of comparable size (E_s values for Me and Br are identical[3c]), the deviation from linearity is in the direction of *larger* $\Delta(\delta)_o$ values with increasing electron-displacing ability than a linear correlation would require. That is, the deviations are not in the direction which would be expected if the usual steric effects of *ortho* substituents were being manifested (diminished interaction between phenol and solvent DMSO). We believe that an *ortho* substituent interferes far less (perhaps not at all) with the solvation of the phenol OH by a *single* molecule of DMSO than it does with the multimolecular solvation usually encountered in situations from which σ constants are evaluated (for example, dissociation of benzoic acid to heavily solvated benzoate ions).

ortho-Substituent σ constants which would be evaluated from our chemical-shift data are a little higher than those reported by Taft,[3c] with larger differences occurring between σ for the stronger electron-displacing halogen substituent than for the weaker electron-displacing methyl one. The magnitudes of σ_p and σ_o^* are nearly the same except for substituents, such as OMe and F, which have steric substituent constants (E_s) substantially larger than zero, in which cases σ_o^* is larger than σ_p.[3c] The minimal steric effects of *ortho* substituents in our study seem to result in a similar apparent enhancement of the polar substituent effect of the *ortho* substituent over the *para* one.

We expect to investigate further the validity of this simple procedure for estimating polar substituent constants of *ortho* substituents.

Experimental Section[14]

Nmr data were obtained with a Varian Associates HA-60 spectrometer for DMSO solutions approximately 5–20% in phenol. Solutions of phenol and *m*-fluorophenol were examined over a range of concentrations to demonstrate the lack of dependence of chemical shift on concentration. Purities of commercially available phenols were checked by melting point and/or gas chromatographic analysis, and only samples which passed the usual criteria of purity were used. Freshly prepared solutions were used, for, although the age of the solutions did not affect the chemical shift observed, phenols substituted with strongly electron-attracting groups (*p*-NO_2 and *p*-CHO) gave diffuse signals when old solutions were used.

(14) We acknowledge with appreciation the assistance provided by Mr. R. Seab and Mr. W. Wegner in the operation of the nmr spectrometer.

Isomerization of 1-Thioacylazetidines and Related Compounds

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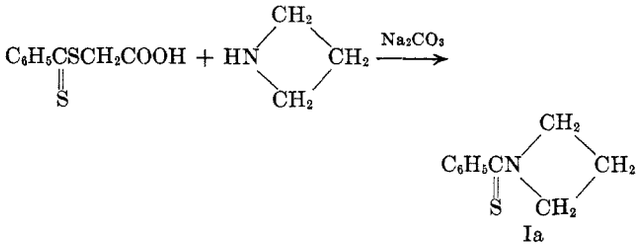
1-Thiobenzoyl-, 1-(aryloxythiocarbonyl)-, and 1-(dithio-*p*-chlorophenyloxycarbonyl)azetidines, 1-(N-phenylthiocarbamyl)-2-methylazetidine, and 1-(N-phenylcarbamyl-)-2-methylazetidine were prepared and isomerized. The 1-thioacylazetidines displayed greater tendency to isomerize than the corresponding 1-acylazetidines. Such a tendency was quite pronounced in the case with urethans and thionurethans; in the former, no isomerization reaction has been observed, while the latter were isomerized with concentrated hydrochloric acid. The isomerization reaction of 1-(N-phenylthiocarbamyl)-2-methylazetidine with acids in refluxing toluene showed more SN2-like character than of 1-(N-phenylcarbamyl)-2-methylazetidine.

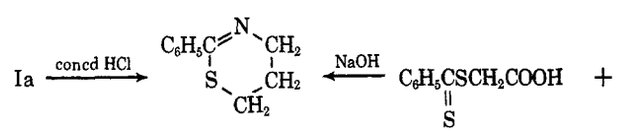
In an earlier paper,[1] the isomerization of 1-(N-phenylcarbamyl)-, 1-(N,N-diphenylcarbamyl)-, 1-(N-phenylthiocarbamyl)-, and 1-benzoylazetidine was reported. With acids, the 1-acyl- or thioacylazetidines were isomerized to 2-substituted dihydro- (or tetrahydro-) oxazines or thiazines quite analogously to the conversion of 1-acyl- or thioacylaziridines to 2-substituted oxazolines or thiazolines. However, in contrast to the aziridine derivatives, the azetidine derivatives were found to be stable to heat and nucleophilic reagents, and especially lacking in self-polymerization property under moderate conditions. The fact prompted us to prepare several 1-thioacylazetidines in order to elucidate the isomerization reaction especially in relation to the effect of the structural change on ease of the rearrangement.

1-Thiobenzoylazetidine (Ia) was prepared by the reaction of azetidine with thiobenzoylthioglycolic acid.[2] Ia was converted to 2-phenyl-4,5-dihydro-6H-1,3-thiazine (IIa) in 24% yield (based on the quantity of IIa picrate) on standing in concentrated hydrochloric acid at room temperature for 10 days. Reaction with dichloroacetic acid or boron trifluoride etherate in



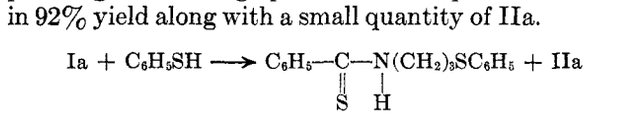
Ia

refluxing toluene also gave IIa in 28 or 75% yield, respectively. Sodium iodide in refluxing *n*-butyl ethyl



IIa $H_2N(CH_2)_3Br \cdot HBr$

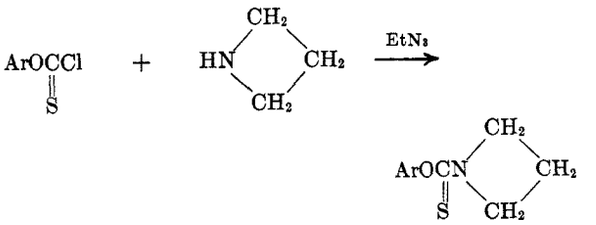
ketone was also effective for the isomerization. Thiophenol gave the ring-opened addition product with Ia in 92% yield along with a small quantity of IIa.



1-(Aryloxythiocarbonyl)azetidines were prepared from chlorothionformic acid aryl esters and azetidine.

(1) Y. Iwakura, A. Nabeya, T. Nishiguchi, and Y. Ichikawa, *J. Org. Chem.*, **30**, 3410 (1965).

(2) J. C. Crawhall, and D. F. Elliott, *J. Chem. Soc.*, 2071 (1951).



Ib, Ar = *p*-tolyl
c, Ar = *p*-chlorophenyl
d, Ar = *p*-nitrophenyl

These thionurethans were converted to 2-aryloxy-4,5-dihydro-6H-1,3-thiazines by the action of concentrated hydrochloric acid at 60°. *p*-Toluenesulfonic acid in refluxing toluene was less effective for the isomerization.

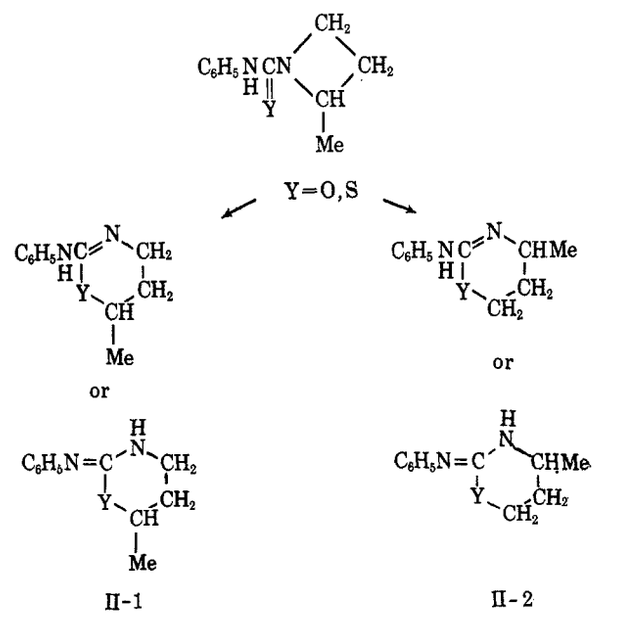
1-(Dithio-*p*-chlorophenyloxycarbonyl)azetidine (Ie), which was prepared from azetidine and chlorodithioformic acid *p*-chlorophenyl ester, was also isomerized to 2-(*p*-chlorophenylthio)-4,5-dihydro-6H-1,3-thiazine (IIe) in concentrated hydrochloric acid.

In contrast to the result with Ia, 1-benzoylazetidine[1] gave N-(3-chloropropyl)benzamide in a quantitative yield on standing in concentrated hydrochloric acid for 10 days. Dichloroacetic acid in refluxing xylene also seemed to give the ring-opened addition product. As described in the previous paper,[1] the isomerization and the addition reaction of the 1-acyl- or thioacylazetidines with acids are considered to occur competitively. In the case with Ia, only the strongly nucleophilic thiophenol gave the addition product prevailing over the attack by the strongly nucleophilic thiocarbonyl sulfur. This is in good contrast to the results with 1-benzoylazetidine, the poorer nucleophilicity of the carbonyl oxygen of which allowed hydrochloric or dichloroacetic acid to add.

In 1-(alkyl- or aryloxycarbonyl)aziridines, no isomerization reaction has been observed. 1-(*p*-Chlorophenyloxycarbonyl)azetidine[3] gave 3-chloropropylcarbamic acid *p*-chlorophenyl ester in high yields on standing in concentrated hydrochloric acid both at room temperature or at 60°. Reaction with *p*-toluenesulfonic acid in refluxing toluene resulted in the recovery of the starting material after 8 hr. Under forcing conditions (refluxed in xylene for 25 hr), the azetidine derivative seemed to have partially decomposed. 1-(*p*-Chlorophenyloxycarbonyl)aziridine[4] and *p*-toluenesulfonic acid gave the addition product instantaneously after admixture of each solution in benzene at room temperature.

It has been a matter of interest why 1-(alkyl- or aryloxycarbonyl)aziridines or azetidines gave no isomerized products. The fact that *p*-toluenesulfonic acid, in spite of the poor nucleophilicity of its conjugate base, gave the addition product with 1-(*p*-chlorophenyloxycarbonyl)aziridine would show the poorer nucleophilicity of the carbonyl oxygen in urethans. Such poor nucleophilicities of the urethan carbonyls are also seen in the rate of ring-closure of N- (or O-) (2-bromoethyl)amide, urea, and urethans reported by Scott, *et al.*[5] In 80% ethanolic water at 50° the relative rate of ring closure was 340 for $PhCONHCH_2CH_2Br$, 138 for $PhNHCONHCH_2CH_2Br$, 7.5 for $PhNHCOOCH_2CH_2Br$, and 1 for *n*-$PrOCONHCH_2CH_2Br$. Substitution of the oxygen of urethan carbonyl by sulfur facilitated the isomerization as expected. Incidentally, it was found that N-(4-hydroxybutyl)-thiobenzamide gave the seven-membered 2-phenyl-4,5,6,7-tetrahydro-1,3-thiazepine rather than the five-membered 1-thiobenzoylpyrrolidine on treatment with polyphosphoric acid or hydrobromic acid.

The question arose if there exists a mechanistic difference between the acid-catalyzed isomerization reaction of the 1-acyl- and of the corresponding 1-thioacylazetidines. As to the acid-catalyzed isomerization reaction of azetidine derivatives, we have advanced the following mechanism.[1] First, protonation to the azetidine compound would occur to make the N–C bond in the ring more polarized, and, after that, carbonyl oxygen or the thiocarbonyl sulfur would attack the ring carbon to give the product. However, we have not determined whether the attack of the oxygen or the sulfur would proceed by an SN1 or SN2 mechanism. The greater nucleophilic reactivity of the sulfur made us to expect that the attack of the sulfur would assume more SN2 character than of the oxygen. 1-(N-Phenylthiocarbamyl)-2-methylazetidine (If) and 1-(N-phenylcarbamyl)-2-methylazetidine (Ig) were prepared and the isomerization reaction with acids were investigated. If the attack of the oxygen or the sulfur assumes SN1 character, more N–CHMe bond cleavage would result, and, on the other hand, if it assumes SN2 character, more $N–CH_2$ bond would be favored. In every reaction with *p*-toluenesulfonic or picric acid, a mixture of the two isomerized products, the one arising from the cleavage of N–CHMe bond (II-1) and the other from $N–CH_2$ bond cleavage (II-2), was obtained. Nmr spectral analysis was conveniently



applied to the composition determination of the mixture, because the two isomers II-1 and II-2 in both IIf and g have absorption of methyl hydrogens at

(3) Y. Iwakura, T. Nichiguchi, and A. Nabeya, *J. Org. Chem.*, **31**, 1651 (1966).

(4) Y. Iwakura and A. Nabeya, *ibid.*, **25**, 1118 (1960).

(5) F. L. Scott, R. E. Glick, and S. Winstein, *Experientia*, **13**, 183 (1957).

considerably different τ values to enable to measure the area of each absorption band. Results are shown in Table I.

TABLE I

RESULTS OBTAINED BY THE REACTION OF If AND g WITH ACIDS

Compd	Acid	Total yield of II, %	Ratio of II-1	Ratio of II-2
If	*p*-Toluenesulfonic[a]	77	36	64
If	Picric[a]	80	21	79
If	$BF_3 \cdot OEt_2$[a]	23		100[b]
Ig	*p*-Toluenesulfonic[c]	79	89	11
Ig	Picric[c]	80	86	14
Ig	$BF_3 \cdot OEt_2$[c]	14	100	

[a] Refluxed in toluene for 2 hr. [b] Nmr spectral analysis was not adopted because of the difficulty of separation of II from polymeric material. Recrystallization of the product from petroleum ether (bp 40–80°) gave almost pure IIf-2. [c] Refluxed in toluene for 8 hr.

As expected, the reaction of If with acids displayed more SN2-like character than of Ig. Such a tendency was quite marked when boron trifluoride etherate was used as a catalyst. As reported in the previous paper,[1] boron trifluoride etherate was not so strong a catalyst to induce the isomerization of 1-(N-phenylcarbamyl)-azetidine. The fact that the introduction of a methyl group in the 2-carbon in the ring facilitated the isomerization reaction suggests that the ring-opening reaction in Ig would only proceed *via* carbonium cation. In the case with If, on the other hand, soon after the N–C bond is polarized by the weak action of boron trifluoride etherate, the sulfur would attack the ring carbon bimolecularly.

Experimental Section[6]

Preparation of 1-Thiobenzoylazetidine (Ia).—To an aqueous solution of 11.9 g (0.056 mole) of thiobenzoylthioglycolic acid and 3 g (0.028 mole) of sodium carbonate, an aqueous solution of 3.2 g (0.028 mole) of azetidine was added, and the mixture was stirred for 1 hr. The crystals obtained were collected on a filter, dried, and recrystallized from benzene to give 8.3 g (84%) of Ia, melting at 102–103.5°. The nmr spectrum of Ia (in carbon tetrachloride (CCl_4) with tetramethylsilane (TMS) as the internal standard) showed a multiplet centered at about τ 5.75 (2- and 4-CH_2 in the ring) and a quintet at τ 7.72 (3-CH_2 in the ring) with 2:1 area.

Anal. Calcd for $C_{10}H_{11}NS$: C, 67.75; H, 6.26; N, 7.90. Found: C, 67.92; H, 6.17; N, 7.72.

Isomerization of Ia in Concentrated Hydrochloric Acid.—Compound Ia (1.77 g, 0.01 mole) was dissolved in 10 g of concentrated hydrochloric acid, and the mixture was left at room temperature for 10 days. When the solution was made weakly acidic with sodium hydroxide, crystals separated out, which were filtered and found to be Ia recovered (0.94 g, 54%). After making the filtrate alkaline, it was extracted with ether. Evaporation of ether and addition of picric acid solution to the residue gave 0.94 g (24%) of IIa picrate, mp 176–180°. Recrystallization of the picrate from ethyl acetate raised the melting point to 180–182° (lit.[7] mp 183–185°).

Anal. Calcd for $C_{16}H_{14}O_7S$: C, 47.29; H, 3.47; N, 13.79. Found: C, 47.78; H, 3.53; N, 13.84.

An authentic sample of IIa was prepared from thiobenzoylthioglycolic acid and 3-bromopropylamine, and converted to the picrate. Admixture of the picrate with the above obtained sample showed no melting point depression. IIa freed from the picrate by addition of aqueous sodium hydroxide melted at 44–43° (lit.[7] oil). The infrared spectrum of free IIa showed a band of C=N at 1680 cm^{-1}. The nmr spectrum of IIa gave signals at τ 6.15, 6.98 (both triplet), and 8.24 (quintet) with equal areas (in CCl_4 with TMS as the internal standard).

Anal. Calcd for $C_{10}H_{11}NS$: C, 67.75; H, 6.26; N, 7.90. Found: C, 67.53; H, 6.35; N, 8.04.

Isomerization of Ia with Sodium Iodide.—A mixture of 0.89 g (0.005 mole) of Ia and 0.30 g (0.002 mole) of sodium iodide in 5 ml of *n*-butyl ethyl ketone was refluxed for 8 hr. After removal of the solvent under reduced pressure, the residue was treated with dilute hydrochloric acid solution. The portion insoluble in dilute hydrochloric acid solution weighed 0.73 g (83%), mp 91–95° and the infrared spectrum of which was identical with that of Ia. Treatment of the acidic solution as in the preceding experiment gave 0.29 g (14%) of IIa picrate, mp 174–178°. A control run was made by refluxing the solution of Ia in *n*-butyl ethyl ketone for 8 hr. Compound Ia was recovered quantitatively.

Reaction of Ia with Thiophenol.—A mixture of Ia (1.77 g, 0.01 mole) and thiophenol(1.10 g, 0.01 mole) was placed in a glass tube, and the tube was sealed under an atmosphere of nitrogen. The ampoule was heated at 150° for 8 hr. The content of the tube solidified on cooling, and was dissolved in benzene and petroleum ether (bp 40–80°) and crystallized to give 2.4 g of N-(3-phenylthiopropyl)thiobenzamide, mp 70–71°. Extraction of the filtrate with dilute hydrochloric acid gave 0.04 g of IIa picrate after addition of picric acid (1% from Ia). An additional crop of the addition product was obtained from the organic layer to give the total yield of 2.6 g (92%). The infrared spectrum of the thioamide had an absorption band of NH at 3310 cm^{-1}. The structure of the thioamide was further confirmed by comparison with an authentic sample prepared from thiobenzoylthioglycolic acid and 3-phenylthiopropylamine.

Anal. Calcd for $C_{16}H_{17}NS_2$: C, 66.85; H, 5.96; N, 4.87. Found: C, 67.56; H, 5.97; N, 4.63.

Preparation of 1-(*p*-Chlorophenylthiocarbonyl)azetidine (Ic).—Chlorothionformic acid *p*-chlorophenyl ester was prepared from thiophosgene and *p*-chlorophenol according to Rivier.[8] A solution of 65.5 g (0.57 mole) of thiophosgene in 200 ml of chloroform was placed in a blender. While the solution was agitated vigorously under cooling, an aqueous solution of 73.5 g (0.57 mole) of *p*-chlorophenol and 23 g (0.57 mole) of sodium hydroxide was added dropwise, the temperature being kept below 10°. The organic layer was separated, washed with water, and dried with calcium chloride. After evaporation of chloroform, the residue was submitted to vacuum distillation to give 100 g (85%) of the sample, bp 95° (1 mm).

Other esters were prepared in similar manners. *p*-Tolyl ester boiled at 86° (3 mm), and *p*-nitrophenyl ester melted at 57–59° after recrystallizations from petroleum ether.

Into an ethereal solution of 10.4 g (0.05 mole) of chlorothionformic acid *p*-chlorophenyl ester, a solution of 2.9 g (0.05 mole) of azetidine and 5.0 g (0.05 mole) of triethylamine in ether was added, the temperature being kept at −5°. After triethylamine hydrochloride was filtered, ether was evaporated. The residue was recrystallized from petroleum ether to give 9.0 g (79%) of Ic, mp 67°. The nmr spectrum of Ic showed a multiplet at τ 5.74 and a quintet at τ 7.73 with 2:1 area (in CCl_4 with TMS as the internal standard).

Anal. Calcd for $C_{10}H_{10}ClNOS$: C, 52.75; H, 4.43; N, 6.15. Found: C, 53.13; H, 4.41; N, 5.73.

Compounds Ib (mp 70–72°) and d (mp 138–139°) were prepared in the same way. The yield of Id was lower (60%).

Anal. Calcd for $C_{11}H_{13}NOS$ (Ib): C, 63.75; H, 6.32; N, 6.76. Found: C, 63.82; H, 6.25; N, 6.56.

Anal. Calcd for $C_{10}H_{10}N_2O_3S$ (Id): C, 50.42; H, 4.23; N, 11.76. Found: C, 50.49; H, 4.15; N, 11.93.

Isomerization of Ic with Concentrated Hydrochloric Acid.—A mixture of 1.1 g (0.005 mole) of Ic and 5 g of concentrated hydrochloric acid was kept at 60° for 1 day. The odor of sulfur became pronounced. Extraction of the aqueous solution with benzene and evaporation of benzene gave an oily material with phenolic odor. After making the aqueous solution alkaline, it was extracted with benzene. About 0.55 g (50%) of 2-(*p*-chlorophenyloxy)-4,5-dihydro-6H-1,3-thiazine (IIc) was obtained from the benzene layer. Compound IIc was recrystallized from petroleum ether.

(6) Melting points and boiling points are uncorrected.

(7) A. Lowson, and C. E. Searle, *J. Chem. Soc.*, 1556 (1957).

(8) H. M. Rivier, *Bull. Soc. Chim.*, **35**, 837 (1906).

TABLE II

2-ARYLOXY-4,5-DIHYDRO-6H-1,3-THIAZINES

Aryl	Mp, °C	Formula	Calcd, % C	Calcd, % H	Calcd, % N	Found, % C	Found, % H	Found, % N
p-Tolyl	30–32	$C_{11}H_{13}NOS$	63.75	6.32	6.76	63.80	6.37	6.65
p-Chlorophenyl	75–77	$C_{10}H_{10}ClNOS$	52.75	4.43	6.15	53.13	4.50	5.94
p-Nitrophenyl	63–65	$C_{10}H_{10}N_2O_3S$	50.42	4.23	11.76	50.43	4.28	11.81

TABLE III

THE PICRATES OF 2-ARYLOXY-4,5-DIHYDRO-6H-1,3-THIAZINES

Aryl	Mp, °C	Formula	Calcd, % C	Calcd, % H	Calcd, % N	Found, % C	Found, % H	Found, % N
p-Tolyl	160	$C_{17}H_{16}N_4O_8S$	46.79	3.70	12.84	47.02	3.70	13.00
p-Chlorophenyl	170 dec	$C_{16}H_{13}ClN_4O_8S$	42.07	2.87	12.26	42.16	3.04	12.76
p-Nitrophenyl	145	$C_{16}H_{13}N_5O_{10}S$	41.12	2.80	14.99	41.12	2.95	14.90

Reaction of Ic with an equimolar amount of *p*-toluenesulfonic acid in refluxing toluene gave a poor yield (less than 10%) of IIc.

The nmr spectrum of IIc gave signals at τ 6.48, 6.96 (both triplet), and 8.23 (quintet) with equal areas (in CCl_4 with TMS as the internal standard).

Isomerization of Ib or d with concentrated hydrochloric acid was carried out in a similar manner. The yields of IIb and d were 40 and 60%, respectively. Compound Ib or d was not recovered. The infrared spectra of IIb, c, and d had bands of C=N at 1653, 1653, and 1660 cm^{-1}, respectively.

The melting points and the analytical data of II and the picrates are shown in Tables II and III.

Preparation of 1-(Dithio-*p*-chlorophenyloxycarbonyl)azetidine (Ie).—Chlorodithioformic acid *p*-chlorophenyl ester was prepared from thiophosgene and sodium *p*-chlorothiophenolate as in the preparation of chlorothionformic acid esters described above, bp 128–129° (1 mm). Condensation reaction of the dithioformic acid ester with azetidine was carried out as in the preparation of Ic. Compound Ie melted at 96–98° after recrystallization from benzene and petroleum ether. The nmr spectrum of Ie showed a multiplet at τ 5.75, and a quintet at τ 7.66 with 2:1 area (in CCl_4 with TMS as the internal standard).

Anal. Calcd for $C_{10}H_{10}ClNS_2$: C, 49.27; H, 4.13; N, 5.75. Found: C, 49.68; H, 4.11; N, 5.68.

Isomerization of Ie with Concentrated Hydrochloric Acid.—A mixture of 1.2 g (0.005 mole) of Ie and 5 g of concentrated hydrochloric acid was kept at 70° for 1 day. Extraction of the aqueous solution with benzene gave Ie recovered (0.7 g, 59%). By making the aqueous layer alkaline, 0.46 g (38%) of 2-(*p*-chlorophenylthio)-4,5-dihydro-6H-1,3-thiazine (IIe), mp 47–49°, was obtained. Recrystallization from petroleum ether gave a pure sample, mp 49–50°. It had a band at 1588 cm^{-1} (C=N) in the infrared spectrum. The nmr spectrum showed signals at τ 6.53, 7.02 (both triplet), and 8.27 (quintet) with equal areas (in CCl_4 with TMS as the internal standard).

Anal. Calcd for $C_{10}H_{10}ClNS_2$: C, 49.27; H, 4.13; N, 5.75. Found: C, 49.14; H, 4.12; N, 5.82.

Compound Ie and *p*-toluenesulfonic acid in refluxing toluene gave a poorer yield of IIe (17%) with recovered Ie (33%). Compound IIe gave the picrate, mp 180° with decomposition.

Anal. Calcd for $C_{16}H_{13}ClN_4O_7S_2$: C, 40.64; H, 2.77; N, 11.85. Found: C, 40.47; H, 2.68; N, 11.85.

Reaction of 1-Benzoylazetidine with Concentrated Hydrochloric Acid.—1-Benzoylazetidine (0.81 g, 0.005 mole) was dissolved in 5 g of concentrated hydrochloric acid, and the solution was left standing at room temperature for 10 days. After neutralization of the solution, crystals were collected on a filter and dried to give 0.98 g (98%) of N-(3-chloropropyl)benzamide, mp 49–52°. Recrystallization from ether and petroleum ether gave a pure sample melting at 53–53.5°. The infrared spectrum of the sample had bands at 3340 cm^{-1} (NH) and 1645 cm^{-1} (C=O).

Anal. Calcd for $C_{10}H_{12}ClNO$: C, 60.76; H, 6.12; N, 7.09. Found: C, 61.03; H, 6.07; N, 7.08.

Reaction of 1-(*p*-Chlorophenyloxycarbonyl)azetidine with Concentrated Hydrochloric Acid.—A mixture of 1-(*p*-chlorophenyloxycarbonyl)azetidine (1.06 g, 0.005 mole) and 5 g of concentrated hydrochloric acid was kept at 60° for 1 day. After dilution of the mixture, the precipitate was filtered and dried to give 1.2 g (95%) of 3-chloropropylcarbamic acid *p*-chlorophenyl ester, mp 98–100°. Recrystallization from ether and petroleum ether gave an analytical sample melting at 99.5–100.5°. It had bands at 3320 cm^{-1} (NH) and 1702 cm^{-1} (C=O) in the infrared spectrum.

Anal. Calcd for $C_{10}H_{11}Cl_2NO_2$: C, 48.41; H, 4.47; N, 5.65. Found: C, 48.48; H, 4.64; N, 5.61.

Reaction of 1-(*p*-Chlorophenyloxycarbonyl)aziridine with *p*-Toluenesulfonic Acid.—To a solution of 1.72 g (0.01 mole) of *p*-toluenesulfonic acid in benzene, a solution of 1.98 g (0.01 mole) of 1-(*p*-chlorophenyloxycarbonyl)aziridine in benzene was added. White crystals separated out. They were collected on a filter to give 3.08 g (84%) of 3-tosyloxypropylcarbamic acid *p*-chlorophenyl ester. It was recrystallized from benzene and petroleum ether, mp 101–102°. The infrared spectrum of the compound had bands at 3470 cm^{-1} (NH) and 1745 cm^{-1} (C=O).

Anal. Calcd for $C_{16}H_{16}ClNO_5S$: C, 51.96; H, 4.36; Cl, 9.59; N, 3.79; S, 8.67. Found: C, 51.98; H, 4.47; Cl, 9.46; N, 4.20; S, 8.71.

Treatment of the above reaction mixture with water gave no basic material. Thus, no evidence for the formation of the isomerized product was observed.

Cyclization Reaction of N-(4-Hydroxybutyl)thiobenzamide.—N-(4-Hydroxybutyl)thiobenzamide, mp 47–48° (2.1 g, 0.01 mole) was heated in polyphosphoric acid (20 g) at 100–110° for 15 hr. The mixture was added to ice–water, and the acidic solution was extracted with ether. Evaporation of ether left brown material, the infrared spectrum of which was quite different from that of an authentic sample of 1-thiobenzoylpyrrolidine. After the aqueous solution was made alkaline, it was extracted with ether. Evaporation of ether and the subsequent addition of picric acid to the residue gave 3.2 g (76%) of crude 2-phenyl-4,5,6,7-tetrahydro-1,3-thiazepine picrate melting at 159–164° after recrystallization from ethyl acetate. Repeated recrystallization from the same solvent gave a pure sample, mp 168–170.5°.

Anal. Calcd for $C_{17}H_{16}N_4O_7S$: C, 48.57; H, 3.84; N, 13.33. Found: C, 48.43; H, 4.01; N, 13.35.

The freed 2-phenyl-4,5,6,7-tetrahydro-1,3-thiazepine melted at 20–21°. The infrared spectrum of the freed sample had a band at 1603 cm^{-1} (C=N). The nmr spectrum of the sample gave signals at τ 6.05, 7.25 (both triplet), and about 8.16 (multiplet) with areas of 1:1:2 ratio (in CCl_4 with TMS as the internal standard).

Preparation of 1-(N-Phenylthiocarbamyl)-2-methylazetidine (If), and 1-(N-Phenylcarbamyl)-2-methylazetidine (Ig).—2-Methylazetidine was prepared from 4-amino-2-butanol according to the method reported by Vaughan, *et al.*,[9] bp 74–75° (lit.[9] bp 72–76°).

1-(N-Phenylthiocarbamyl)-2-methylazetidine (If) was prepared from 2-methylazetidine and phenylisothiocyanate. It could not be crystallized. The infrared spectrum of If had a band of NH at 3250 cm^{-1}.

Anal. Calcd for $C_{11}H_{14}N_2S$: C, 64.06; H, 6.84; N, 13.58. Found: C, 64.96; H, 6.90; N, 13.00.

1-(N-Phenylcarbamyl)-2-methylazetidine (Ig) was prepared from 2-methylazetidine and phenylisocyanate, mp 115–116°

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TABLE IV

2-PHENYLIMINO-6-METHYLTETRAHYDRO-1,3-THIAZINE (IIF-1), 2-PHENYLIMINO-4-METHYLTETRAHYDRO-1,3-THIAZINE (IIF-2), 2-ANILINO-6-METHYL-4,5-DIHYDRO-6H-1,3-OXAZINE (IIG-1), AND 2-ANILINO-4-METHYL-4,5-DIHYDRO-6H-1,3-OXAZINE (IIG-2)

			Calcd, %				Found, %			
Compd	Mp, °C	Formula	C	H	N	S	C	H	N	S
IIf-1	103–104	$C_{11}H_{14}N_2S$	64.06	6.84		15.52	63.84	6.91		15.47
IIf-2	146–147	$C_{11}H_{14}N_2S$	64.06	6.84		15.52	64.09	6.93		15.08
IIg-1	109–110	$C_{11}H_{14}N_2O$	69.44	7.42	14.73		69.89	7.23	14.59	
IIg-2	111–113	$C_{11}H_{14}N_2O$	69.44	7.42	14.73		69.15	7.39	14.59	

TABLE V

THE PICRATES OF IIF-1, IIF-2, IIG-1, AND IIG-2

			Calcd, %				Found, %			
Compd	Mp, C°	Formula	C	H	N	S	C	H	N	S
IIf-1	165–166	$C_{17}H_{17}N_5O_7S$	46.90	3.94		7.37	46.52	3.97		7.97
IIf-2	187–188	$C_{17}H_{17}N_5O_7S$	46.90	3.94		7.37	46.88	4.05		7.56
IIg-1	176–178	$C_{17}H_{17}N_5O_8$	48.69	4.09	16.69		48.96	4.11	16.73	
IIg-2	180–182	$C_{17}H_{17}N_5O_8$	48.69	4.09	16.69		49.11	4.25	16.32	

after recrystallization from benzene and petroleum ether. It had bands at 3275 cm^{-1} (NH) and 1643 cm^{-1} (C=O) in its infrared spectrum.

Anal. Calcd for $C_{11}H_{14}N_2O$: N, 14.73. Found: N, 14.55.

2-Phenylimino-6-methyltetrahydro-1,3-thiazine (IIf-1) was prepared from 1-(3′-hydroxybutyl)-3-phenylthiourea by the cyclization reaction in concentrated hydrochloric acid. Other samples of II-1 and II-2 were prepared in a similar way. Analytical data are summarized in Table IV.

Analytical data of the picrates are summarized in Table V. The nmr signals of methyl hydrogens were located at τ 8.71, 8.82 (IIf-1), 8.89, 9.00 (IIf-2), 8.64, 8.75 (IIg-1), and 8.84, 8.95 (IIg-2), in chloroform with TMS as the internal standard.

Reaction of Ig with *p*-Toluenesulfonic Acid.—A mixture of 1.9 g (0.01 mole) of Ig and 1.7 g (0.01 mole) of *p*-toluenesulfonic acid in 10 ml of toluene was refluxed for 8 hr. The organic layer was extracted with 1 *N* sulfuric acid several times. After the aqueous solution was made alkaline, it was extracted with benzene. Evaporation of benzene gave 1.5 g (79%) of a mixture of IIg-1 and IIg-2 (by comparison of the infrared spectrum with those of IIg-1 and IIg-2). The mixture was dissolved in chloroform (in 10% concentration), and the solution was submitted to the nmr analysis. The errors in the determination of the ratio of II-1 and II-2 were about 5%.

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The Reduction Products of a Dibenzo[*b*,*f*][1,5]diazocine[1]

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Reductions of 2,8-dichloro-6,12-diphenyldibenzo[*b*,*f*][1,5]diazocine gave both dihydro and tetrahydro derivatives. One of the dihydro products was found to be an indoloindole derivative (V) while the tetrahydro compounds were shown to be diastereomeric diphenyldibenzodiazocines (II and III). The interconversions of these products as well as those of their methyl derivatives are described. The condensation of the two diastereomeric tetrahydro derivatives II and III with formaldehyde led to the isolation of three methylene bridged isomers. The stereochemistry of these products was determined by nmr spectroscopy and in turn constitutes unequivocal proof for the stereochemical assignment for II and III.

The pharmacological interest[2] in 2,8-dichloro-6,12-diphenyldibenzo[*b*,*f*][1,5]diazocine[3] (I) prompts us to describe the products obtained by the reduction of this compound. Initial experiments gave mixtures which contained the products II, III, IV, and V in varying amounts. By changing the conditions used for these reductions we were able to separate, identify, and assign structures for these products.

Reduction of I with lithium aluminum hydride gave II, III, and IV. It was found that the ratio of these products was strongly influenced by the choice of solvent.

In pyridine, for example, a 78% yield of the dihydro derivative IV was obtained. The structure was proved by oxidation to I with chromic acid and, more conclusively, by further reduction to a mixture of the diastereomeric tetrahydro derivatives II and III.

The nmr spectra of IV and its monoacetyl derivative, as well as its monomethyl derivative XII, show peculiarities which are worthy of discussion. Compound XII, for instance, shows unsymmetrical doublets for the aliphatic C*H* and also for the CH_3 groups. The ratio of the areas of the two peaks in each doublet is approximately 1:4.

An explanation for the spectral properties was suggested by an inspection of the Dreiding models for these compounds (see Figure 1). The C=N double bond in the eight-membered ring makes the model so rigid that the two preferred conformations are interconvertible only by the use of considerable force. It is, therefore, assumed that each of these compounds consists of a mixture of pairs of relatively stable conformational isomers. This was confirmed by nmr spectra

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