alkaline conditions. GCP, PCP, synthetic ethyleneglycol cyclic phosphate (ECP), and 2,3-butanediol cyclic phosphate (BCP) were tested for their stabilities to hydrolysis at various pHs.

(Received December 10, 1956)

U.D.C. 547.632

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19. **Zen-ichi Horii, Tatsuo Sakai, and Yasumitsu Tamura**: A Modified Leuckart Reaction. III.[1] Rearrangement in the Leuckart Reaction.

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In the preceding papers[1,2] we reported that a mixture of urea or 1,3-dimethylurea and formic acid can be used in the place of formamide or N-methylformamide in the Leuckart reaction. Subsequently, this method has been successfully extended to the synthesis of N-alkylamino compounds from corresponding carbonyl compounds by using 1,3-dialkylurea (Table I).

TABLE I.

Carbonyl compd.	$CO(NHR)_2$ R	Product Formula	Yield (%)	b.p. (°C/mm.)	Hydrochloride m.p. (°C)	Found C%	Found H%	Calcd. C%	Calcd. H%
$C_6H_5COCH_3$	C_2H_5	$C_6H_5CH(NHC_2H_5)CH_3$	47	60/3	199	64.68	8.68	64.75	8.85
$C_6H_5COC_6H_5$	C_2H_5	$C_6H_5CH(NHC_2H_5)C_6H_5$	35	160/15	245	72.71	7.32	72.54	7.55
$C_6H_5COCH_3$	n-C_4H_9	$C_6H_5CH(NHC_4H_9)CH_3$	40	72～74/4	153	67.42	9.43	67.25	9.53
C_6H_5CHO	n-C_4H_9	$C_6H_5CH_2NHC_4H_9$	<10	80/3	240	66.14	9.08	66.20	9.15

In order to extend this method to the synthesis of N-arylamino compounds, we have now investigated the reaction of a mixture of 1,3-diphenylurea and formic acid with benzophenone. Unexpectedly, it was found that the reaction does not proceed normally, giving a mixture of *o*- and *p*-aminotriphenylmethane instead of the expected product, i.e. N-benzhydrylaniline. We now wish to discuss the chemical structures of the reaction products and to propose a possible mechanism for this reaction.

A mixture of benzophenone, 1,3-diphenylurea, and formic acid was treated according to the general procedure proposed by us.[1,2] From a reaction mixture we obtained a substance having a wide melting range of 82～95° which was somewhat higher than that of the expected N-benzhydrylaniline, m.p. 53～54°. It had a basic property and gave a positive diazo reaction. On chromatographic purification there were obtained two pure crystalline compounds which melted at 127～127.5° and 84～84.5°, respectively. The former m.p. was identical with that of *o*-aminotriphenylmethane and the latter m.p. with that of *p*-aminotriphenylmethane. The identity of the reaction products with the authentic specimens was established by direct comparison of m.p., mixed m.p., and ultraviolet absorption spectra.

The same reaction products were also obtained by the normal Leuckart reaction using a mixture of benzophenone, formanilide, and formic acid. On heating a mixture of 1,3-diphenylurea and formic acid at 180° for 1 hour, formanilide was obtained in a good yield (88%). From this result it is assumed that formanilide is also a reactant in

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[1] Part II: This Bulletin, 3, 159(1955).

[2] Z. Horii, Y. Tamura, Y. Murakami: J. Pharm. Soc. Japan, **72**, 1208(1952).

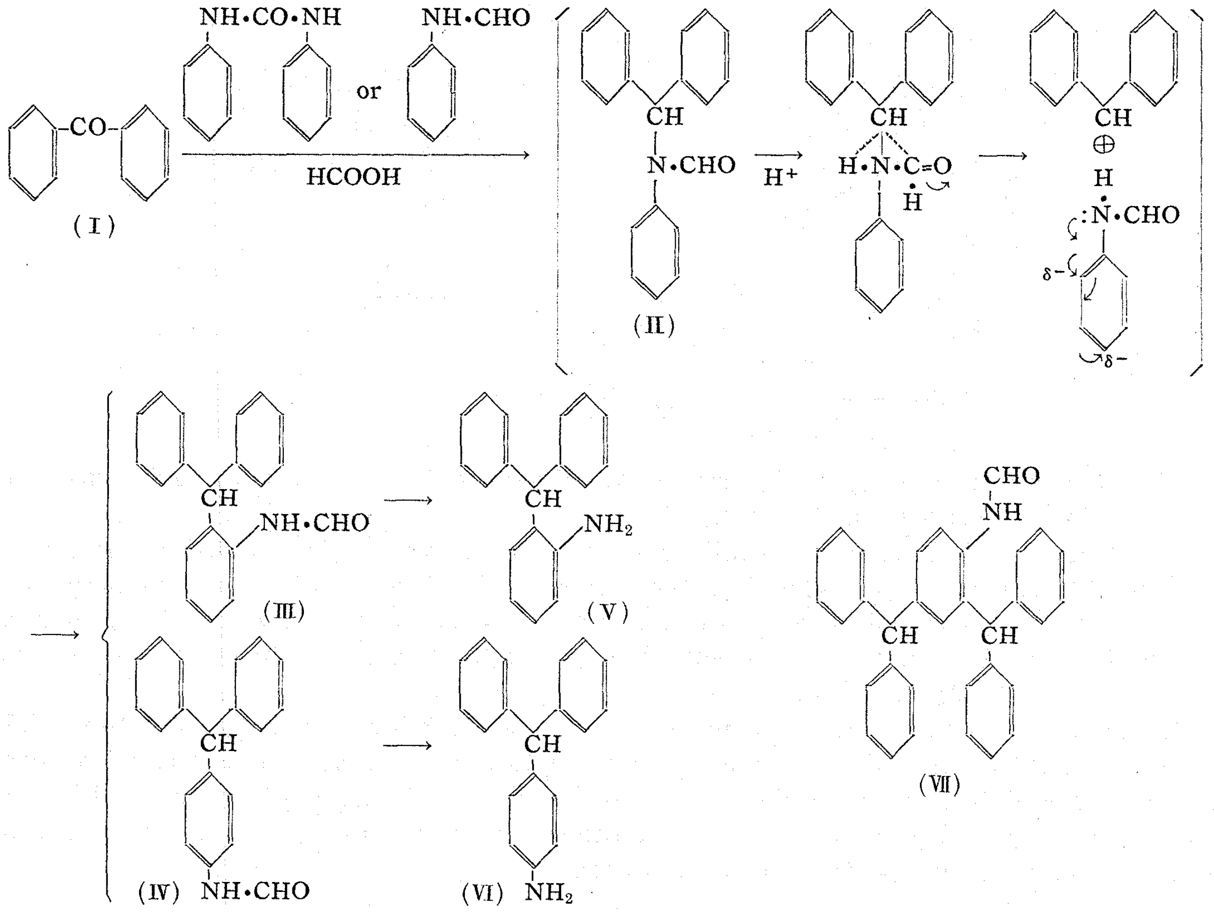

Chart 1.

this modified Leuckart reaction.

Formerly, Busch[3] reported that N-benzhydrylaniline is converted into *p*-aminotriphenylmethane on heating it with aniline hydrochloride in a sealed tube. Later, similar rearrangement reactions, i.e. the Hofmann-Martius rearrangement[4] and the Reilly-Hickinbottom rearrangement,[5] were often reported in literatures. In these reactions the alkyl group in the N-alkylaniline migrated to the *para*-position of aniline. Recently, Cantarel[6] reported that the C-N bond of N-benzhydrylaniline is cleaved easily on heating it with *N* hydrochloric acid or by heating its hydrochloride alone, yielding a mixture of aniline, *p*-aminotriphenylmethane, and N-dibenzhydryl-*p*-aminotriphenylmethane.

From these reports it may be assumed that the N-formyl derivative of N-benzhydrylaniline will be formed first and then converted into a mixture of *o*- and *p*-aminotriphenylmethane. In order to examine this mechanism for the reaction, the following experiments were carried out.

(1) Isolation of the pure product from the Leuckart reaction mixture prior to hydrolysis with 15% hydrochloric acid was attempted but in vain.

(2) On treating N-benzhydrylaniline with a mixture of formanilide and formic acid under the same reaction conditions mentioned above, the same reaction products, i.e. *o*- and *p*-aminotriphenylmethane, were obtained, but N-benzhydrylaniline was mostly unchanged on refluxing it with 15% hydrochloric acid.

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3) M. Busch, *et al.*: Ber., **38**, 1761(1905).
4) C. K. Ingold: "Structure and Mechanism in Organic Chemistry," 615(1953).
5) *Idem.*, 617(1953).
6) R. Cantarel: Compt. rend., **226**, 931(1948); **227**, 286(1948).

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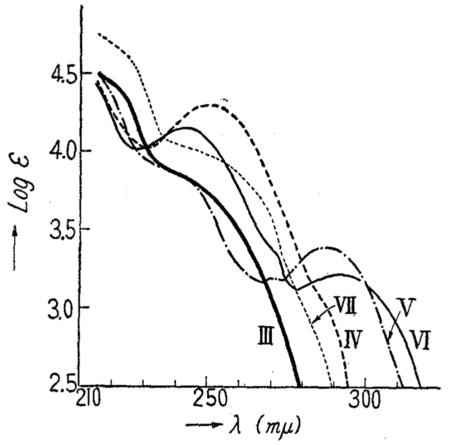

Fig. 1. Ultraviolet Spectra of Aminotriphenylmethane Derivatives (in EtOH)

(3) Heating of *o*- or *p*-aminotriphenylmethane with 98.5% formic acid gave the corresponding N-formyl derivatives.

(4) Heating of N-benzhydrylaniline with 98.5% formic acid yielded a crystalline product (VII) melting at 160~160.5°. The chemical structure of this compound was studied through its chemical properties, elemental analysis, molecular weight determination, and infrared and ultraviolet absorption spectra, and was thought to have a tentative formula, 2,4-dibenzhydrylformanilide.

Thus, we wish to propose the mechanism shown in Chart 1 for this reaction. The sequence would be as follows : The Leuckart reaction of benzophenone (I) with formanilide or 1,3-diphenylurea in formic acid would proceed normally to give (II) in the first stage. Then (II) would undergo rearrangement to (III) and (IV) in a polar solvent, in the presence of proton in successive stages.

Experimental

Leuckart Reaction of Benzophenone with 1,3-Diphenylurea—A mixture of 6.1 g.(0.033 mole) of benzophenone, 11.5 g. (0.05 mole) of 1,3-diphenylurea, and 30 cc. of 80% formic acid was heated at 108~109° for 2 hrs., and then raised to 190° during 1.5 hrs., maintaining the temperature between 190~200° for 3 hrs.

The reaction mixture[when it was distilled immediately under a reduced pressure, no distillate was obtained below 270°/1 mm. except formanilide (b.p$_4$ 133~134°)] was added to 30 cc. of 15% HCl and, after refluxing for 2 hrs., the solution was cooled, washed with a little ether, basified with 20% NaOH solution, and extracted with ether. The ether extract was dried over anhyd. Na_2SO_4, the solvent removed, and the residue distilled under a reduced pressure. The distillate (b.p$_2$ 185~187°) gave a white solid, m.p. 82~95°; yield, 3.8 g.(44%).

This solid was dissolved in petr. benzine, passed through an alumina column (40 g., 19×175 mm.), and sucessively eluted with petr. benzine and ether.

Evaporation of the first eluate (petr. benzine : 250 cc.) gave 1.7 g. of white solid, m.p. 117~120°, which melted at 127~127.5° after several recrystallization from EtOH. This compound gave a positive diazo color test (scarlet) and was shown to be *o*-aminotriphenylmethane by analysis, and by its failure to depress the m.p. of the authentic sample m.p. 127~127.5°, prepared by the method of Kliegl.[7] *Anal.* Calcd. for $C_{19}H_{17}N$: C, 87.99; H, 6.90. Found : C, 87.59; H, 6.50. U.V. λ_{max}^{EtOH} mμ (log ε) : 270(3.20), 288(3.39), which are identical with those of the authentic sample.

The second eluate (petr. benzine : 250 cc.) gave 0.8 g. of white solid, m.p. 96~102°, which seems to be a mixture of products.

Further elution with ether (200 cc.) yielded 1.2 g. of white solid, m.p. 75~80°, which after several recrystallization from ether-petr. ether gave white crystals, m.p. 84~84.5°. This compound also showed a distinct diazo color test (scarlet) and was shown to be *p*-aminotriphenylmethane by analysis and by admixture with the authentic sample prepared by the method of Baeyer.[8] *Anal.* Calcd. for $C_{19}H_{17}N$: C, 87.99; H, 6.61. Found : C, 88.08; H, 6.59. U.V. λ_{max}^{EtOH} mμ (log ε) : 243(4.14), 292(3.23), which are identical with those of the authentic sample.

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7) A. Kliegl : Ber., **40**, 4937(1907).
8) A. Baeyer, *et al.* : *Ibid.*, **23**, 1623(1870).

Leuckart Reaction of Benzophenone with Formanilide—A mixture of 9.1 g. of benzophenone, 20.3 g. of formanilide, and 10 cc. of 80% formic acid was treated essentially the same as described above. The reaction product (b.p$_2$ 193~194°, 3.4 g., 26%) solidified, which was chromatographed in petr. benzine on alumina in a like manner as described above. The first eluate with petr. benzine gave white crystals, m.p. 127~128°, which did not depress the melting point of authentic specimen of *o*-aminotriphenylmethane. The last elution with ether furnished white crystals, m.p. 83~84.5°, which was also shown to be identical with the authentic specimen of *p*-aminotriphenylmethane.

Rearrangement of N-Benzhydrylaniline under the Conditions of Leuckart Reaction—A mixture of 5.0 g. of N-benzhydrylaniline, 7.8 g. of formanilide, and 3.6 cc. of 80% formic acid was heated at 114° for 2 hrs., then at 180° during 1 hr., maintaining the temperature between 180~190° for 3 hrs. After cooling, the reaction mixture was worked up according to essentially the same method as described above. The reaction product (b.p$_2$ 188~191°, 1.5 g.) afforded white solid, m.p. 91~96°, which was chromatographed in petr. benzine on alumina. Successive elution with petr. benzine and ether furnished two different compounds of m.p. 127~127.5° and of m.p. 83~84.5°. The former was proved to be *o*-aminotriphenylmethane and the latter to be *p*-aminotriphenylmethane by admixture with authentic specimens.

Formylation of Aminotriphenylmethane (C-Benzhydrylaniline)—(a) A mixture of 0.6 g. of *o*-aminotriphenylmethane and 15 cc. of 98.5% formic acid was refluxed in an oil bath (bath temp. 135°) for 2.5 hrs. Removal of the excess of formic acid *in vacuo* gave a syrupy substance which was dissolved in AcOEt and passed through an alumina column. Evaporation of the solvent and trituration of the gummy residue with a mixture of AcOEt and petr. ether gave colorless plates. Recrystallization from the same solvent gave *o*-formylaminotriphenylmethane which melted at 135~136°. *Anal.* Calcd. for $C_{20}H_{17}ON$: C, 83.59; H, 5.96. Found : C, 82.78; H, 5.74.

(b) Treatment of *p*-aminotriphenylmethane with formic acid under the same conditions afforded a *para*-isomer melting at 112~114°. *Anal.* Calcd. for $C_{20}H_{17}ON$: C, 83.59; H, 5.96. Found : C, 83.47; H, 5.89. U.V. λ_{max}^{EtOH} mμ (log ε) : 251(4.29).

Reaction of Formic Acid on N-Benzhydrylaniline—A solution of 6.5 g. of N-benzhydrylanilne in 30 cc. of 98.5% formic acid was refluxed in an oil bath (bath temp. 125~135°) for 2 hrs. Removal of the excess of formic acid gave a syrupy residue which was dissolved in benzene and passed through an alumina column. Evaporation of the solvent and recrystallization from a mixture of AcOEt and petr. benzine afforded colorless plates (VII) which melted at 160~160.5°. This material showed a positive diazo color test after hydrolysis with HCl in EtOH. *Anal.* Calcd. for $C_{33}H_{27}ON$ (2,4-Dibenzhydrylformanilide) : C, 87.38; H, 6.00; N, 3.09; mol. wt., 453.6. Found : C, 86.87; H, 5.93; N, 3.06; mol. wt.(Rast), 450.4.

Summary

The Leuckart reaction of carbonyl compounds with a mixture of 1,3-dialkylurea and formic acid gave the corresponding N-alkylamino compounds (Table I). However, the same reaction of a mixture of 1,3-diphenylurea and formic acid with benzophenone did not proceed similarly, giving a mixture of *o*- and *p*-aminotriphenylmethane. The mechanism shown in Chart 1 was proposed for this reaction.

(Received December 17, 1956)

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