	83.8	0.67	0.11	0.19	0.03	0.001477	44.2
Benzhydryl azid+44'-p-Dichlorobenzhydrol							
13	95.3	0.50	0.15	0.26	0.09	0.002308	60.7

* 0.00176 mole of azide was used.

than three standard solutions which closed to sample concentration were used for each element of products.

As the peak heights were variable(0-4%) from day to day even if the same experimental conditions such as column temperature, column pressure and filament voltage were maintained, the determination of a sample and standard solution was carried out in the same day.

When the temperature of column was changed during the determination, the values of concentration were calibrated(in #9, 2%/°C).

As shown in Fig 1, a graph of peak height versus concentration, the peak height increases linearly with increasing concentration from 0.5%. Therefore, based on this, the author concludes that for the solutions of 0.5% or more, only two standards are sufficient for inter- or extrapolation of unknowns.

Discussion and Conclusion

In the Schmidt reaction, benzhydryl azide decomposes into benzaldehyde and aniline by strong sulfuric acid. Therefore, if no other reagents were present in the system, we would expect normally the products consisting of aldehyde and aniline. However, as it was assumed in the introduction, if a pre-equilibrium of the type (4) exist within the reaction system, we could acertain this fact by introducing a reagent which is non-reactive
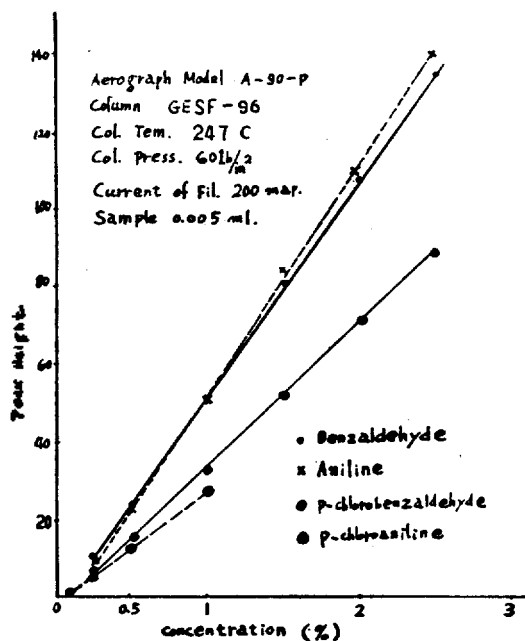

Fig. 1. Concentration versus peak height.

but involves in the pre-equilibrium into the reaction system.

In reactions #3, #6, #9 and #10 in Table 2, p-chlorobenzhydrol was introduced in the Schimdt reaction of benzhydryl azide with no substituent. In this type of reaction, if one assumes no equilibrium, products, i.e. aniline and aldehyde, will consist of those with no substituents.

On the other hand, we would obtain p-chloro species in the products if the pre-equilibrium actually existed, since in the equilibrium radical exchange would certainly involve.
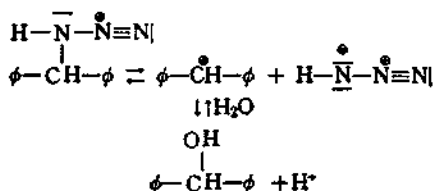
The results in Table 2 indicate that p-chlorobenzaldehyde are approximately 1/4 of the total benzaldehyde as expected from purely statistical ground. The small variations from this, however, may be due to errors in the experiments. According to McEwen[2], the transition state of the Schmidt reaction is a form with the partial bond formed between nitrogen and one of the benzene ring.

In this state, phenyl or substituted phenyl group attaches partially itself with nitrogen atom, and the ratio of aldehydes formed indicated that this migration was assisted by the electron-releasing groups.

Therefore, when chlorine is substituted at p-position (electron withdrawing), we would expect that more p-chloroaldehyde be formed compared with unsubstituted aldehyde in the Schmidt reaction of unsymmetrical benzhydryl azides.

As already mentioned, however, the esults of the products ratio for the reaction with only one substitution on either benzhydryl azide or benzhydrol(first two types, i.e. reaction #3, #6, #9, #10 and #4, #8), conform to this expection only approximately.

However, it is striking that the ratio in these two cases turned out to be the same within experimental error. This could only be the result of a complete pre-equilibrium,

$$\phi-CH-\phi \rightleftarrows \phi-\overset{\bullet}{C}H-\phi + H-\overset{-}{\underline{N}}-\overset{\bullet}{N}\equiv N|$$

This was further confirmed by using dichloro compounds as shown in Table 2(Reaction #11, #12 and #13).

Here again we find the same products ratio regardless of the substrate(benzhydryl azide or benzhydrol) which was substituted with chlorine on p-positions of both benzene rings. The slight decrease of p-chloro-products compared with the reaction with mono-substituted substrate, may be explained as the decreased reactivity of p-substituted phenyl group in the rearrangement step. In other words, the rate is determined by the partial bond formation between phenyl group and nitrogen atom, according to McEwen, and is less reactive when electron-withdrawing group is present.

Agreement shown by these two types of reaction, i. e, mono-substituted and di-substituted, strongly supports the pre-equilibrium theory proposed in this work.

The fact that the recoveries were only about 50% of the expected, can be interpreted as the result of other products formed(especially for anilines) which were the compounds not soluble in n-pentane e. g. aniline sulfate etc. or the compounds which has longer retention times than those of the normal products. This was shown by the fact that the increase in the amount of solvent and the repetition of extraction procedure had almost no effect in the amounts of the normal products obtained(less than 1%).

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