Isomerization of Azetidine Derivatives

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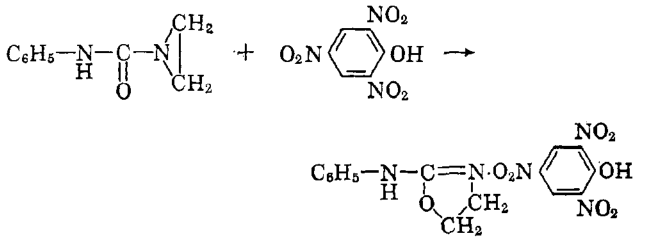
Isomerizations of azetidine derivatives were investigated. 1-(N-Phenylcarbamyl)-, 1-(N,N-diphenylcarbamyl)-, 1-(N-phenylthiocarbamyl)-, and 1-benzoyl-azetidine were isomerized to 2-anilino-5,6-dihydro-4H-1,3-oxazine (or 2-phenyliminotetrahydro-1,3-oxazine), 2-(N,N-diphenylamino)-5,6-dihydro-4H-1,3-oxazine, 2-phenyliminotetrahydro-1,3-thiazine, and 2-phenyl-5,6-dihydro-4H-1,3-oxazine, respectively, by reaction with picric acid or *p*-toluenesulfonic acid in refluxing toluene. Under the same reaction conditions, methanesulfonic acid caused the isomerizations of 1-(N-phenylcarbamyl)azetidine to 2-anilino-5,6-dihydro-4H-1,3-oxazine and of 1-benzoylazetidine to 2-phenyl-5,6-dihydro-4H-1,3-oxazine. Concentrated sulfuric acid or oleum was also effective for the isomerization of 1-(N-phenylcarbamyl)azetidine to 2-anilino-5,6-dihydro-4H-1,3-oxazine and of 1-benzoylazetidine to 2-phenyl-5,6-dihydro-4H-1,3-oxazine. 1-(N-Phenylthiocarbamyl)-azetidine was converted to 2-phenyliminotetrahydro-1,3-thiazine in low yield by the reaction with boron trifluoride etherate or aluminum chloride in refluxing toluene.

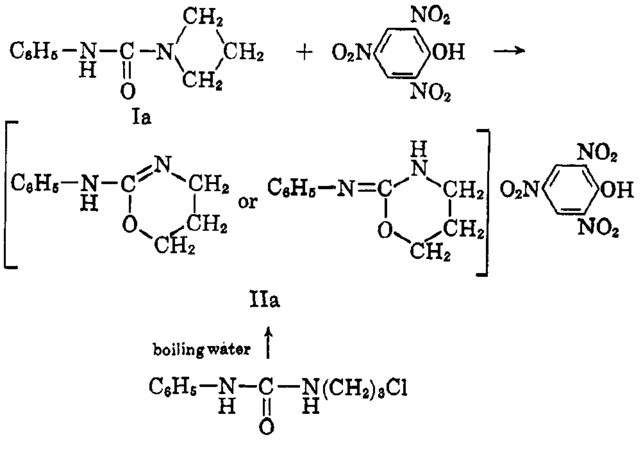
Much study has been done about the isomerization of aziridine derivatives.[1] Concerning azetidine derivatives, however, nothing is known except the isomerization of 1-(N-arylthiocarbamyl)azetidines with concentrated hydrochloric acid.[2] This paper presents the isomerization of N-substituted azetidines.

In one[3] of the papers dealing with isomerization of aziridine derivatives by Heine, *et al.*, it was stated that 1-(N-phenylcarbamyl)aziridine yielded, when treated with sodium iodide in refluxing acetone (as smaller quantities of sodium iodide and larger volumes of acetone were used), some impure 2-anilino-2-oxazoline along with some N,N′-bis(phenylcarbamyl)piperazine and 1-phenyl-1,3-imidazolidin-2-one. In our previous study,[4] it was found that 1-(N-phenylcarbamyl)-aziridine isomerized into 2-anilino-2-oxazoline by the reaction with picric acid in refluxing ethyl acetate.



No other reagent is known, in the literature, to afford such an exclusive conversion of 1-(N-phenylcarbamyl)-aziridine into 2-anilino-2-oxazoline. It is of interest whether picric acid causes the isomerization of 1-(N-phenylcarbamyl)azetidine (Ia) into 2-anilino-5,6-dihydro-4H-1,3-oxazine or 2-phenyliminotetrahydro-1,3-oxazine (IIa), and whether strong acids such as sulfonic or trichloroacetic are also effective for such an isomerization reaction. This study was undertaken to elucidate these matters and extended to other azetidine derivatives, 1-(N,N-diphenylcarbamyl)-, 1-(N-phenylthiocarbamyl)-, and 1-benzoyl-azetidine.

1-(N-Phenylcarbamyl)azetidine (Ia) reacted with picric acid in refluxing toluene to give the picrate of IIa in 60% yield after 8 hr., the structure of which was confirmed by comparison with an authentic sample. Under analogous reaction conditions, *m*-nitrobenzene- and *p*-toluenesulfonic acids gave rise to the isomerization of Ia into IIa. In both cases, the sulfonate of IIa was obtained as an oil. Treatment of each sulfonate with sodium carbonate gave pure IIa in 55 (in the case of *m*-nitrobenzenesulfonic acid), and 77% yields (in the case of *p*-toluenesulfonic acid). Methanesulfonic acid also induced isomerization of Ia to IIa, the sulfonate of which was obtained in crystals.



Reaction with concentrated hydrochloric acid gave several results dependent upon the temperature. At room temperature, a quantitative yield of 1-(3-chloropropyl)-3-phenylurea (IIIa) was obtained after 3 days. At a bath temperature of 100°, IIIa was obtained in lower yield (55%) after 8 hr., while refluxing 8 hr. gave 27% of IIIa along with 11% of IIa. These results and the fact that IIIa is converted to IIa hydrochloride in concentrated hydrochloric acid under reflux suggest that IIa in the above reaction might have formed from Ia *via* the intermediate IIIa, rather than directly from Ia. Actually, it was observed that, when Ia was heated in concentrated hydrochloric acid, white crystals (probably IIIa) increased rapidly as soon as the temperature was raised, and longer period of refluxing resulted in a clear solution again.

p-Nitrobenzoic acid and Ia gave impure 1-[3-(*p*-nitrobenzoyloxy)propyl]-3-phenylurea, m.p. 153–156°. Analytical values deviated from those calculated, probably owing to contamination with unchanged Ia. The infrared spectrum of the above product was very similar to that of 1-[2-(*p*-nitrobenzoyloxy)ethyl]-3-phenylurea[4] with a band of ester carbonyl. By the

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[1] H. W. Heine, *Angew. Chem.*, **74**, 772 (1962).

[2] M. Tisler, *Arch. Pharm.*, **293**, 621 (1960).

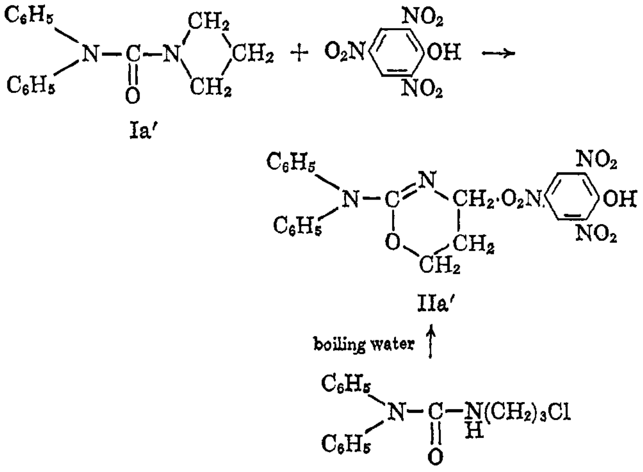
[3] H. W. Heine, W. G. Kenyon, and E. M. Johnson, *J. Am. Chem. Soc.*, **83**, 2570 (1961).

[4] Y. Iwakura and A. Nabeya, *Bull. Tokyo Inst. Technol.*, **42**, 69 (1961).

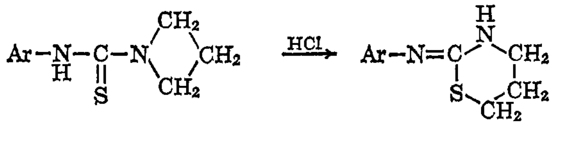
reaction with stronger carboxylic acids, decarboxylation of acids took place. When trichloroacetic acid was heated with Ia in toluene, evolution of gas began as soon as the reaction mixture became a solution, and after that Ia deposited out of the solution. Similar phenomena were observed in the case of 2,4,6-trinitrobenzoic acid, where 1,3,5-trinitrobenzene was isolated along with recovered Ia.

Oleum (30% SO_3) or concentrated sulfuric acid also caused the isomerization of Ia to IIa, when Ia was left standing with these acids at 60° for 1 week. The infrared spectrum of the resulting glassy mass had a band at 1678 $cm.^{-1}$ arising from C=N. After removal of unchanged Ia and polymeric substances from the aqueous solution of the product and treatment with sodium carbonate, a 33% yield of IIa was obtained in both cases. Boron trifluoride etherate or stannic chloride was ineffective for the isomerization of Ia in refluxing toluene in the former case, and without solvent at 100° in the latter case, where Ia was recovered on treatment with sodium carbonate.

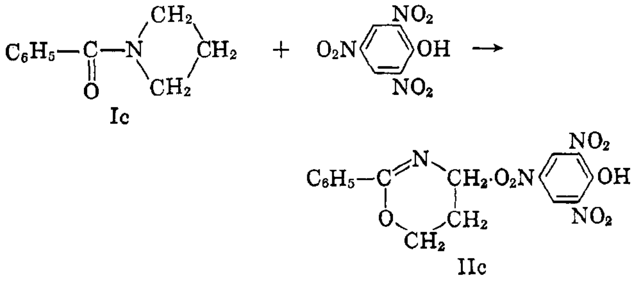
1-(N,N-Diphenylcarbamyl)azetidine (Ia′) and picric acid in refluxing toluene gave the picrate of 2-N,N-diphenylamino-5,6-dihydro-4H-1,3-oxazine (IIa′) (88%). Structure assignment of IIa′ was based on comparison with a sample prepared by cyclization of 1-(3-chloropropyl)-3,3-diphenylurea in boiling water. Reaction with p-toluenesulfonic acid, under similar conditions, resulted in the formation of IIa′ p-toluenesulfonate in 62% yield.



Tisler[2] has reported that 1-(N-arylthiocarbamyl)-azetidines are converted to 2-aryliminotetrahydro-1,3-thiazines in high yields by refluxing in concentrated hydrochloric acid for a short time. When 1-(N-phenylthiocarbamyl)azetidine (Ib) was heated with picric acid in refluxing toluene for 1 hr., the picrate of 2-phenyliminotetrahydro-1,3-thiazine (IIb) was obtained in 90% yield. Reaction with p-toluenesulfonic acid, under analogous conditions, gave an oily product, IIb p-toluenesulfonate, from which IIb was isolated by treatment with sodium carbonate in an over-all yield of 89%. Reaction with concentrated hydrochloric acid gave quite a different result from the others; at room temperature, Ib and excess concentrated hydrochloric acid gave a sticky material after 4 days, and, at 60°, IIb was obtained in high yield after 3 days. Boron trifluoride etherate and aluminum chloride in refluxing toluene were also effective for the isomerization of Ib to IIb, although, in these cases, the yields were lower (about 10% in both cases) owing to the formation of polymeric substances.



1-Benzoylazetidine (Ic) gave the picrate of 2-phenyl-5,6-dihydro-4H-1,3-oxazine (IIc) in 33% yield by reaction with picric acid after being heated in refluxing toluene for 8 hr. Under similar conditions, Ic was converted to p-toluenesulfonate of IIc in 90% yield with p-toluenesulfonic acid, and, with methanesulfonic acid, to IIc methanesulfonate in an oily state, which was converted to IIc picrate (30% yield from Ic). When Ic was left standing with oleum at room temperature for several days, formation of IIc was not recognizable by the infrared spectrum. However, at 90° and after 1 day, an 87% yield of IIc picrate was obtained from the ethereal extract of the alkali-treated reaction product. Aluminum chloride or boron trifluoride etherate was ineffective for the isomerization of Ic in refluxing toluene, although, in the latter case, ether was detected by the gas chromatography in the toluene layer suggesting that some interaction between Ic and boron trifluoride existed. 1-Acylaziridines are known to be easily transformed into 2-substituted 2-oxazolines with sodium iodide in refluxing acetone.[3,5] In the case of 1-benzoylazetidine, only a small quantities of IIc was obtained from reaction with sodium iodide in refluxing cyclohexanone for 8 hr. However, reaction in refluxing acetophenone gave IIc in 41% yield (based on the quantities of IIc picrate derived from the reaction product).



Discussion

Isomerization of Ia to IIa is considered to be affected by strong acids conjugated with weakly nucleophilic bases. Hydrochloric acid is known to be a strong acid, the conjugate base of which being a strong nucleophile. Strong acids such as picric or sulfonic are conjugated with weakly nucleophilic bases. Accordingly, in the reaction of Ia with latter acids, after the protonation to Ia takes place, intramolecular attack of the carbonyl oxygen on the ring carbon would occur preferentially to the competing attack of the conjugate base of the acid, thus giving rise to the isomerization reaction, while in the case of hydrochloric acid, chloride ion would attack the carbon to give addition product, IIIa. This also seems to be the correct explanation of

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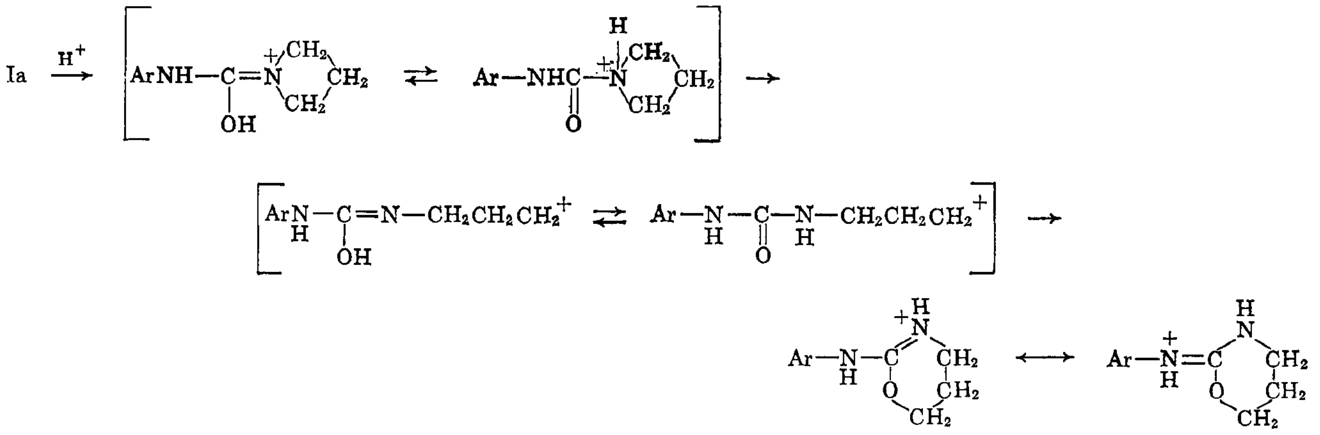
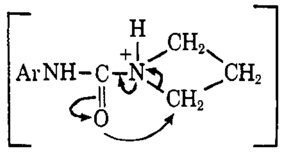
(5) H. W. Heine, M. E. Fetter, and E. M. Nicholson, *J. Am. Chem. Soc.*, **81**, 2202 (1959).



the reaction of Ib with concentrated hydrochloric acid, where the strongly nucleophilic thiocarbonyl sulfur is apt to attack the ring carbon to give IIb.

Exclusive O-alkylation observed in the isomerization of Ia with acids is considered to be related to the fact that, when 1-(2-chloroethyl)-3-phenylurea is heated in boiling water, internal O-alkylation takes place to give 2-anilino-2-oxazoline, while in alkaline solution, N-alkylation takes place to give 1-phenyl-1,3-imidazolidin-2-one.[6] Recently, Capon[7] has widely investigated the ring closure of urethans, amides, and ureas having 2-bromoethyl or 3-bromopropyl groups. He rationalized the O- or N-alkylation of 1-(2-bromoethyl)-3-phenylurea as follows: in neutral solution, O attack predominates, while in basic solution, where the ureido group is ionized to the conjugate base, N attack occurs.

Acid-catalyzed isomerization of Ia would reasonably be depicted as to proceed by the formation of carbonium cation. However, we have not determined whether the reaction of Ia with picric acid or sulfonic acid in dry toluene proceeds through the intermediate formation of a carbonium cation or directly by a concerted mechanism through the attack of carbonyl oxygen on the ring carbon which has positive charge due to polarization.



Comparing with the reaction of aziridine derivatives, those of azetidine derivatives, especially in the case involving direct nucleophilic attack on the ring carbon (*e.g.*, reaction with sodium iodide), require severer conditions. This might be attributed to the larger strain in aziridine ring than in azetidine ring.

Experimental Section[8]

Azetidine was prepared from 3-aminopropanol *via* 1-tosylazetidine according to the method reported by Vaughan, *et al.*,[9] b.p. 60.5–61.5°.

1-(N-Phenylcarbamyl)azetidine (**Ia**) was prepared from azetidine and phenyl isocyanate, m.p. 189–191° (lit.[10] m.p. 189–190°).

Anal. Calcd. for $C_{10}H_{12}N_2O$: N, 15.9. Found: N, 15.5.

1-(N,N-Diphenylcarbamyl)azetidine (**Ia′**) was prepared by the condensation of N,N-diphenylcarbamyl chloride with azetidine using triethylamine as an acid acceptor, m.p. 92–94°, and had a band at 1660 cm.$^{-1}$ (C=O) in the infrared spectrum.

Anal. Calcd. for $C_{16}H_{16}N_2O$: C, 76.16; H, 6.39; N, 11.10. Found: C, 76.28; H, 6.30; N, 11.07.

1-(N-Phenylthiocarbamyl)azetidine (**Ib**) was prepared from azetidine and phenyl isothiocyanate, m.p. 105–107° (lit.[2] m.p. 110°).

Anal. Calcd. for $C_{10}H_{12}N_2S$: N, 14.57. Found: N, 14.38.

1-Benzoylazetidine (**Ic**), m.p. 61–62°, was prepared by the condensation reaction of azetidine with benzoyl chloride and had a band at 1625 cm.$^{-1}$ (C=O) in the infrared spectrum.

Anal. Calcd. for $C_{10}H_{11}NO$: N, 8.69. Found: N, 8.91.

Reaction of Ia with Concentrated Hydrochloric Acid. A. At Room Temperature.—Ia (1.8 g., 0.01 mole) was dissolved in 10 g. of concentrated HCl and was left standing for 3 days at room temperature. After dilution of the reaction mixture with a large volume of water, the precipitate was collected on a filter and dried to give 2.1 g. of 1-(3-chloropropyl)-3-phenylurea (IIIa), m.p. 125–127°. Recrystallization from ethanol did not change the melting point. The infrared spectrum of IIIa showed bands at 3340 (NH) and 1635 cm.$^{-1}$ (C=O).

Anal. Calcd. for $C_{10}H_{13}ClN_2O$: N, 13.2. Found: N, 13.1.

B. At a Bath Temperature of 100°.—A mixture of 0.88 g. of Ia and 2 g. of concentrated HCl was heated at a bath temperature of 100° for 8 hr. After dilution of the mixture with a large volume of water, the precipitate was collected on a filter and dried to give 0.5 g. (55%) of IIIa. Neutralization of the filtrate with sodium carbonate caused no precipitation.

C. At Reflux Temperature.—A mixture of 0.88 g. of Ia and 2 g. of concentrated HCl was refluxed for 8 hr. Treatment of the reaction mixture in the same manner as in part B gave 0.3 g. (27%) of IIIa from the water-insoluble part and 0.1 g. (11%) of IIa on neutralization of the filtrate with sodium carbonate.

Preparation of 2-Anilino-5,6-dihydro-4H-1,3-oxazine (or 2-Phenyliminotetrahydro-1,3-oxazine) (IIa).—A 1.9-g. sample of IIIa was heated in boiling water. After 2 hr., the solution was almost clear. Cooling the reaction mixture, removal of some unchanged IIIa, and neutralization with sodium carbonate gave 1.0 g. (68%) of crude IIa. Recrystallization from benzene and petroleum ether (b.p. 40–80°) gave a sample melting at 125–127°. The infrared spectrum had bands at 3450 (NH) and 1670 cm.$^{-1}$ (C=N). The n.m.r. spectrum in chloroform, with tetramethylsilane as the internal standard (τ 10.0), exhibited signals at τ 8.16 (quintet), 6.61, and 5.82 (both triplet) with equal areas.

Anal. Calcd. for $C_{10}H_{12}N_2O$: C, 68.16; H, 6.86; N, 15.90. Found: C, 68.21; H, 7.02; N, 15.89.

Reaction of Ia with Picric Acid.—A mixture of 0.88 g. (0.005 mole) of Ia, 1.15 g. (0.005 mole) of picric acid, and 5 ml. of dry toluene was refluxed for 8 hr. Yellow crystals were recrystallized from Methyl Cellosolve to give 1.2 g. (60%) of an analytically pure sample, m.p. 205° dec. Infrared spectra and melting points were identical for the product and the authentic sample of IIa picrate (ν_{NH} 3230 cm.$^{-1}$, $\nu_{C=N}$ 1678 cm.$^{-1}$.)

Anal. Calcd. for $C_{16}H_{15}N_5O_8$: N, 17.3. Found: N, 17.4.

Reaction of Ia with Sulfonic Acids.—Reactions of Ia with sulfonic acids were performed under the same conditions as in the reaction with picric acid.

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[6] S. Gabriel and R. Stelzner, *Ber.*, **28**, 2929 (1895).

[7] B. Capon, *Quart. Rev.* (London), **18**, 72 (1964).

[8] Melting points and boiling point are uncorrected.

[9] W. R. Vaughan, R. S. Klonowski, R. S. McElhinney, and B. B. Millward, *J. Org. Chem.*, **26**, 138 (1961).

[10] Ya. M. Yanbikov, *J. Gen. Chem. USSR*, **8**, 1470 (1938).

Reaction with *p*-toluenesulfonic acid gave an oily product which separated out of toluene as a lower layer. Infrared spectra of the oily product obtained above and the sample (also an oil) prepared from IIa and *p*-toluenesulfonic acid in dry toluene were identical ($\nu_{\mathrm{C=N}}$ 1675 cm.$^{-1}$). Removal of toluene and neutralization with sodium carbonate gave 77% of IIa melting at 119–124°. After recrystallization from benzene and petroleum ether, the mixture melting point was undepressed.

Reaction with *m*-nitrobenzenesulfonic acid proceeded quite similarly, and gave 55% of IIa melting at 122–126°.

Ia and methanesulfonic acid gave IIa methanesulfonate, m.p. 128–138°, in 86% yield after recrystallization from acetone and petroleum ether. Another recrystallization did not change the melting point. An authentic sample of IIa methanesulfonate melted at 142–145°. Infrared spectra were identical for both samples (ν_{NH} 3230 cm.$^{-1}$, $\nu_{\mathrm{C=N}}$ 1680 cm.$^{-1}$). A part of the sulfonate from the reaction of Ia with methanesulfonic acid was treated with sodium hydroxide, and the formation of IIa was confirmed by the melting point and mixture melting point with authentic sample of IIa.

Anal. Calcd. for $C_{11}H_{16}N_2O_4S$: C, 48.52; H, 5.92; N, 10.29. Found: C, 48.51; H, 6.06; N, 10.46.

Reaction of Ia with *p*-Nitrobenzoic Acid.—A mixture of 0.88 g. of Ia, 0.84 g. (0.005 mole) of *p*-nitrobenzoic acid, and 10 ml. of dry toluene was refluxed for 8 hr. The crystalline product was treated with sodium bicarbonate to remove unreacted *p*-nitrobenzoic acid and was recrystallized from benzene. Repeated recrystallizations did not narrow the melting range, 153–156°. The infrared spectrum had bands at 3375 (NH), 1700 (ester C=O), and 1628 cm.$^{-1}$ (urea C=O), and was similar to that of 1-[2-(*p*-nitrobenzoyloxy)ethyl]-3-phenylurea which had bands at 3330 (NH), 1720 (ester C=O), and 1635 cm.$^{-1}$ (urea C=O).

Anal. Calcd. for $C_{17}H_{17}N_3O_5$: C, 59.47; H, 4.99; N, 12.24. Found: C, 61.15; H, 5.01; N, 12.85.

Reaction of Ia′ with Concentrated Hydrochloric Acid.—Ia′ (2.5 g., 0.01 mole) was dissolved in 5 g. of concentrated HCl and the mixture was left standing at room temperature for 3 days. After dilution of the reaction mixture with a large volume of water, the precipitated crystals were collected on a filter and dried to give 2.9 g. of 1-(3-chloropropyl)-3,3-diphenylurea, m.p. 120–123°. Recrystallization from benzene and petroleum ether gave a pure sample melting at 122–123°. The infrared spectrum had bands at 3330 (NH) and 1653 cm.$^{-1}$ (C=O).

Anal. Calcd. for $C_{16}H_{16}ClN_2O$: C, 66.55; H, 5.93; N, 9.70. Found: C, 66.44; H, 5.84; N, 9.73.

Preparation of 2-(N,N-Diphenylamino)-5,6-dihydro-4H-1,3-oxazine (IIa′).—IIa′ was prepared from 1-(3-chloropropyl)-3,3-diphenylurea in quite the same manner as IIa from IIIa. It melted at 94–96° after recrystallization from petroleum ether, and had a band at 1663 cm.$^{-1}$ (C=N) in the infrared spectrum. The n.m.r. spectrum obtained under quite the same conditions for IIa gave signals at τ 8.15 (quintet), 6.59, and 5.82 (both triplet) with equal areas.

Reaction of Ia′ with Picric Acid.—A mixture of 1.25 g. (0.005 mole) of Ia′, 1.15 g. (0.005 mole) of picric acid, and 5 ml. of dry toluene was refluxed for 4 hr., and the precipitated crystals were filtered while hot to separate them from picric acid and dried to give 2.1 g. (88%) of IIa′ picrate, melting at 145° with brown coloration. It was recrystallized from ethanol, and had an identical infrared spectrum with that of an authentic IIa′ picrate.

Anal. Calcd. for $C_{22}H_{19}N_5O_8$: C, 54.88; H, 3.98; N, 14.55. Found: C, 54.96; H, 3.92; N, 14.5.

Reaction of Ia′ with *p*-Toluenesulfonic Acid.—The reaction was made in quite the same manner as that with picric acid except that the reaction time was 8 hr. The product, IIa′ *p*-toluenesulfonate, melted at 195° with violet coloration (yield 62%). Melting point and infrared spectra were identical for the above obtained product and an authentic sample of IIa′ *p*-toluenesulfonate.

Anal. Calcd. for $C_{23}H_{24}N_2O_4S$: C, 65.07; H, 5.70; N, 6.60. Found: C, 65.01; H, 5.76; N, 6.45.

Reaction of Ib with Picric Acid and *p*-Toluenesulfonic Acid.—Reactions were performed in quite the same manner as in the case of Ia except that the refluxing period was 1 hr. (after longer heating, the reaction mixture gave off a bad smell, probably due to decomposition of IIb).

From 0.96 g. (0.005 mole) of Ib and 1.15 g. (0.005 mole) of picric acid, 1.9 g. (90%) of IIb picrate was obtained and recrystallized from Methyl Cellosolve, m.p. 193–195°. The infrared spectra and melting point were identical for the product and for an authentic sample.

Anal. Calcd. for $C_{16}H_{15}N_7O_7S$: C, 45.60; H, 3.59; N, 16.62. Found: C, 45.80; H, 3.93; N, 16.40.

From 0.96 g. of Ib and 0.86 g. of *p*-toluenesulfonic acid, 0.85 g. (89%) of IIb was obtained after treatment with sodium carbonate.

Reaction of Ib with Boron Trifluoride Etherate.—A mixture of 0.96 g. of Ib, 0.7 g. of boron trifluoride etherate, and 5 ml. of dry toluene was refluxed for 1 hr. The reaction mixture was very sticky. Treatment with sodium hydroxide gave 0.1 g. (11%) of IIb after recrystallization from benzene and petroleum ether.

Reaction of Ic with Picric Acid.—Refluxing a mixture of 0.80 g. (0.005 mole) of Ic, 1.15 g. (0.005 mole) of picric acid, and 5 ml. of dry toluene for 8 hr. gave 0.6 g. (33%) of 2-phenyl-5,6-dihydro-4H-1,3-oxazine picrate, m.p. 144–149° (lit.[11] m.p. 151°).

Anal. Calcd. for $C_{16}H_{14}N_4O_8$: C, 49.23; H, 3.62; N, 14.36. Found: C, 49.51; H, 3.68; N, 14.5, 14.4.

2-Phenyl-5,6-dihydro-4H-1,3-oxazine (IIc) was prepared from N-(3-bromopropyl)benzamide according to the known method.[11] The infrared spectrum had a band at 1660 cm.$^{-1}$ (C=N). The n.m.r. spectrum in carbon tetrachloride, with tetramethylsilane as the internal standard (τ 10.0), exhibited signals at τ 8.25 (quintet) 6.57, and 5.88 (both triplet) with equal areas.

Reaction of Ic with Sulfonic Acids.—Reaction of Ic (0.80 g.) and *p*-toluenesulfonic acid (0.67 g.) in the same manner as above gave 1.4 g. (84%) of IIc *p*-toluenesulfonate, m.p. 152–154° after recrystallization from acetone and ethanol. Another recrystallization from the same mixed solvent gave a pure sample melting at 153.3–154.5°. The infrared spectrum had a band at 1670 cm.$^{-1}$ (C=N).

Anal. Calcd. for $C_{17}H_{19}NO_4S$: C, 61.20; H, 5.73; N, 4.20. Found: C, 61.03; H, 5.73; N, 3.96.

Following the method just given, Ic and methanesulfonic acid gave an oily product. Infrared spectrum showed a band at 1660 cm.$^{-1}$ (C=N). Treatment of the product with sodium hydroxide, extraction of the alkaline solution with ether, and subsequent addition of picric acid to the ethereal extract gave a 33% yield of IIc picrate, m.p. 146–149°. Admixture with an authentic sample gave no depression of melting point.

Reaction of Ic with Oleum.—A mixture of 0.80 g. of Ic and 0.50 g. of oleum (30% SO_3) was left standing at 90° for 1 day. Treatment of the reaction mixture in an analogous way as in the reaction with methanesulfonic acid gave 1.5 g. (80%) of IIc picrate, m.p. 146.5–149°.

Reaction of Ic with Sodium Iodide in Acetophenone.—A mixture of 0.80 g. of Ic, 0.75 g. of sodium iodide, and 10 ml. of acetophenone was refluxed for 8 hr. Extraction of the solution with dilute sulfuric acid, treatment of the acidic solution with sodium hydroxide, extraction of the resulting alkaline solution with ether, and subsequent addition of picric acid to the extract gave 0.76 g. (41%) of IIc picrate, m.p. 148–150°.

A control run was done by refluxing a solution of Ic in acetophenone for 8 hr. The resulting solution was treated as above except for the addition of picric acid. Evaporation of ether left very little material, the infrared spectrum of which was different from that of IIc.

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[11] S. Gabriel and P. Elfeldt, *Ber.*, **24**, 3214 (1891).